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The Clinical and Cost-effectiveness of HIV Self-testing in Blantyre, Malawi

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A thesis submitted in fulfillment of the requirements for the degree of

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TABLE OF CONTENTS

LIST OF TABLES	10
LIST OF FIGURES	13
DEDICATION	16
ACKNOWLEDGEMENTS	17
DECLARATION.....	18
ABBREVIATIONS	19
ABSTRACT	21
CHAPTER 1: Introduction	23
1 Overview of Chapter 1	24
1.1 Introduction	25
1.2 Origin of my interest	27
1.3 Research question.....	29
1.4 Overview of the PhD thesis	29
1.5 Summary of Chapter 1	32
CHAPTER 2: Background.....	33
2. Overview of Chapter 2	34
2.1 Malawi country profile	35
2.1.1 Introduction	35
2.1.2 The population of Malawi.....	36
2.1.3 The economy and living standards in Malawi.....	37
2.1.4 Health of Malawians.....	43
2.2 Human Immunodeficiency Virus (HIV)	45
2.2.1 Introduction	45
2.2.2 Clinical consequences of HIV infection	45
2.2.2.1 Tuberculosis (TB).....	47
2.2.2.2 Common infections	48
2.2.2.3 Opportunistic infections – AIDS defining.....	49
2.2.2.4 Common cancers and other complications – AIDS defining.....	50
2.2.3 HIV care and treatment	50

2.3 The HIV epidemic in sub-Saharan Africa and Malawi	54
2.3.1 HIV in sub-Saharan Africa	54
2.3.2 Malawi and HIV.....	56
2.4 Financing HIV services	60
2.5 HIV testing and counselling	62
2.5.1 Introduction	62
2.5.2 Approaches to HIV testing and counselling	63
2.5.3 Community-based HIV testing and counselling	64
2.5.4 HIV self-testing.....	65
2.6 Study sites and study populations.....	68
2.6.1 Study site: Blantyre, Malawi.....	68
2.6.2 HitTB study.....	69
2.6.2.1 Introduction to HitTB study.....	69
2.6.2.2 HIV self-testing in the HitTB study.....	70
2.6.2.3 HitTB cluster-randomised trial	71
2.6.2.3 Provision of HIV care and treatment in HitTB study.....	72
2.6.3 Queen Elizabeth Central Hospital	74
2.6.4 Primary health clinics: Ndirande and Chilomoni.....	75
2.7 Summary of Chapter 2	76
 CHAPTER 3: Methodological Issues around Economic Evaluations of HIV	
interventions in sub-Saharan Africa.....	77
3. Overview of Chapter 3	78
3.1 Economic evaluations in resource-poor sub-Saharan settings	79
3.1.1 Introduction	79
3.1.2 Findings from previous reviews.....	80
3.2 Economic evaluations of HIV testing strategies	82
3.2.1 Introduction	82
3.2.2 Comparing costs of different HIV testing strategies.....	82
3.2.3 Community-based HIV testing strategies	84
3.2.4 Cost of providing HIV treatment.....	86
3.2.5 Impact of HIV treatment on health-related quality of life.....	87
3.2.6 Economic evaluation of HIV testing strategies	88
3.3 Decision-analytic modelling of HIV interventions	92
3.3.1 Overview.....	92
3.3.2 Modelling HIV prevention strategies.....	93

3.3.3 Modelling HIV treatment strategies	95
3.4 Summary of Chapter 3	103
CHAPTER 4: Overview of PhD Research Methods	104
4. Overview of Chapter 4	105
4.1 Overview of PhD research	106
4.1.1 Primary research question.....	106
4.1.2 Rationale of overall study design	107
4.1.3 Aims and objectives	108
4.2 Economic evaluation	111
4.2.1 Overview.....	111
4.2.2 Why undertake an economic evaluation.....	111
4.2.3 Why undertake economic evaluations in resource-poor sub-Saharan settings	114
4.2.4 Types of economic evaluation	115
4.2.5 Rationale for undertaking a cost-utility analysis in this PHD.....	117
4.3 Decision-analytic models.....	118
4.3.1 Introduction	118
4.3.2 Approaches to decision-analytic modeling.....	119
4.3.3 Decision trees	120
4.3.4 Markov models.....	122
4.3.5 Individual sampling models (ISM).....	125
4.3.6 Decision models that allow interaction	125
4.3.7 Summary of modeling approaches	126
4.4 Cross-sectional and longitudinal studies.....	129
4.4.1 Introduction	129
4.4.2 Cross-sectional studies	129
4.4.3 Longitudinal studies	130
4.5 Cost analysis	132
4.5.1 Introduction	132
4.5.2 Costing perspective	133
4.5.3 Health provider costing.....	134
4.5.4 Patient incurred costs	137
4.5.5 Adjusting and communicating costs	139
4.6 Health outcomes and health-related quality of life	141
4.6.1 Introduction	141
4.6.2 Measuring health-related quality of life	141

4.6.3 Quality-adjusted life weights and QALY estimation	143
4.6.4 The EuroQol EQ-5D measure	144
4.7 Summary of Chapter 4	147
CHAPTER 5: A comparison of the costs and consequences of Facility HIV	
testing and Home HIV self-testing	148
5 Overview of Chapter 5	149
5.1 Introduction	150
5.2 Methods.....	152
5.2.1 Ethical statement	152
5.2.2 Study setting and study population.....	152
5.2.3 Cost analysis.....	154
5.2.3.1 Direct health provider costs	154
5.2.3.2 Direct non-medical and indirect costs.....	156
5.2.3.3 Cost conversions.....	157
5.2.4 Health-related quality of life.....	158
5.2.5 Statistical analysis.....	159
5.2.6 Sensitivity analysis	162
5.3 Results	163
5.3.1 Participant characteristics	163
5.3.2 Direct health provider costs of HTC service	165
5.3.3 Direct non-medical and indirect costs for HTC participants	165
5.3.4 Total societal costs of HTC	166
5.3.5 Health-related quality of life of HTC participants.....	170
5.3.6 Findings from sensitivity analysis	175
5.4 Discussion	177
5.5 Summary of Chapter 5	182
CHAPTER 6: A comparison of the costs and consequences of Accessing HIV	
treatment.....	183
6 Overview of Chapter 6.....	184
6.1 Introduction	185
6.2 Methods.....	187
6.2.1 Ethical statement	187
6.2.2 Overview.....	187
6.2.3 Study setting and study population.....	188
6.2.4 Cost analysis.....	191

6.2.4.1 Direct health provider costs	191
6.2.4.2 Direct non-medical and indirect costs	194
6.2.4.3 Cost conversions	195
6.2.5 Health-related quality of life.....	196
6.2.6 Statistical analysis.....	197
6.2.7 Sensitivity analysis	200
6.3 Results	201
6.3.1 Participant characteristics	201
6.3.2 Direct health provider costs of HIV treatment clinics	204
6.3.3 Pre-ART observation	206
6.3.3.1 Cost analysis for pre-ART observational period	206
6.3.3.2 Health-related quality of life analysis	214
6.3.4 ART observation period	221
6.3.4.1 Cost analysis	221
6.3.4.2 Health-related quality of life analysis	234
6.3.5 Findings from sensitivity analysis	242
6.4 Discussion	243
6.5 Summary of Chapter 6	253
CHAPTER 7: Economic and Health-Related Quality of Life Outcomes for Hospitalised Patients Co-infected with HIV in Blantyre, Malawi.....	255
7 Overview of Chapter 7.....	256
7.1 Introduction	257
7.2 Methods.....	259
7.2.1 Ethics.....	259
7.2.2 Study overview	259
7.2.3 Study setting and study population.....	260
7.2.4 Medical data extraction	262
7.2.5 Cost analysis.....	264
7.2.5.1 Direct health provider costs	264
7.2.5.2 Direct non-medical and indirect costs.....	272
7.2.5.3 Cost conversions.....	273
7.2.6 Health-related quality of life.....	274
7.2.7 Statistical analysis.....	275
7.2.8 Sensitivity analysis	279
7.3 Results	280

7.3.1. Participant characteristics	280
7.3.2 Direct health provider unit costs for healthcare resources.....	285
7.3.3 Cost analysis.....	292
7.3.5 Health-related quality of life analysis.....	301
7.3.5 Findings from sensitivity analysis	309
7.4 Discussion	313
7.5 Summary of Chapter 7	322
CHAPTER 8: Cost-utility analysis of providing HIV self-testing in addition to facility-based HIV testing and counselling in Blantyre, Malawi.....	323
8 Overview of Chapter 8.....	324
8.1 Introduction	325
8.2 Methods.....	327
8.2.1 Study overview	327
8.2.2 Model description.....	328
8.2.2.1 Model overview.....	328
8.2.2.2 Individual simulation in the model.....	330
8.2.3 Model parameters.....	336
8.2.3.1 Overview of model parameter synthesis.....	336
8.2.3.2 Initial characteristics of individuals modeled.	338
8.2.3.3 Transition probabilities.....	340
8.2.3.3.1 HIV incidence.....	340
8.2.3.3.2 Changes in CD4 counts amongst those not on ART	341
8.2.3.2.3 Risk of mortality and HIV associated co-morbidities	342
8.2.3.2.3 Uptake of HIV testing and linkage.....	343
8.2.3.2.4 Outcomes of HIV care.....	345
8.2.3.4 Health provider and societal costs.....	347
8.2.3.5 Health state utility scores	347
8.2.4 Model validation.....	356
8.2.5 Sensitivity analysis	357
8.2.6 Alternative model scenarios.....	358
8.2.6 Decision rules	359
8.3 Results	360
8.3.1 Findings from model validation.....	360
8.3.2 Primary findings.....	363
8.3.3 Findings over different time horizons.....	370

8.3.3 Sensitivity analysis	370
8.3.4 Public health impact of offering HIVST	375
8.3.4 Alternative scenarios – Earlier initiation of ART	376
8.4 Discussion	380
8.5 Summary of Chapter 8	384
CHAPTER 9: Discussion of Findings	385
9 Overview of Chapter 9	386
9.1 Introduction	387
9.2 Main findings of PhD	391
9.3 Comparison to previous findings.....	397
9.4 Strengths and limitations of PhD	401
9.5 Policy implications.....	412
9.6 Original contribution to research from PhD	418
9.7 Recommendations for future research	419
9.8 Reflection of research training during PhD	423
9.9 Conclusion.....	425
References.....	426
APPENDIX I: Malawi and Warwick Ethics committee approval documents	492
APPENDIX II: WHO and CDC classification of HIV clinical stage	493
APPENDIX III: Uptake, Accuracy, Safety, and Linkage into Care over Two Years of Promoting Annual Self-Testing for HIV in Blantyre, Malawi: A Community- Based Prospective Study	495
APPENDIX IV: Effect of Optional Home Initiation of HIV Care Following HIV Self-testing on Antiretroviral Therapy Initiation Among Adults in Malawi: A Randomized Clinical Trial	496
APPENDIX V: Literature search strategy to review cost-effectiveness studies of HIV interventions.....	497
Appendix VI: Participant information leaflet (English version) – HIV testing and HIV cohort studies	500
Appendix VII: Participant information leaflet (Chichewa version) – HIV testing and HIV cohort studies.....	501

Appendix VIII: Consent form (English version) – HIV testing and HIV cohort studies.....	502
Appendix IX: Consent form (Chichewa version) – HIV testing and HIV cohort studies.....	503
Appendix X: HTC-103 Baseline socio-demographics questionnaire – HIV testing and HIV cohort studies.....	504
Appendix XI: HTC-104 Post HIV testing questionnaire: Patient costs and health-related quality of life – HIV testing and HIV cohort studies	505
Appendix XII: Resource use data extraction tool.....	506
Appendix XIII: HTC-105 Patient costs and health-related quality of life – HIV cohort study	507
Appendix XIV: Participant information leaflet (Chichewa version) - Hospital cohort study	508
Appendix XV: Consent form (Chichewa version) - Hospital cohort study.....	509
Appendix XVI: Ward template for assessing participant’s eligibility for recruitment - Hospital cohort study	510
Appendix XVII: HTC-DOC Medical data extraction tool - Hospital cohort study	511
Appendix XVIII: Adapted ICD codebook used to code primary medical diagnosis - Hospital cohort study	512
Appendix XIX: HTC ward - Hospital cohort study.....	513
Appendix XX: HTC 501 Baseline socio-demographic questionnaire - Hospital Cohort study.....	514
Appendix XXI: HTC 502 Admission direct non-medical and indirect cost data collection tool - Hospital cohort study	515
Appendix XXII: HTC 503 Previous day direct non-medical and indirect cost data collection tool - Hospital cohort study	516
Appendix XXIII: HTC QoL health-related quality of life questionnaire - Hospital cohort study	517

LIST OF TABLES

Table 1: Malawi’s Progress on Millennium Development Goals	43
Table 2: Comparison of costs of HIV testing through different modalities	83
Table 3: Comparison of costs of community-based HIV testing strategies	85
Table 4: Cost-effectiveness of HIV self-testing from Cambiano et al., 2015	90
Table 5: Overview of Models evaluating cost-effectiveness of Prevention of Mother-To-Child Transmission (PMTCT) of HIV	100
Table 6: Overview of Models evaluating cost-effectiveness of interventions to tackle transmission and acquisition of HIV infection	101
Table 7: Modelling approaches to evaluating cost-effectiveness of HIV treatment interventions	102
Table 8: Approaches to performing an economic evaluation	116
Table 9: Characteristics of HIV testers	164
Table 10: Annual Direct Health Provider costs of HIV testing and counselling	167
Table 11: Direct non-medical and indirect costs and time	168
Table 12: Multivariable analysis exploring relationship between modality of HIV testing and total Societal cost of testing*	169
Table 13: Health-related quality of life of HIV testers	172
Table 14: Estimated predicted values compared to actual utility scores	173
Table 15: MSE and MAE for regression models by utility score range	173
Table 16: Multivariable analysis exploring relationship between modality of HIV testing and EQ-5D utility scores*	174
Table 17: Sensitivity Analysis for multivariable regression of total societal cost (Model 2)*	176
Table 18: Characteristics of recruited participants.....	203
Table 19: Direct Health Provider costs of consultation with health professional	204
Table 20: Annual Direct Health Provider costs of HIV Treatment Clinics (excluding clinical contact).....	205
Table 21: Mean total costs for pre-ART observations.....	209
Table 22: Mean total costs of pre-ART observations by modality of HIV testing received.....	210
Table 23: Multivariable analysis exploring relationship between CD4 count and modality of HIV testing received and the total pre-ART Health Provider costs*	212
Table 24: Multivariable analysis exploring relationship between CD4 count and modality of HIV testing received and the total pre-ART Societal costs*	213
Table 25: Health-related quality of life outcomes for pre-ART sample by CD4 counts	216

Table 26: Health-related quality of life outcomes for pre-ART sample by modality of HIV testing received and CD4 counts	217
Table 27: Estimated predicted values compared to actual utility scores.....	218
Table 28: MSE and MAE for regression models by utility score range	218
Table 29: Multivariable analysis exploring relationship between CD4 count and modality of HIV testing received and the EQ-5D utility score before starting anti-retroviral therapy*.....	220
Table 30: Mean total monthly and first year costs (in 2014 US Dollars) after initiation of anti-retroviral therapy by baseline CD4 count.....	223
Table 31: Mean total monthly and first year costs (in 2014 INT Dollars) after initiation of anti-retroviral therapy by baseline CD4 count.....	225
Table 32: Mean total monthly and first year costs (in 2014 US Dollars) after initiation of anti-retroviral therapy by modality of HIV testing	229
Table 33: Mean total monthly and first year costs (in 2014 INT Dollars) after initiation of anti-retroviral therapy by modality of HIV testing	229
Table 34: Multivariable analysis exploring relationship between CD4 count and modality of HIV testing received and the monthly cost of providing HIV treatment*	233
Table 35: Health-related quality of life outcomes amongst those started onto ART by month from initiation of treatment	235
Table 36: Health-related quality of life outcomes before and after initiation of anti-retroviral therapy by modality of HIV testing.....	238
Table 37: Multivariable analysis exploring relationship between CD4 count and modality of HIV testing received on the EQ-5D utility score after starting ART*	241
Table 38: Average annual HIV treatment costs for patients on ART	246
Table 39: Overview of data collection and timing of administering questionnaires	262
Table 40: Characteristics of participants eligible for recruitment	281
Table 41: Characteristics of recruited participants.....	283
Table 42: Characteristics of participants by the primary medical diagnosis	284
Table 43: Mean Health Provider costs - Radiological and Imaging Investigations.....	286
Table 44: Mean Health Provider costs - Laboratory Investigations	287
Table 45: Mean Health Provider costs - Ward-based Investigations and Procedures.....	288
Table 46: Mean Health Provider costs - Pharmacy department	288
Table 47: Mean Health Provider costs - Ward Stay.....	289
Table 48: Total Health Provider costs by primary medical diagnosis.....	293
Table 49: Total direct non-medical and indirect costs.....	295
Table 50: Total societal cost of hospital admission.....	297
Table 51: Multivariable analysis exploring relationship between HIV status and anti-retroviral treatment status on the Total Health Provider Costs*	299
Table 52: Multivariable analysis exploring relationship between HIV status and anti-retroviral treatment status on the Total Societal costs*	300

Table 53: EQ-5D utility scores by primary medical diagnosis (Zimbabwean Tariff)	303
Table 54: Visual analogue scale scores by primary medical diagnosis	304
Table 55: Estimated predicted values compared to actual utility scores.....	306
Table 56: MSE and MAE for regression models by utility score range	306
Table 57: Multivariable analysis exploring relationship between HIV status and anti-retroviral treatment status and the EQ-5D utility scores* derived from the Zimbabwean tariff (Primary analysis).....	308
Table 58: Sensitivity analysis: EQ-5D utility scores from UK Tariff by primary medical diagnosis	310
Table 59: Multivariable analysis exploring relationship between HIV status and anti-retroviral treatment status on EQ-5D utility scores derived from the UK tariff (Sensitivity analysis)*	312
Table 60: Distribution of costs by cost category amongst hospitalised medical patients from previous hospital costing studies in the region.	315
Table 61: Comparison of duration of hospital admission	316
Table 62: Parameters used to determine baseline characteristics of individuals in model	349
Table 63: Monthly transition probabilities in model.....	350
Table 64: Monthly risk of Severe HIV associated illness and HIV disease progression by current CD4 count.....	351
Table 65: Health provider costs for model (2014 US and INT Dollars).....	352
Table 66: Societal costs for model (2014 US and INT Dollars)	353
Table 67: EQ-5D Utility scores for model (Zimbabwean and UK tariff)	354
Table 68: Targeted literature search findings for synthesis of parameters in model.....	355
Table 69: Alternative model scenarios evaluated.....	358
Table 70: Findings from model validation for outcomes of offering HIV testing	361
Table 71: Findings from model validation for outcomes on Anti-retroviral therapy.....	362
Table 72: Cost-effectiveness findings from primary analysis (2014 US Dollars)	365
Table 73: Cost-effectiveness findings from primary analysis (2014 INT Dollars)	365
Table 74: Cost-effectiveness findings from primary analysis over different time horizons (2014 US Dollars).....	372
Table 75: Findings from sensitivity analysis and different time horizons, including probability of intervention cost-effective.....	374
Table 76: Public health Impact of implementing HIV self-testing.....	375
Table 77: Cost-effectiveness findings for alternative scenario from the health provider perspective (20 year time horizon)	377

LIST OF FIGURES

Figure 1: Map of Africa.....	35
Figure 2: Population characteristics of Malawi.....	36
Figure 3: Population demographics and life expectancy in Malawi	37
Figure 4: Gross Domestic Product in Malawi from 1980-2014	38
Figure 5: Global changes in Gross Domestic Product in comparison to 2010	38
Figure 6: Inflation in consumer prices in Malawi from 1981-2014.....	39
Figure 7: Labour force participation and Economic productivity in Malawi	40
Figure 8: Malawian government spending on health and education	41
Figure 9: Non-government funding of health services in Malawi.....	41
Figure 10: Access to Electricity and Water in Malawi	42
Figure 11: Educational attainment in Malawi.....	42
Figure 12: Changes in mortality rates in Malawi 1980-2014.....	44
Figure 13: Child health and Tuberculosis incidence, Malawi 1980-2014	44
Figure 14: WHO guideline changes for ART initiation and numbers of Africans on ART	51
Figure 15: Impact of starting anti-retroviral drugs on the risk of developing HIV- associated comorbidities*	52
Figure 16: Number of people living with HIV	54
Figure 17: Percentage of people living with HIV who are receiving anti-retroviral therapy	55
Figure 18: Number of Malawians living with HIV, on ART and newly initiated onto ART ...	58
Figure 19: Provision and uptake of HIV testing and counseling (HTC) services in Malawi	59
Figure 20: Funding of HIV programmes in low and middle-income countries in the last decade	60
Figure 21: Forecasts for spending on HIV services in Africa (2015-2030)	61
Figure 22: Map of Malawi and Location of Blantyre City	69
Figure 23: Map of Blantyre City and HitTB Study Clusters.....	72
Figure 24: Approaches to performing an economic evaluation	112
Figure 25: Simple Decision trees	121
Figure 26: Markov models	123
Figure 27: An approach to determining the appropriate model structure	128
Figure 28: Recruitment of HIV testing participants.....	163
Figure 29: Comparison of EQ-5D utility scores to Visual Analogue Scale scores.....	170
Figure 30: EQ-5D utility scores by response to Self-assessed health	171
Figure 31: Quality of life adjusted survival without ART	181
Figure 32: Quality of life adjusted survival with ART	181
Figure 33: Description of observation period for HIV cohort study.....	188

Figure 34: Recruitment and follow-up of participants	202
Figure 35: Box plot showing the distribution of total health provider costs (2014 US Dollars) by HIV testing modality and CD4 count (n=297)	206
Figure 36: Box plot showing the distribution of total direct non-medical and indirect costs (2014 US dollars) by HIV testing modality and CD4 count (n=297)	207
Figure 37: Box plot showing the distribution of total societal costs (2014 US dollars) by HIV testing modality and CD4 count (n=297)	207
Figure 38: Box plot showing distribution of EQ-5D utility scores (Zimbabwean tariff) by HIV testing modality and CD4 count	214
Figure 39: Box plot showing distribution of EQ-5D utility scores (UK tariff) by HIV testing modality and CD4 count	215
Figure 40: Box plot showing distribution of scores from the visual analogue scale by HIV testing modality and CD4 count.....	215
Figure 41: Mean monthly costs* (in 2014 US Dollars) after initiation of anti-retroviral therapy by the baseline CD4 count.....	224
Figure 42: Mean monthly costs* (in 2014 INT Dollars) after initiation of anti-retroviral therapy by the baseline CD4 count.....	226
Figure 43: Mean monthly costs* (in 2014 US Dollars) after initiation of anti-retroviral therapy by modality of HIV testing received	230
Figure 44: Mean monthly costs* (in 2014 INT Dollars) after initiation of anti-retroviral therapy by modality of HIV testing received	231
Figure 45: Changes in health-related quality of life outcomes over time since initiating anti-retroviral therapy by baseline CD4 count	236
Figure 46: Changes in health-related quality of life outcomes after initiating anti-retroviral therapy by modality of HIV testing.....	239
Figure 47: Overview of study design	260
Figure 48: Bottom-up approach to costing resources used	265
Figure 49: Top-down approach to allocating support	265
Figure 50: Comparison of drug prices between Malawi MoH and international market price (prices< US\$0.05)	268
Figure 51: Comparison of drug prices between Malawi MoH and international market price (prices> US\$ 0.05)	269
Figure 52: Recruitment of participant.....	280
Figure 53: Comparison of Investigation/Procedure prices between QECH and Private healthcare provider 1.....	290
Figure 54: Comparison of Investigation/Procedure prices between QECH and Private Healthcare Provider 2	291
Figure 55: Comparison of EQ5D utility Scores to Visual Analogue Scale Scores	305
Figure 56: Comparison of EQ-5D utility scores estimated from Zimbabwean and UK tariffs	311

Figure 57: Overview of HIV model structure.....	330
Figure 58: Overview of HIV disease progression module.....	333
Figure 59: Overview of HIV Testing and Linkage module	334
Figure 60: Overview of HIV treatment module	336
Figure 61: Cost-effectiveness plane showing incremental costs and effectiveness of offering HIVST (Health provider perspective).....	366
Figure 62: Cost-effectiveness plane showing incremental costs and effectiveness of offering HIVST (Societal perspective)	367
Figure 63: Cost-effectiveness acceptability curve – Health provider perspective	368
Figure 64: Cost-effectiveness acceptability curve – Societal perspective.....	369
Figure 65: Tornado diagram showing findings from sensitivity analysis	373
Figure 66: Cost-effectiveness plane showing incremental costs and effectiveness for alternative scenarios (Health provider perspective).....	378
Figure 67: Cost-effectiveness acceptability frontier for alterative scenarios (Health provider perspective)	379

DEDICATION

I would like to dedicate this thesis to the people of Malawi. I thank you all for welcoming me to your country and making my three years there a thoroughly enjoyable and unforgettable experience.

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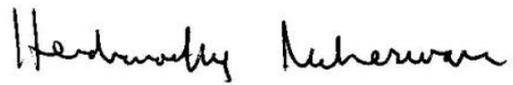
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DECLARATION

This thesis is submitted to the University of Warwick in support of my application for the degree of Doctor of Philosophy. It has been composed by myself and has not been submitted in any previous application for any degree.



Hendramoorthy Maheswaran

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ABBREVIATIONS

AIDS	Acquired Immunodeficiency Syndrome
ART	Anti-Retroviral Therapy
ARV	Anti-Retroviral
CBA	Cost-Benefit Analysis
CDC	Centers for Disease Control and Prevention
CEA	Cost-Effectiveness Analysis
CEAC	Cost-Effectiveness Acceptability Curves
CEAF	Cost-Effectiveness Acceptability Frontier
CI	Confidence Interval
CLAD	Censored Least Absolute Deviations
CPT	Cotrimoxazole Preventative Therapy
CRF	Case Report Form
CUA	Cost-Utility Analysis
DALY	Disability-Adjusted Life Year
DES	Discrete Event Simulation
EPTB	Extra-Pulmonary Tuberculosis
FDA	Food and Drug Administration
Flogit	Fractional logit
GDP	Gross Domestic Product
GEE	Generalised Estimating Equation
GLM	Generalized Linear Models
GPS	Global-Positioning Satellites
HIV	Human Immunodeficiency Virus
HIVST	HIV Self-Testing
HRQoL	Health-Related Quality of Life
HTC	HIV Testing and Counselling
ICER	Incremental Cost-Effectiveness Ratio
IeDEA	International Epidemiologic Databases to Evaluate AIDS
IQR	Interquartile Range
INT	International Dollars
IPT	Isoniazid Preventative Therapy
ISM	Individual Sampling Model
ISPOR	International Society for Pharmacoeconomics and Outcomes Research
MAE	Mean Absolute Error
M+E	Monitoring and Evaluation

MoH	Ministry of Health
MSE	Mean Squared Error
MWK	Malawian Kwacha
OLS	Ordinary Least Squares
PCP	Pneumocystis Carinii Pneumonia
PITC	Provider-Initiated HIV Testing and Counselling
PMTCT	Prevention of Mother to Child Transmission
PSA	Probabilistic Sensitivity Analysis
PTB	Pulmonary Tuberculosis
QA	Quality Assurance
QALY	Quality-Adjusted Life Year
QECH	Queen Elizabeth Central Hospital
RDT	Rapid Diagnostic Test
SAH	Self-Assessed Health
TB	Tuberculosis
VAS	Visual Analogue Scale
VCT	Voluntary Counselling and Testing
WHO	World Health Organisation
WTP	Willingness To Pay

ABSTRACT

Background: Human immunodeficiency virus (HIV) remains a global health problem. In sub-Saharan Africa, where the majority of HIV infected individuals live, 1.5 million HIV positive individuals die and 1.2 million become infected every year. Ensuring timely access to anti-retroviral therapy (ART) and efficacious HIV prevention strategies could potentially end the epidemic. To realise these benefits, individuals need access to frequent HIV testing and retesting. Facility-based HIV testing and counseling (HTC) is not popular in the region. HIV self-testing (HIVST), where individuals test in the privacy of their own homes, has been found to potentially achieve the required levels of HIV testing needed to achieve these goals. However no economic analysis of HIVST has been undertaken to inform policy makers whether it is a cost-effective option to scale-up in the region.

Objective: To undertake a cost-utility analysis (CUA), from the health provider and societal perspectives, that estimates the incremental cost per quality-adjusted life year (QALY) gained by providing Malawian communities HIVST, in addition to routine provision of facility-based HTC.

Methods: A decision-analytical model parameterised using primary cost and health-related quality of life (HRQoL) data collected from three observational studies: (1) a cross-sectional study recruiting individuals (n=1,241) who accessed HIVST and facility-based HTC; (2) a cohort study following up HIV positive individuals (n=330) accessing HIV treatment after HIVST or facility-based HTC; and (3) a cohort study of adults (n=822) admitted to the medical wards at Queen Elizabeth Central Hospital. In addition, evidence from the literature was synthesised to estimate epidemiological parameter inputs. Primary costing was undertaken to estimate health provider costs. Participants were asked about the direct non-medical and indirect costs they incurred, and their HRQoL measured using the EuroQol EQ-5D. Costs were adjusted

to 2014 US and INT Dollars, and the primary cost-effectiveness outcome was expressed in terms of incremental cost per QALY gained.

Results: The health provider cost per participant tested through HIVST (US\$8.78) was comparable to that for facility-based HTC (US\$7.53-US\$10.57), although the mean societal costs of HTC were US\$ 2.38 (95%CI: US\$0.87-US\$3.89) lower with HIVST. The mean total health provider (US\$22.74 v US\$28.33) and societal cost (US\$25.56 v US\$32.22) during the pre-ART period was lower for those who had accessed HIVST to learn their status than for those who accessed facility-based HTC. Mean total health provider and societal costs during the first year of accessing ART were comparable between those who had accessed HIVST and facility-HTC (mean total societal cost: US\$251.14 v US\$261.57). HIV positive individuals who had more advanced HIV disease, measured by the CD4 count, had lower EQ-5D utility scores. Health-related quality of life improved once individuals started ART, with the majority of participants reporting perfect health one year after starting ART. The mean cost of hospital admission was high, for example the mean health provider cost of managing Cryptococcal Meningitis and Pulmonary Tuberculosis was US\$837.92 and US\$473.11, respectively, and was associated with low EQ-5D utility scores. The CUA found the incremental cost-effectiveness ratio (ICER) of providing HIVST in addition routine facility-based HTC to be US\$316.18 per QALY gained from the health provider perspective (societal perspective: US\$332.05 per QALY gained). The sensitivity analysis found the ICER was comparable if the cost of HIVST was higher, if there were lower rates of linkage into HIV treatment after HIVST and if the HIV prevalence in the population was lower.

Conclusion: HIVST was found to be an affordable and cost-effective option for Malawi based on International guidelines (ICER below three times the gross domestic product: US\$250 in Malawi). Undertaking primary economic data collection in resource-constrained settings was feasible and provided robust estimates for use in decision-analytic models.

CHAPTER 1: Introduction

1 Overview of Chapter 1

In this chapter, I will introduce my PhD thesis and research question. I will provide a brief introduction to HIV and HIV self-testing. I will introduce my primary research question, the importance of investigating it and how my interest in it arose. I will then provide an overview of the structure of the thesis, and provide a brief description of the individual chapters within it.

1.1 Introduction

Human immunodeficiency virus (HIV) is a viral infection that without treatment leads to acquired immunodeficiency syndrome (AIDS) and death. The syndrome was first described in 1981 (Gottlieb et al., 1981), the virus isolated in 1984 (Gallo et al., 1984) and the first anti-HIV drug treatment became available in 1987 (Yarchoan and Broder, 1989). Over subsequent decades the virus spread across Africa with millions of individuals becoming infected and millions dying. In 2014, 35 million people worldwide were living with HIV, with over two thirds living in Africa (UNAIDS, 2014b). During this time, HIV treatment was becoming more widely available, improving the health outcomes of HIV positive individuals, however there was a need to improve uptake of HIV testing in Africa.

“Good quality HIV counseling and testing services are few and far between, clinical care and the resources to treat opportunistic infections are minimal, and for most people with HIV and AIDS, there is no access to antiretroviral drugs” (Harries et al., 2001)

The situation changed after 2000. International health organisations and National Ministries of Health realised there was an urgent need to provide HIV care to the millions dying in Africa. HIV services, supported by national governments and international donors were massively scaled-up with millions being successfully started onto life-saving anti-retroviral treatment. People with HIV were living longer, and fewer children were born with HIV.

However, whilst many of those with HIV had better access to treatment, millions continued to fall between the cracks (UNAIDS, 2014b). Of more concern was that we still did not understand how to effectively prevent the millions of new individuals becoming infected with the virus (Galarraga et al., 2009). The high incidence, combined with high costs of delivering life-long anti-retroviral therapy (ART), now threaten the long-term viability of HIV services which have increased delivery of ART by twenty-fold since 2003 (UNAIDS, 2012, 2010).

The last few years of HIV prevention research has yielded promising findings. There are promising strategies that will effectively prevent new HIV infections. The majority of these new approaches revolve around the benefits of anti-HIV drugs in terms of significantly reducing the risk of transmission and infection (Abdool Karim et al., 2010, Grant et al., 2010, Cohen et al., 2011, Gray et al., 2007a, Granich et al., 2009). A key requirement of all proposed strategies is high uptake of HIV testing and counselling (HTC), with the most promising (early ART for HIV prevention) (Granich et al., 2009) having significant requirements for regular repeat testing in order to identify HIV infection early.

In Africa human and financial resources are scarce. HIV testing services, as currently provided, have poor uptake amongst the population (Staveteig et al., 2013). People do not like attending health facilities that require them to travel distances and spend their own money to visit, and where testing and counseling are offered in very busy

places with little privacy (Morin et al., 2006, Kalichman and Simbayi, 2003, WHO, 2015). Testing for HIV is a life-changing event and has major implications for an individual. A large volume of research suggests that offering HIV testing and counseling closer to an individual's home, or in the privacy of their home, would significantly increase uptake (Suthar et al., 2013, Sabapathy et al., 2012). However, the costs of these services are high, and new approaches are being investigated.

HIV self-testing is seen to offer promise (WHO, 2013b, UNAIDS, 2014a). The first HIV oral self-test kit was approved for over the counter sale in the USA in 2012. HIV self-testing allows individuals to learn their HIV status in privacy, and can be provided through a number of flexible delivery strategies. Research in Malawi has identified HIV self-testing has high population uptake, and used by those individuals who have been traditionally hard to reach by current HIV testing strategies (Choko et al., 2011, MacPherson et al., 2014, Choko et al., 2015b). However, there have been no empirical investigations into the costs and cost-effectiveness of HIV self-testing to inform policy makers on its affordability and value for money.

1.2 Origin of my interest

In 2007, I worked as a medical doctor in a rural hospital in South Africa. During my two years working there, I witnessed the large-scale scale-up of HIV treatment that was taking place all over sub-Saharan Africa. As a doctor, I saw many HIV infected individuals, and would assess and start anti-retroviral therapy. Some days we would

start treatment on as many as 30 individuals who had visited the hospital or one of the many primary health care clinics that served the local population. One of the things that struck me, and which is commonly seen in research contexts, was the late presentation of HIV infected individuals at the clinics and hospitals. The majority of people I saw presented with late stage HIV infection, often presenting with Tuberculosis or more severe opportunistic diseases. Many of these individuals had only recently had an HIV test or only tested after they presented to the health facility with an AIDS defining illness.

HIV testing and counselling was only being offered in the health facilities in the region. I then became involved in setting up and evaluating a home and mobile HIV testing and counseling service in the region (Maheswaran et al., 2012). In working on this programme, I became interested in approaches to evaluating public health services. After returning to the UK and beginning my public health training, I undertook a Masters degree in health economics. During this degree and the Master's dissertation, I became interested in economic evaluations and decision-analytic models (Maheswaran and Barton, 2012). I decided to combine these two interests, and consequently decided to investigate the cost-effectiveness of HIV self-testing for my PhD topic.

1.3 Research question

In this PhD, I investigated the cost-effectiveness and broader economic impact of a population-level strategy based on providing home-based HIV self-testing in Malawi. Specifically, my research question is:

“How cost-effective is home-based HIV self-testing in Blantyre, Malawi?”

1.4 Overview of the PhD thesis

The thesis consists of nine chapters. Chapter Two provides the context: the location of my study, the characteristics of the study population, and it includes an overview of HIV infection and the medical consequences of the infection more generally. I also provide an overview of the HIV epidemic in sub-Saharan Africa, and in Malawi and then describe HIV testing and counseling, how it is provided, and issues regarding current uptake of HIV testing in sub-Saharan Africa and, more specifically, in Malawi. I further describe HIV self-testing and why it may provide a solution to the problem of how to increase uptake of HIV testing in the region. I also provide a description of the study population for the studies undertaken in the PhD and the HIV self-testing intervention that was being investigated in Blantyre, Malawi (HitTB Study)

Chapter Three provides a review of the literature relating to economic evaluations undertaken in sub-Saharan Africa. I provide a description of the growth of this research area over the last decade, and of previous economic evaluations of HIV

testing and counseling, and other HIV management strategies in sub-Saharan Africa. I describe how these influenced my methodological approach to answering my research question.

Chapter Four provides an overview of the research question and the methods used in answering the research question. I discuss the rationale for my choice of methods and their strengths and limitations.

Chapter Five provides a description of the study undertaken amongst those accessing facility-based HIV testing and counselling and HIV self-testing (HIVST). The aim of the study was to investigate the health provider costs of providing both modalities of HTC, the costs incurred by users in accessing the services, and the health-related quality of life amongst those who underwent HIV testing.

Chapter Six provides a description of the study undertaken amongst HIV positive individuals who accessed HIV treatment after being diagnosed HIV positive. In this study, I recruited a cohort of those who tested HIV positive after accessing either facility-based HIV testing or HIV self-testing. I provide a description of the costs and health-related quality of life impact of accessing HIV care. I investigate whether the modality of HIV testing has an impact on health provider costs, on the costs incurred by HIV positive individuals as they accessed care, or on the quality of life of HIV positive individuals as they accessed HIV care.

Chapter Seven provides a description of the study undertaken amongst hospitalised patients in the main hospital in Blantyre, Malawi. In this study, individuals admitted to the hospital were followed-up during their admission to investigate the health provider costs of providing medical care, the costs incurred by patients and their families and carers during the hospital admissions, and the health-related quality of life of the patients during their hospital admission. The primary aim of this part of the thesis was to investigate the economic outcomes associated with providing hospital care to those with more advanced HIV infection.

Chapter Eight is the main decision-analytic modeling component of the thesis. In this chapter I provide a description of the economic modeling work undertaken to investigate the primary research question, and of the economic data collected in the preceding chapters to populate the models. The chapter generates estimates of the incremental cost-effectiveness of providing HIVST in addition to facility-based HIV testing services, in Blantyre, Malawi.

In Chapter Nine I provide a summary of my research, and discuss its strengths and limitations. I relate the findings to previous research and discuss implications for future research and policy. The Chapter concludes by providing the key conclusions of my thesis, and the implications for health policy in Malawi and the region.

1.5 Summary of Chapter 1

In this chapter I have provided a brief introduction to HIV, and HIV testing in Africa. I have discussed the changes in HIV and HIV care in Africa, and how my interest in this subject arose. I have also provided an overview of the chapters within my PhD.

In the following Chapter I will provide a detailed background to the country of Malawi, and the setting the research was undertaken. I will provide an overview of HIV and HIV testing, and public health issues relating to them

CHAPTER 2: Background

2. Overview of Chapter 2

In this chapter I will briefly describe the country of Malawi. I will provide a detailed overview of HIV and of how the infection impacts on an individual's health. I will discuss the progression of HIV disease and the additional illnesses to which individuals are susceptible because of the effect of HIV on the immune system.

I will describe the public health impact the HIV epidemic has had on Malawi, and how the country's health care providers have responded. I will discuss the treatment of HIV positive individuals and link this to the importance of HIV testing and counselling. I will then provide a detailed overview of HIV testing and HIV self-testing.

I will introduce the HITTb study that was investigating the provision of HIV self-testing in Blantyre, and the population from which I recruited participants to investigate my research question.

2.1 Malawi country profile

2.1.1 Introduction

Malawi is a land-locked, low-income country in southern Africa (Figure 1) with a population of approximately 16 million and a gross domestic product (GDP) per capita of approximately US\$250 in 2014 (World Bank, no date, WHO, no date-a). It is one of the poorest countries in the world. The country is facing a generalised HIV epidemic, which predominantly affects the general heterosexual population. The HIV prevalence amongst adults aged 15 to 49 years is approximately 10% (UNAIDS, 2014b).

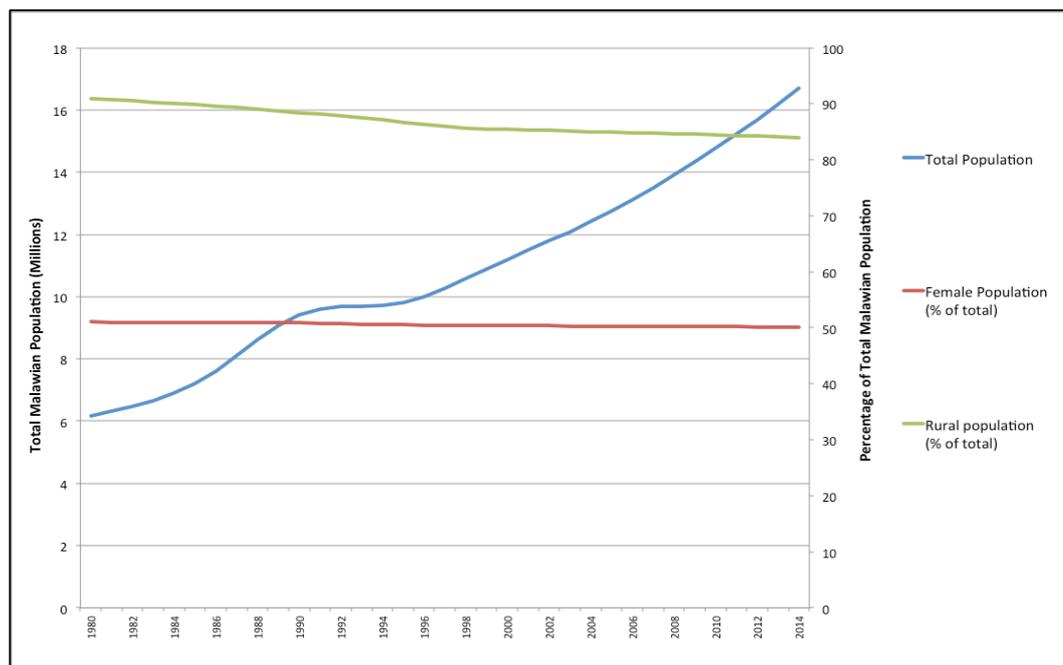
Figure 1: Map of Africa



2.1.2 The population of Malawi

The population of Malawi grew from 6 million in 1980 to over 16 million in 2014 (Figure 2). Approximately half the population are female, and over 80% of the population live in rural settings. In Malawi, 40% of the population is aged less than 15 years, and only 5% is aged over 60 years (Figure 3).

Figure 2: Population characteristics of Malawi

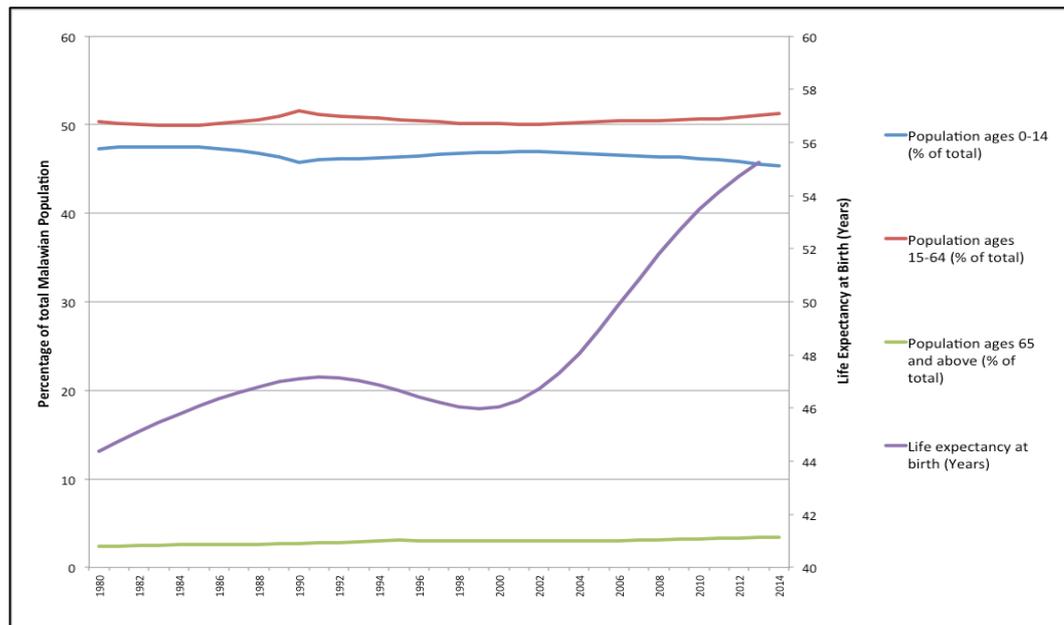


(Source: World Bank)

Life expectancy at birth in Malawi rose during the 1980's, but fell during the 1990's. The last decade has seen a significant increase in the life expectancy at birth from 48 years in 2004 to over 55 years in 2013. Strong evidence suggests that the changes in life expectancy over the last 20 years are directly related to the emergence of the HIV epidemic in the 1990's, with subsequent increases in life expectancy directly attributable to the scale-up of anti-retroviral therapy in the region (Jahn et al., 2008,

Glynn et al., 2014). Mortality and morbidity amongst the population is high, with Malawians losing on average 8 years of full health during their lifetime (WHO, no date-a).

Figure 3: Population demographics and life expectancy in Malawi



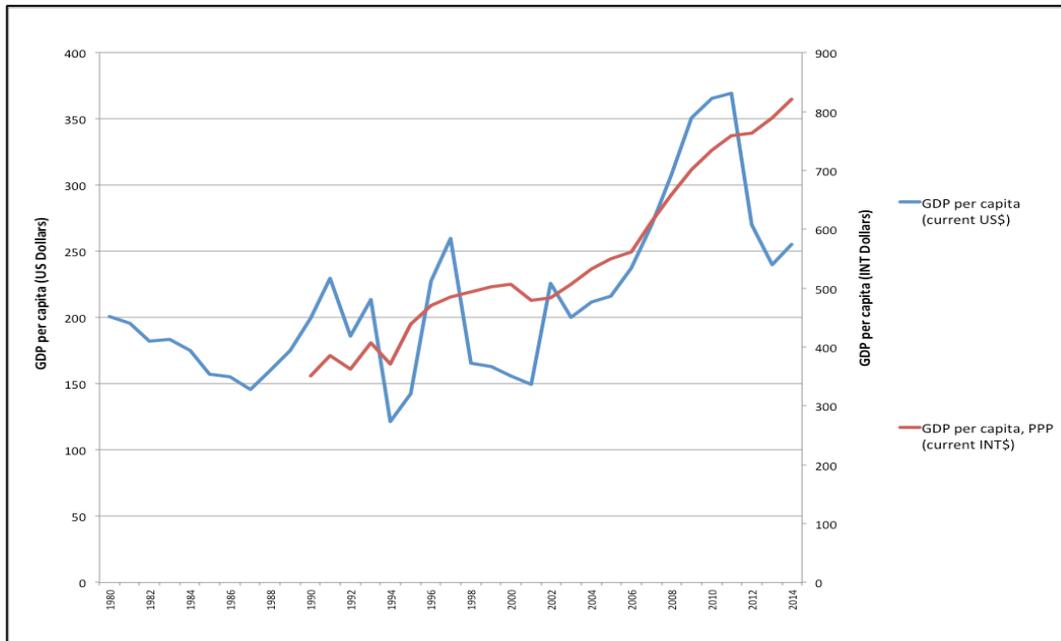
Source: World Bank (no date)

2.1.3 The economy and living standards in Malawi

Malawi is a low-income country that has experienced slow and fluctuating levels of growth in its economy over the last two decades (Figure 4). The gross domestic product (GDP) of Malawi grew at a rate approximately 5% in 2014 (World Bank, no date). Although the global financial crisis in 2008 affected the Malawian economy, its recovery has been in keeping with other countries in the region (Figure 5). The country continues to experience high rates of inflation in the prices for consumer goods (23.4% in 2014) (Figure 6), and an unstable local currency, the Malawian

Kwacha (MWK). The currency was devalued in 2011 and its exchange value against the US dollar is approximately 450 MWK (in 2014) (World Bank, no date).

Figure 4: Gross Domestic Product in Malawi from 1980-2014



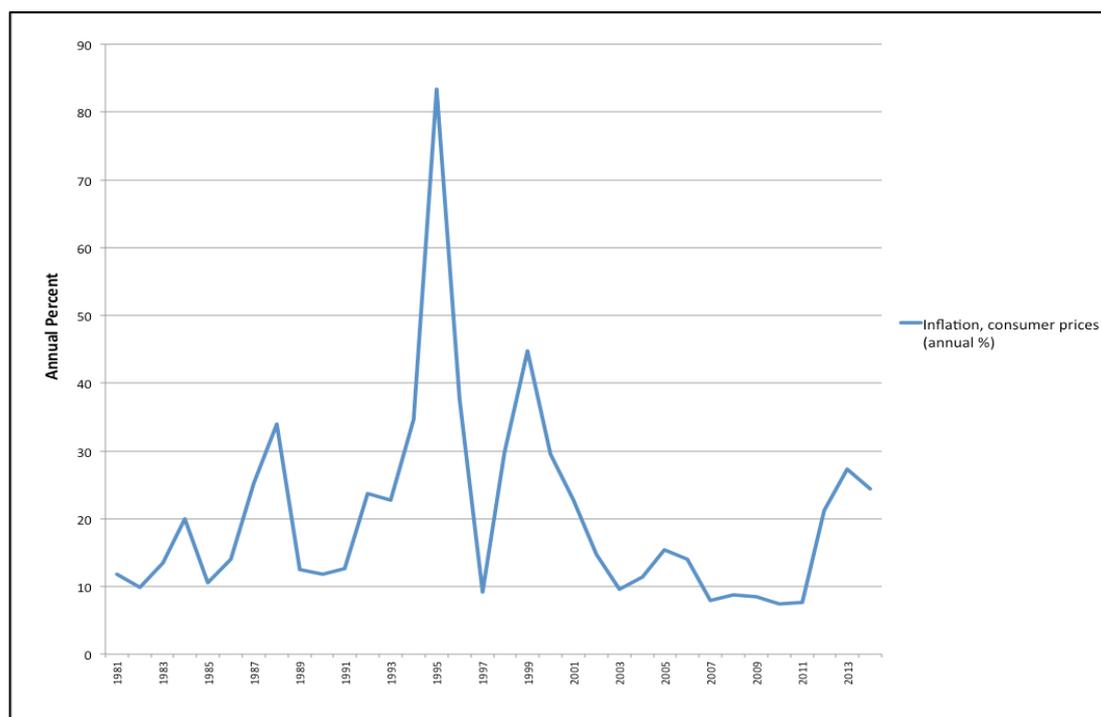
Source: World Bank (no date)

Figure 5: Global changes in Gross Domestic Product in comparison to 2010



Source: World Bank (no date)

Figure 6: Inflation in consumer prices in Malawi from 1981-2014

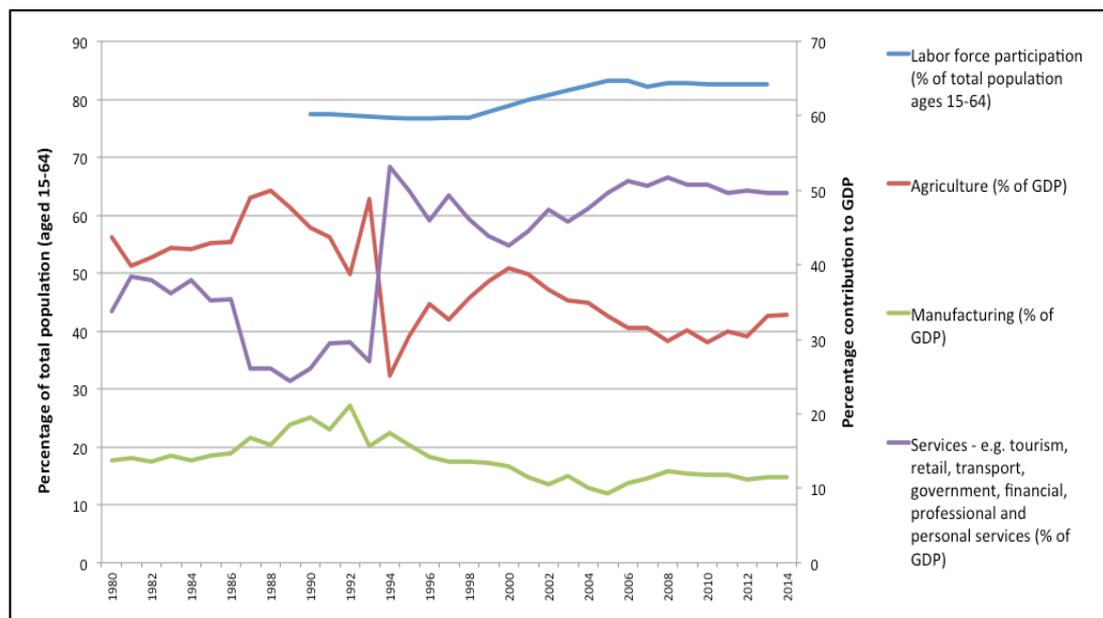


Source: World Bank (no date)

Figure 7 highlights how the economy has historically been built around an agricultural base, especially in rural areas where the majority of the population is composed of subsistence farmers. Agriculture contributes for approximately a third of the GDP in Malawi (in 2014), and accounts for the majority of exports; products include tobacco, tea and coffee.

The last two decades have seen a rise in the service industry (Figure 7), coinciding with the gradual migration of rural inhabitants to the urban cities (Figure 2). Over 80% of adults aged 15-64 are economically active. The average income in Malawi was approximately US\$250 per annum in 2014, with three-quarters of the population living on less than US\$2 a day (World Bank, no date).

Figure 7: Labour force participation and Economic productivity in Malawi



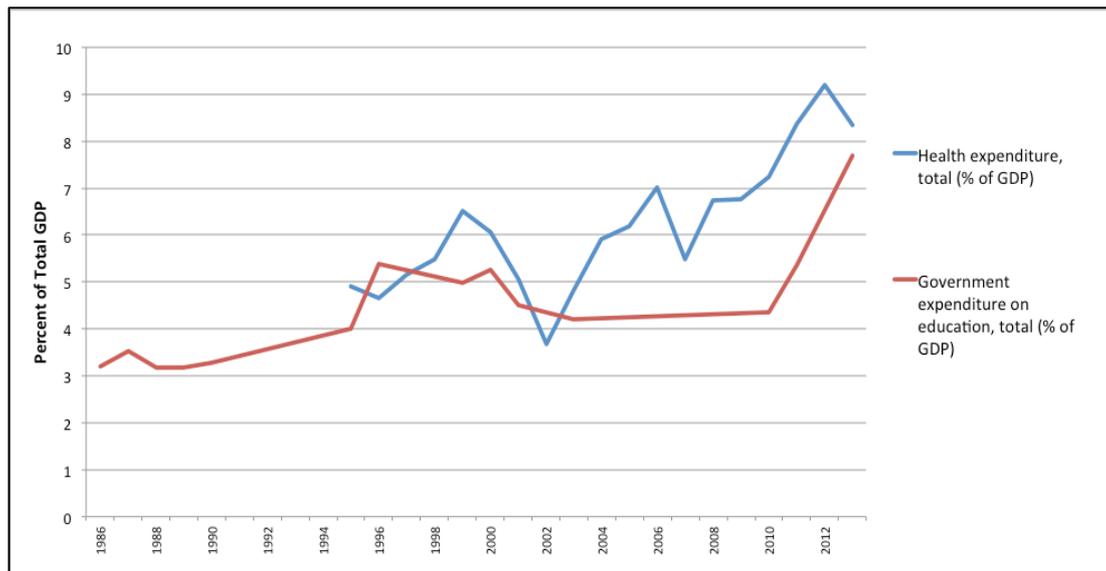
Source: World Bank (no date)

The Malawian government spends approximately 8% of the GDP on healthcare (Figure 8); in 2014 this equated to approximately US\$80 per capita per annum (World Bank, no date, WHO, no date-a). However, a significant amount of funding (approx. 90%) for HIV services in Malawi comes from international donors (World Bank, 2010). The last few years have seen a significant loss of budgetary support from international donors (Figure 9). This has been partly as a consequence of the global financial crisis in 2008 (The aids2031 Consortium 2010).

Living standards in Malawi have improved over the last decade (Figure 10). Only 10% of the population has access to electricity, primarily because of lack of infrastructure to supply the predominantly rural population. The majority of the population has access to clean drinking water. There has also been a significant increase in

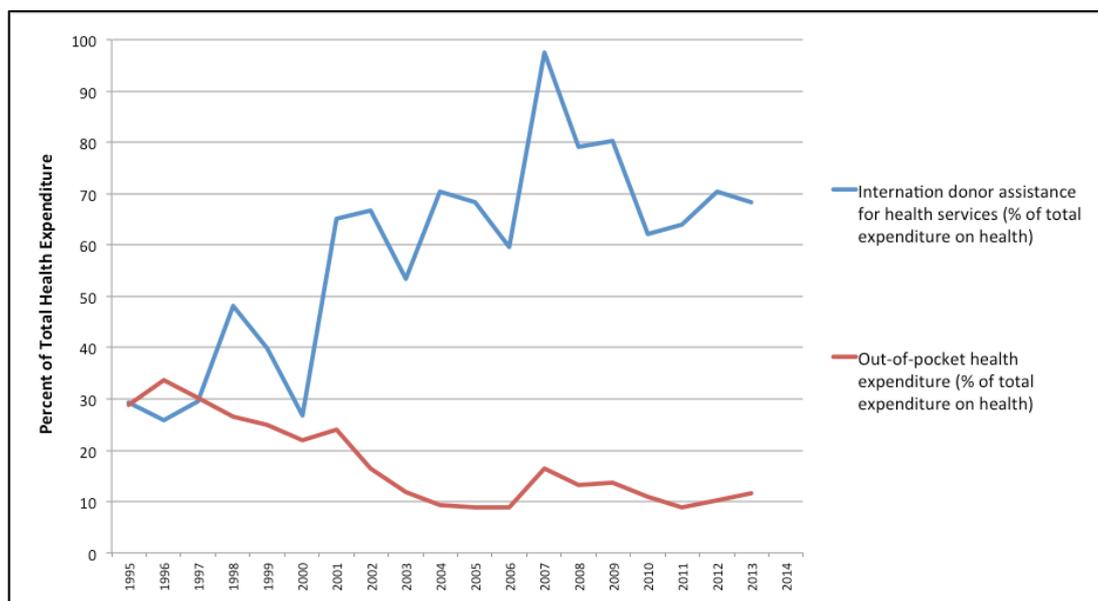
educational attainment in Malawi, however this has predominantly been seen in completion of primary school education and not for secondary educational attainment (Figure 11).

Figure 8: Malawian government spending on health and education



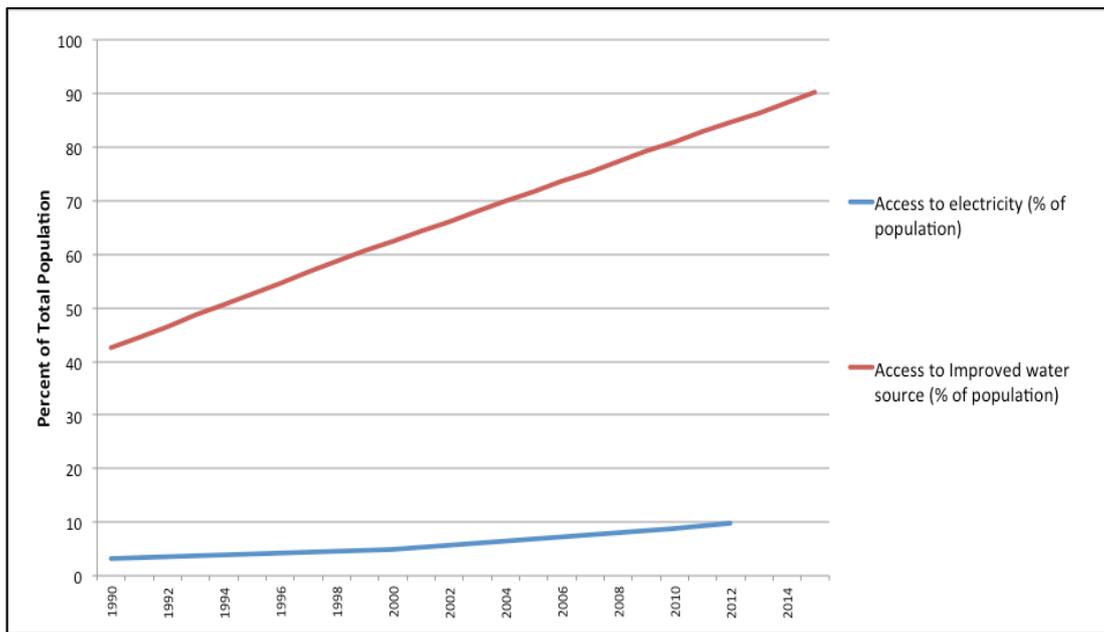
Source: World Bank (no date)

Figure 9: Non-government funding of health services in Malawi



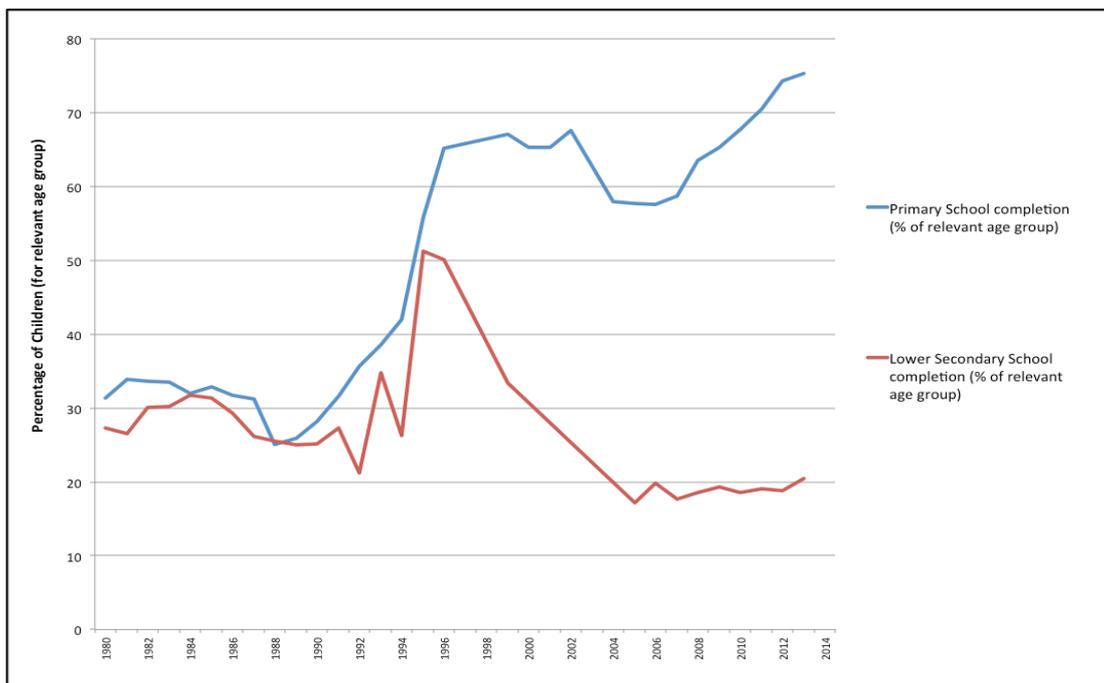
Source: World Bank (no date)

Figure 10: Access to Electricity and Water in Malawi



Source: World Bank (no date)

Figure 11: Educational attainment in Malawi



Source: World Bank (no date)

2.1.4 Health of Malawians

Table 1 highlights that there have been outstanding improvements in the health of the population (WHO, no date-a). This is mainly as a result of reduced maternal and childhood mortality (Figure 12), alongside improvements in childhood nutrition and immunisations, and reduced incidence and mortality from infectious diseases including Tuberculosis and Malaria (Table 1 & Figure 13). Nevertheless this reduced mortality from infectious diseases has been partially replaced by an increase in mortality from 'Western' causes such as hypertension, cardiovascular disease and road traffic accidents (Soliman and Juma, 2008, Bowie, 2007, Chokothe et al., 2014). However, much of the improved outcomes amongst the adult population in Malawi have been attributed to improved provision of HIV care and treatment (Jahn et al., 2008, Glynn et al., 2014).

Table 1: Malawi's Progress on Millennium Development Goals

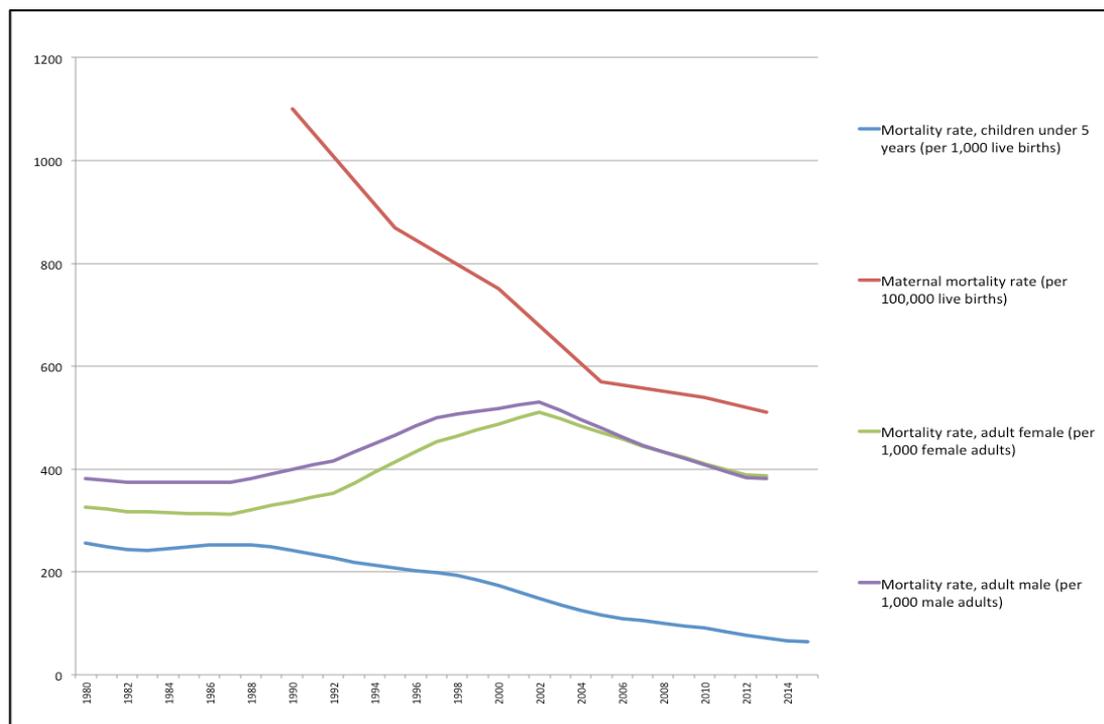
Indicator	Baseline (2000)*	Current (2013)**
Under-five mortality rate (per 1000 live births)	245	68
Maternal mortality ratio (per 100,000 live births)	1100	510
Deaths due to HIV/AIDS (per 100,000 population)	723.1	256.6
Deaths due to malaria (per 100,000 population)	159.4	59.6
Deaths due to tuberculosis among HIV-negative people (per 100,000 population)	32	9.3

Data from World Health Organization (WHO, no date-a)

*1990: under-five mortality & maternal mortality

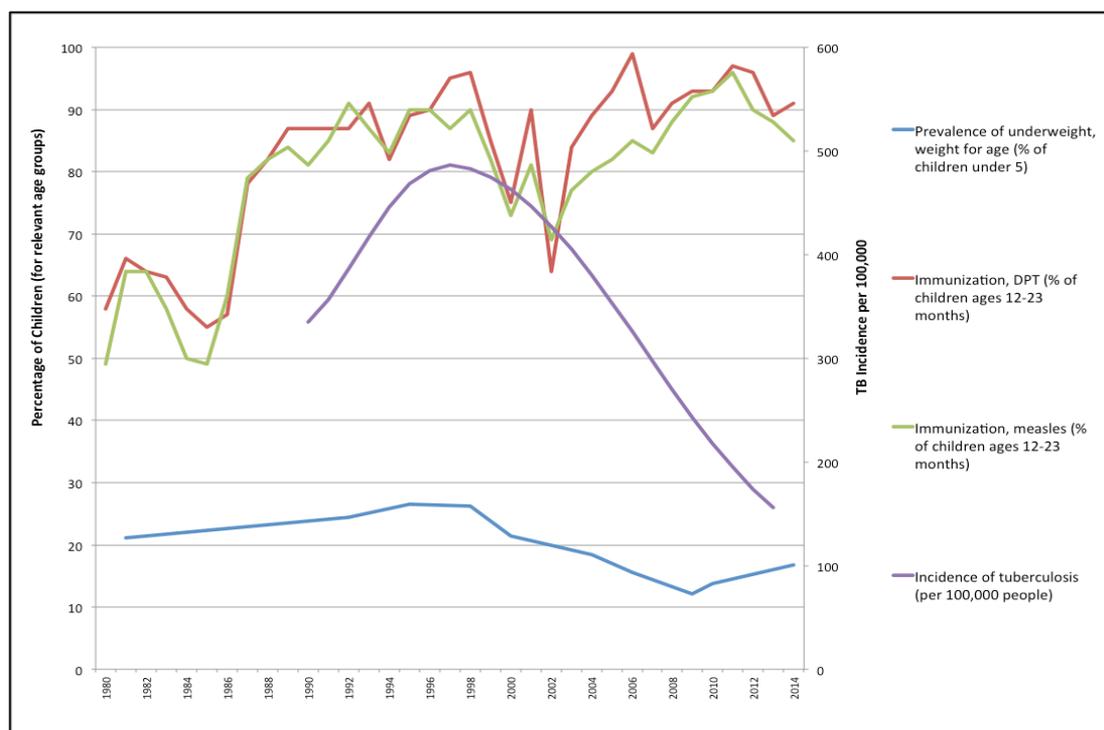
**2012: for deaths due to HIV/AIDS and malaria

Figure 12: Changes in mortality rates in Malawi 1980-2014



Source: World Bank (no date)

Figure 13: Child health and Tuberculosis incidence, Malawi 1980-2014



Source: World Bank (no date)

2.2 Human Immunodeficiency Virus (HIV)

2.2.1 Introduction

HIV is a viral infection that is transmitted between humans through sexual contact, blood products or from infected mothers to their children during pregnancy or breast-feeding. The impact of HIV at the population level differs across regions depending on predominant modes of transmission, populations affected and treatments available. In sub-Saharan Africa, HIV transmission has mainly been amongst the general heterosexual population. As a consequence HIV prevalence in some of the most severely affected countries in sub-Saharan Africa is as high as 18%, with the prevalence highest amongst economically and sexually active 25-35 year olds (Hallett et al., 2010).

2.2.2 Clinical consequences of HIV infection

HIV infection results in a slowly progressive immunodeficiency syndrome characterised by declining levels of CD4 T-helper cells. As a consequence, individuals are at increased risk of other communicable and non-communicable diseases, and without treatment will die within 8-11 years, on average. The illnesses that HIV infected individuals are susceptible to are viewed by many as: (1) AIDS-defining diseases; or (2) non-AIDS diseases. AIDS defining diseases are seen as posing a particular risk to individuals with HIV because their immune system is already significantly weakened. These infections or malignancies are known as “opportunistic” as they take advantage of a weakened immune system. Importantly,

AIDS-defining illnesses rarely occur in healthy HIV negative individuals. Non-AIDS diseases occur in HIV negative individuals, but tend to occur at a higher rate with poorer outcomes in HIV infected individuals. These illnesses generally occur during the early stages of HIV infection when the immune system is only slightly weakened.

The link between HIV-infection and non-AIDS defining illnesses is more complex. In HIV-infected individuals, these illnesses may be more common because of complications of treatment, including ART (Group et al., 2007), or because of co-infection with other infectious agents (Rockstroh, 2006), or simply because of chronic immunosuppression. Recent evidence highlights that the risk of non-AIDS diseases decreases with increasing CD4+ counts, though to a lesser degree than for AIDS-defining diseases (Baker et al., 2008). Importantly, whilst AIDS-defining illness occur more commonly when an individual's CD4 count falls below 200 cell/ μ l, non-AIDS diseases are commonly seen in individuals with CD4 counts above 200 cells/ μ l (Baker et al., 2008).

At the beginning of the HIV epidemic, when knowledge of HIV was limited and there was an urgent need for monitoring the epidemic as well as understanding clinical impact and disease progression, two classification systems were developed: the U.S. Centers for Disease Control and Prevention (CDC) classification system (Schneider et al., 2008) and the World Health Organization (WHO) Clinical Staging and Disease Classification System (WHO, 2007). These two systems continue to be used,

especially in resource-poor settings, to provide clinicians and patients with important information about HIV disease stage and clinical management. **Appendix II** summarises the WHO and CDC classifications of HIV associated clinical conditions.

The CDC disease staging system assesses the severity of HIV disease in three broad categories by CD4 cell count and by the presence of specific HIV-related conditions. The definition of AIDS includes all HIV-infections with CD4 counts of <200 cells/ μ L (or CD4 percentage <14%) as well as certain HIV-related conditions and symptoms.

The WHO system classifies HIV disease into four clinical stages on the basis of clinical manifestations that can be recognised and treated by clinicians in diverse settings, including resource-constrained settings, and by clinicians with varying levels of HIV expertise and training. In the following section, I describe the common HIV-associated medical illnesses.

2.2.2.1 Tuberculosis (TB)

TB infection can occur in a variety of human organs, commonly in the lungs, brain, heart and abdomen. If TB infection results in TB disease of the lungs it is referred to as Pulmonary Tuberculosis (PTB). If TB infection results in TB disease that affects any organ outside of the lung it is referred to as Extra-Pulmonary Tuberculosis (EPTB).

TB is the commonest cause of mortality and morbidity in HIV infected individuals (De Cock et al., 1992, Connolly et al., 1999, Mukadi et al., 2001) and remains so even after patients are initiated onto ART (Lawn et al., 2005, Lawn et al., 2006, Etard et al., 2006, Saraceni et al., 2008). The interaction between HIV and TB is very strong. One in four individuals dying with TB in sub-Saharan Africa is HIV co-infected, and about 15% of new TB cases are HIV positive (WHO, 2009a). In resource-poor settings, many individuals infected with TB may need hospital care at some point during their illness. Individuals infected with TB often present late with severe illness that necessitates admission to hospital. Individuals may also be admitted to hospital for further diagnostic investigation, whilst in many resource-poor settings those needing re-treatment for TB are given their treatment in hospital.

2.2.2.2 Common infections

Bacterial Pneumonia is one of the commonest causes of mortality and morbidity in resource-poor settings (Murray et al., 2012, Lozano et al., 2012), with excess rates seen in people with HIV infection (Polsky et al., 1986, Hirschtick et al., 1995). Risk increases with decreasing CD4 cell count (Boschini et al., 1996).

Bacterial meningitis is a common cause of death in resource-poor settings (Murray et al., 2012, Lozano et al., 2012). *Streptococcus pneumoniae* is the most common causative organism. HIV infected individuals are at increased risk of developing bacterial meningitis (Gilks et al., 1996).

Urinary Tract infections have higher incidence in those infected with HIV, with early evidence suggesting that the risk increases with falling CD4 count (Evans et al., 1995).

Salmonellosis is a bacterial infection from contaminated food or water, and is also found more commonly in people who are HIV-positive (Gordon et al., 2002).

2.2.2.3 Opportunistic infections – AIDS defining

Cryptococcal meningitis is a common opportunistic infection in the central nervous system associated with HIV. It is caused by a fungus that is present in soil. Individuals nearly always need hospital admission for treatment, and despite this mortality remains high (Jarvis et al., 2014). Infection mainly appears in HIV-infected individuals when their CD4 count falls below 100 cells/ μ l (Jarvis and Harrison, 2007).

Pneumocystis Carinii Pneumonia (PCP) is an opportunistic infection of the lungs that occurs in the late stages of HIV infection and is associated with very high mortality (Phair et al., 1990).

Candidiasis is a common HIV-related infection. In HIV infected individuals it is often localised to the mouth or throat, or oesophagus. Whilst the associated risk of mortality is low, infection affects an individual's ability to eat (Sangeorzan et al., 1994).

2.2.2.4 Common cancers and other complications – AIDS defining

Kaposi's sarcoma is a tumor of the blood vessel walls, and the commonest HIV-associated malignancy. Kaposi's sarcoma can also affect the internal organs, including the digestive tract and lungs. The incidence has reduced significantly with the introduction of ART (Brodt et al., 1998).

Wasting syndrome is defined as an involuntary weight loss of >10%, and is commonly, but not necessarily, associated with chronic diarrhoea (Mangili et al., 2006).

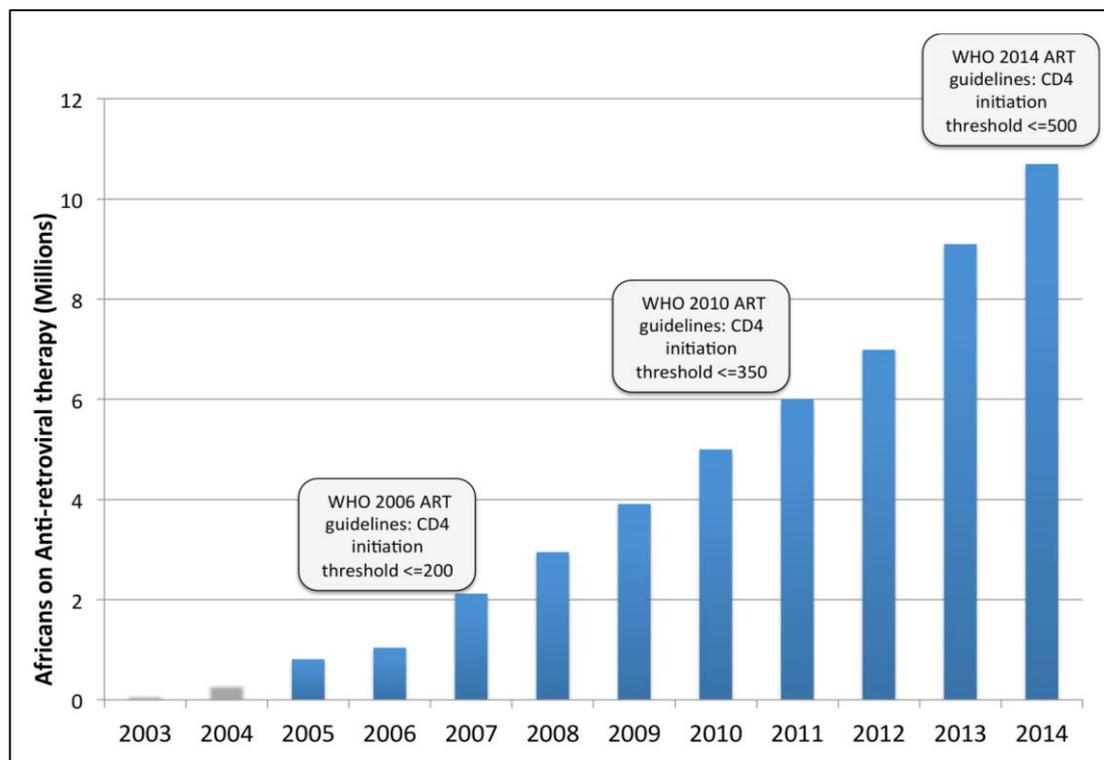
Neurological complications: one of the most common neurological complications is AIDS dementia complex, which leads to behavioural changes and diminished mental functioning (Nath et al., 2008).

2.2.3 HIV care and treatment

The advent of anti-retroviral therapy (ART) has had a major impact. ART consists of a combination of anti-retroviral drugs that reduce HIV viral loads, allowing an individual's immune system to recover. ART has become increasingly available in sub-Saharan Africa. In 2003 there were only about 100,000 people with access to treatment (WHO, 2004). How we provide HIV treatment in Africa has evolved over the last few years with HIV infected individuals being initiated earlier and earlier onto anti-retroviral treatment (Figure 14) (WHO, 2009b, WHO, 2010b, WHO, 2014,

UNAIDS, 2014b). There are now over 9 million individuals alive on treatment, however this still only accounts for about one third of those in need of ART (UNAIDS, 2014b).

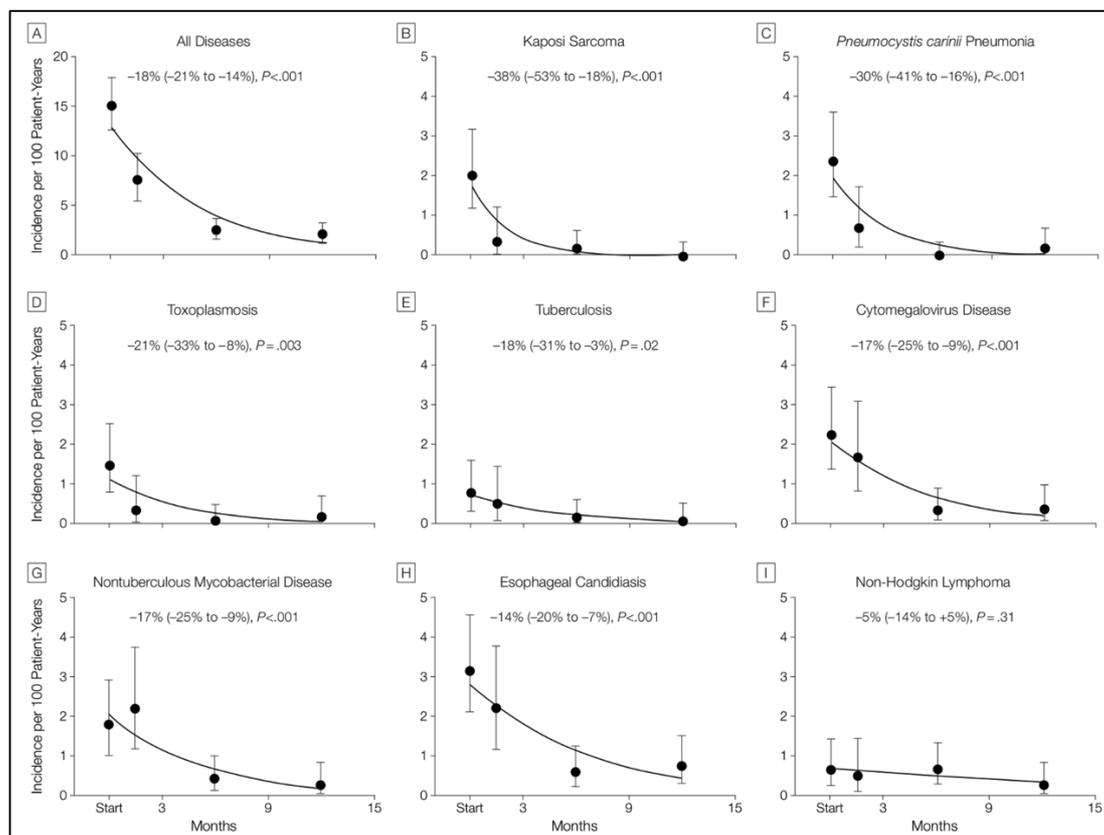
Figure 14: WHO guideline changes for ART initiation and numbers of Africans on ART



The successful scale-up of ART in sub-Saharan Africa has had a major impact on the health outcomes of those affected (May et al., 2010a). HIV infected individuals in the region have life expectancies comparable to HIV uninfected individuals with timely initiation of ART (Johnson et al., 2013, Mills et al., 2011). They also have a 96% reduction in the risk of transmission to uninfected sexual partners (Cohen et al., 2011). ART also reduces the risk of HIV associated illnesses (Ledergerber et al., 1999,

Palella et al., 1998). Figure 15 shows data from high-income settings highlighting the fall in incidence of many AIDS-defining illness after initiation of ART (Ledergerber et al., 1999). In sub-Saharan Africa, initiation of ART has been found to reduce the risk of HIV associated illnesses and progression to AIDS (Lawn et al., 2006, Jarvis and Harrison, 2007, Badri et al., 2006a, Ford et al., 2010).

Figure 15: Impact of starting anti-retroviral drugs on the risk of developing HIV-associated comorbidities*



*Figure taken from: Ledergerber et al., 1999

HIV treatment in Malawi and many countries in sub-Saharan Africa is provided utilising the WHO's public health approach to scaling-up access to anti-retroviral therapy (Gilks et al., 2006). The majority of care is provided by health professionals

other than doctors, using a simplified approach to assessing patient's eligibility for treatment and subsequent management on anti-retroviral therapy (Malawi MoH, 2011a).

The cost of providing ART in sub-Saharan Africa, whilst low in comparison to costs in high-income countries, represents a considerable burden and is likely to increase over the coming years (The aids2031 Consortium 2010). The continued high HIV incidence and improved outcomes in those already initiated will result in an ever-expanding treatment population and in larger numbers needing more costly second and third-line drug regimens.

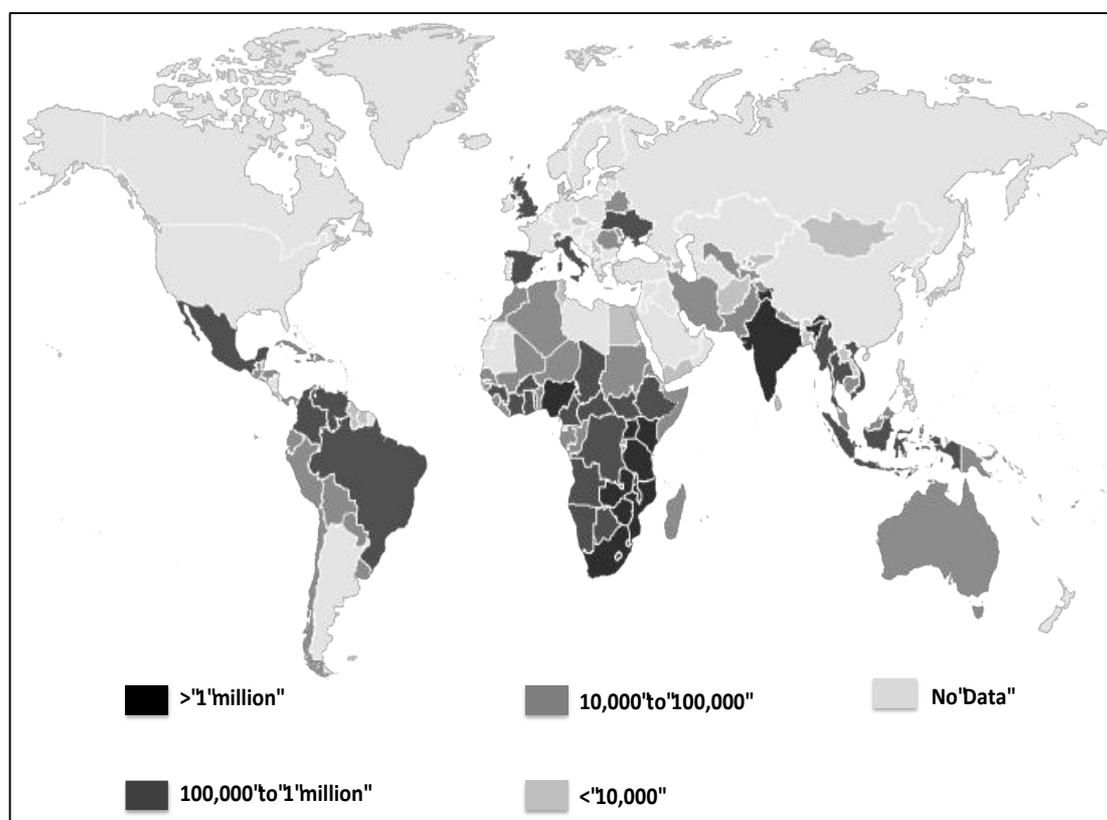
In addition the WHO guidelines for when to initiate individuals onto ART have been continually updated. At the time of starting this PhD the World Health Organisation (WHO) recommended initiating ART when an individual's CD4 count falls below 350 cells/ μ l, unless there are clear benefits of earlier initiation on HIV transmission, namely amongst pregnant women or where an individual's sexual partner is HIV negative (WHO, 2013a). The WHO updated their guidelines in 2014 advising initiation of ART in individuals whose CD4 count was below 500 cells/ μ l (WHO, 2014). Taking into account recent evidence that suggests immediate initiation of ART in all those infected with HIV (Cohen et al., 2011, Group et al., 2015b, Group et al., 2015a), it is likely all of the 25 million HIV infected individuals in the region will need access to ART.

2.3 The HIV epidemic in sub-Saharan Africa and Malawi

2.3.1 HIV in sub-Saharan Africa

In 2014, over 35 million people are currently living with HIV worldwide, whilst HIV accounts for 10.7% and 14.7% of deaths in 15-49 year old men and women, respectively (UNAIDS, 2014b, Murray et al., 2014). Figure 16 shows the number of people currently living with HIV worldwide, and highlights the disproportionate burden in sub-Saharan Africa, especially in Southern Africa, where Malawi is located.

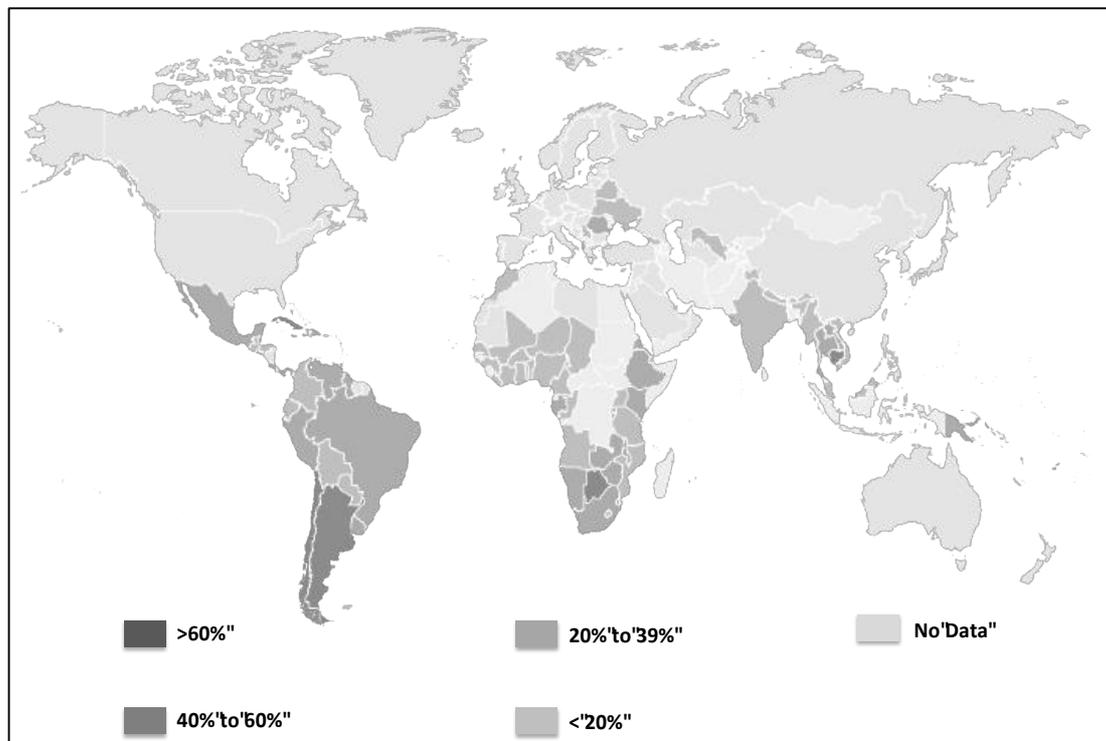
Figure 16: Number of people living with HIV



Source: (UNAIDS, 2013a)

In most parts of sub-Saharan Africa, HIV remains the most common cause of years of life lost due to premature mortality and years lived with disability (Murray et al., 2012). In 2012, an estimated 7 million Africans were on anti-retroviral treatment (ART); however, 1.2 million lives were lost to HIV/AIDS and 1.6 million people were newly infected in the region (UNAIDS, 2013a). Figure 17 highlights that despite the large numbers on ART, the majority of people living with HIV in sub-Saharan Africa do not have access to treatment. Despite the scale-up of HIV prevention and treatment services, HIV associated co-morbidities continues to place a significant financial burden on health systems in the region (Padian et al., 2011).

Figure 17: Percentage of people living with HIV who are receiving anti-retroviral therapy



Source: (UNAIDS, 2013a)

2.3.2 Malawi and HIV

Malawi has been severely affected by the HIV epidemic with an HIV prevalence of approximately 11%, and as high as 18% in urban areas (WHO, no date-a, Choko et al., 2011). Its transmission is predominantly heterosexual (UNAIDS, 2012).

In 2004, Malawi scaled up its HIV services by providing free HIV care, decentralised from hospitals to primary health clinics, and by shifting much of the clinical responsibilities of care to non-physician clinicians, nurses and lay workers (Bemelmans et al., 2010, Lowrance et al., 2008). This has enabled Malawi to achieve higher anti-retroviral treatment coverage than many of its better-resourced neighbouring countries (Bemelmans et al., 2010, UNAIDS, 2012), with comparable individual-level health outcomes (Weigel et al., 2012), and a significant beneficial impact on population-level mortality (Floyd et al., 2010). Malawi supports its HIV treatment and prevention services primarily from funds provided by international donors, which currently account for over 90% of the HIV budget (MoH, 2012).

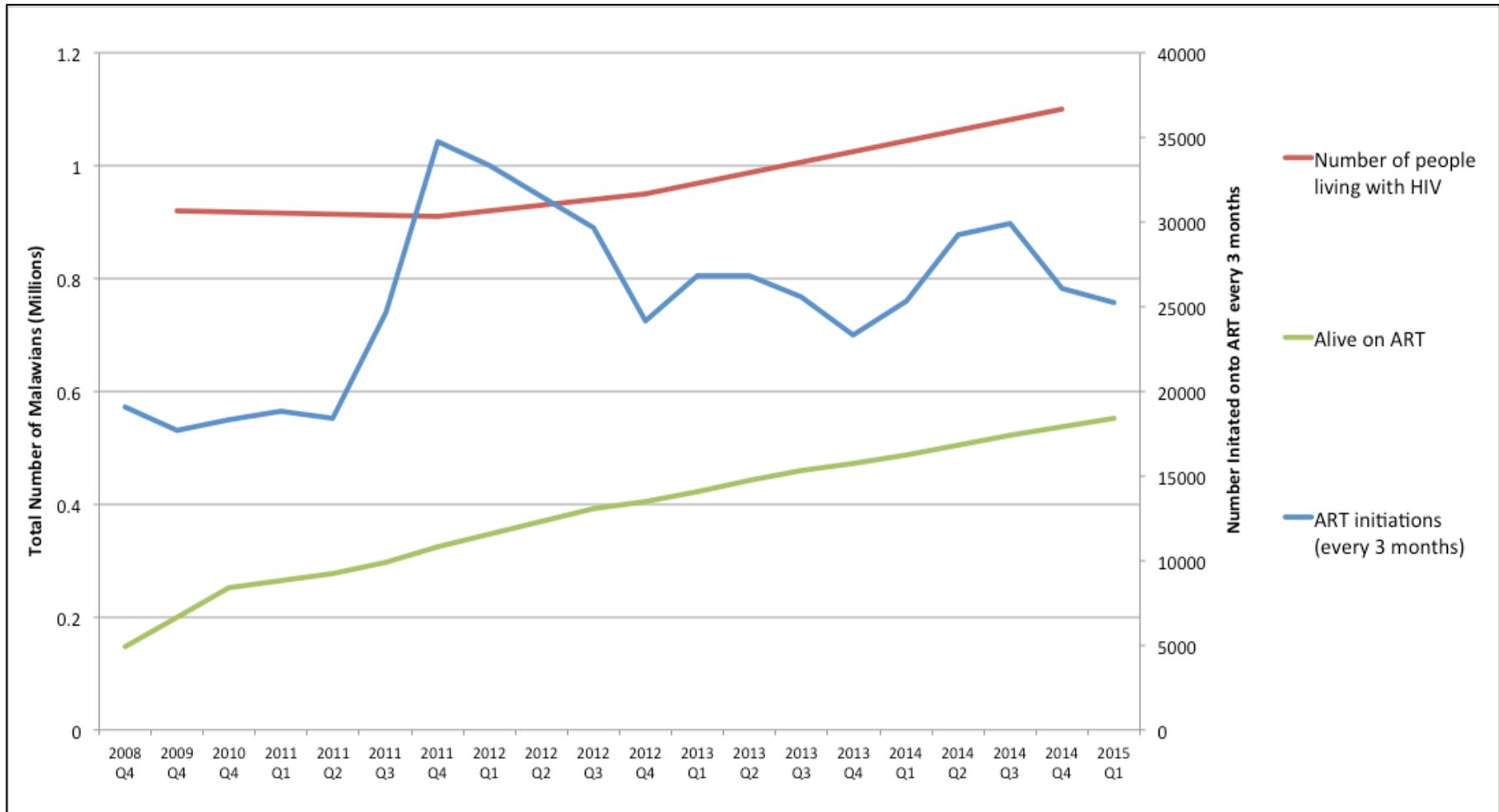
By 2010, the Malawian health sector had successfully initiated ART in approximately 300,000 HIV positive individuals and was offering HIV testing to approximately 1.2 million individuals per year (MoH, 2011b, MoH, 2012). While all this has been achieved at relatively low cost, the WHO revised its guidelines in 2010, and again in 2013. On both revisions, the WHO has progressively recommended earlier and earlier initiation of ART (WHO, 2010c, WHO, 2013a). This has led not only to a

significant increase in the number of HIV positive individuals in need of ART, but now means that nearly 95% of people living with HIV should be starting ART for their own individual benefit.

Figure 18 shows the estimated number of HIV positive individuals living in Malawi (UNAIDS, 2012, UNAIDS, 2013a, UNAIDS, 2014b), the number of HIV positive individuals initiated onto ART every three months and the total number alive and receiving ART (MoH, 2014). Figure 18 shows that despite the numbers being initiated onto ART in Malawi, ART coverage at the population level remains below 50%. The most recent UNAIDS estimates suggests that about one half of those in need of ART do not currently receive treatment (UNAIDS, 2012). In 2014, approximately 540,000 Malawians were alive and receiving anti-retroviral therapy for their HIV infection. However, HIV testing services were not testing more individuals, reaching more first time HIV testers or detecting more HIV positive individuals than in 2010 (Figure 19) (MoH, 2014).

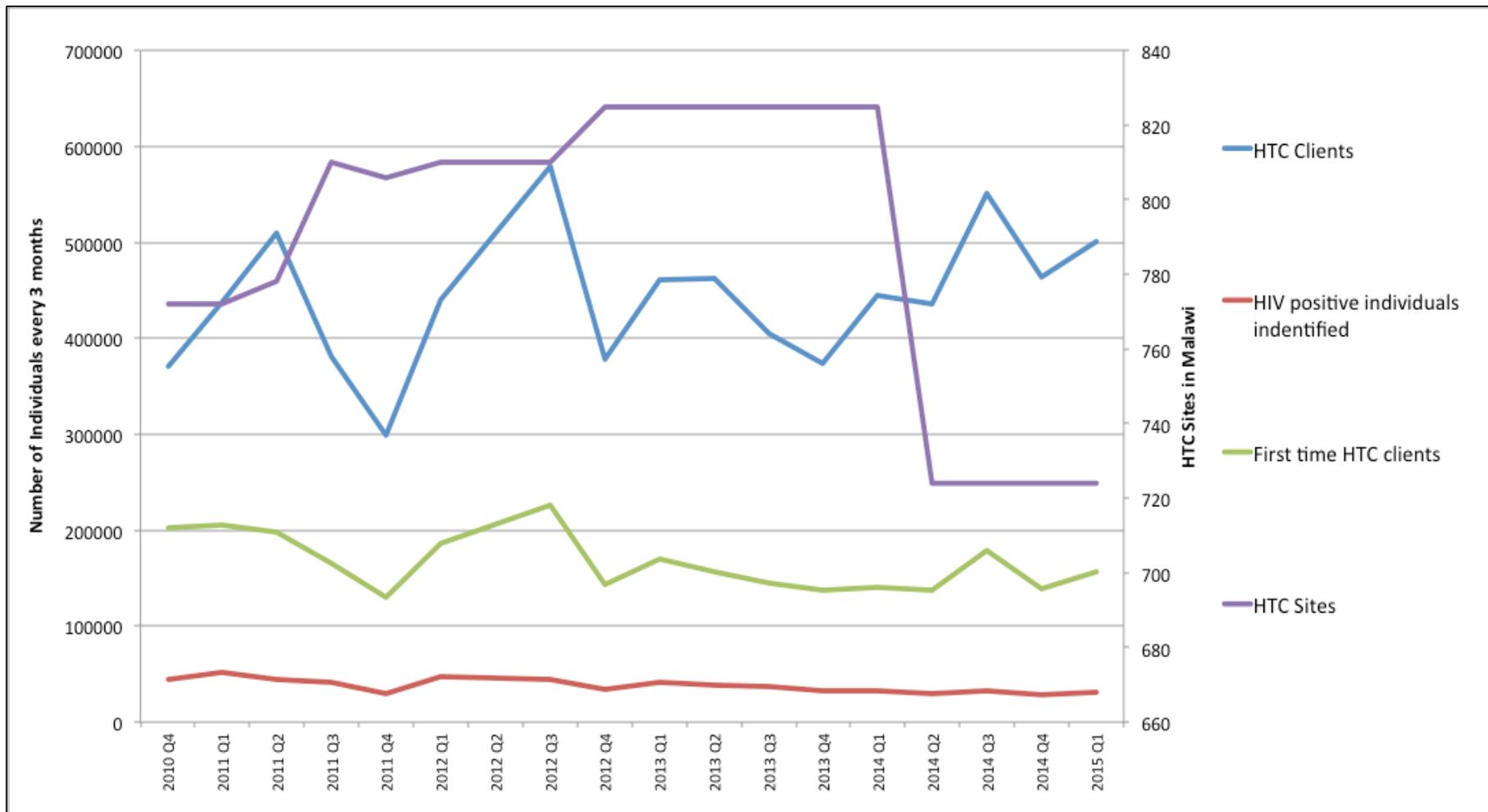
Malawi needs to not only sustain current efforts in providing anti-retroviral therapy, but to increase provision and uptake of HIV testing services, which remain sub-optimal (Macpherson et al., 2012c).

Figure 18: Number of Malawians living with HIV, on ART and newly initiated onto ART



Source: Malawi MoH; UNAIDS

Figure 19: Provision and uptake of HIV testing and counseling (HTC) services in Malawi

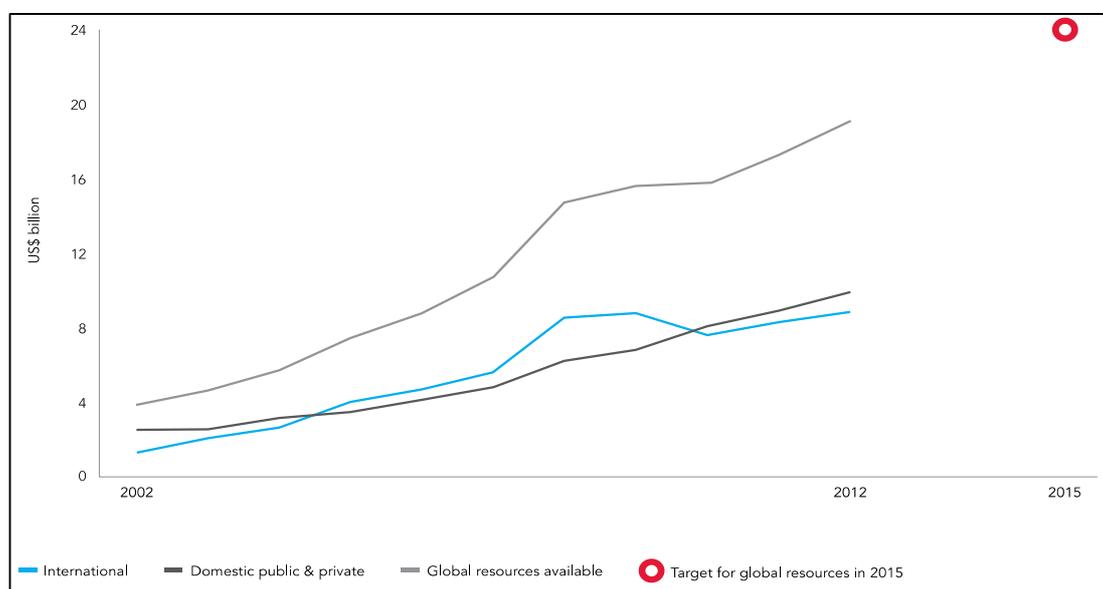


Source: Malawi MoH; UNAIDS

2.4 Financing HIV services

HIV programmes in sub-Saharan Africa have seen significant increases in funding through both international donors and domestic public sources. Figure 20 shows that over the last decade, funding for HIV programmes in low and middle-income has increased by approximately five-fold, with an estimated US\$ 19 billion spent annually, with approximately US\$10 billion coming from International funding organisations (UNAIDS, 2013a). Countries in Eastern and Southern Africa account for approximately one half of all HIV-related spending. Care and treatment services consume 55% of HIV expenditure (UNAIDS, 2013a).

Figure 20: Funding of HIV programmes in low and middle-income countries in the last decade

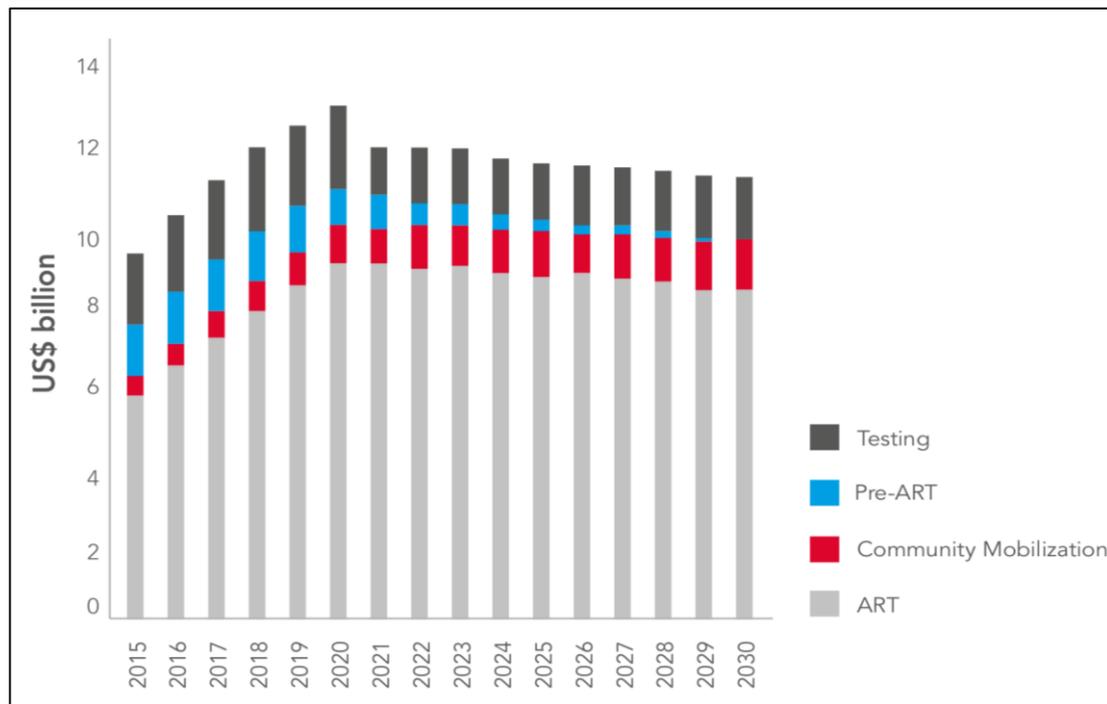


Source: (UNAIDS, 2013a)

Whilst the last decade has seen year on year increases in available funds for HIV programmes in the region, there are concerns over the long-term sustainability of

these programmes, which are heavily reliant on international funding sources (The aids2031 Consortium, 2010). This is likely to rise over the coming years with strong evidence suggesting that initiating ART in HIV infected individuals earlier than current recommendations, effectively immediate initiation of treatment once HIV diagnosis is known, improves health outcomes (Group, 2015b, Group, 2015a). Even without considering the financial impact of immediate initiation of ART, the costs of providing HIV treatment is expected to increase substantially over the coming few years (Figure 21). This has increased the need to monitor and evaluate HIV financial resources critically over time as part of the overall response to the HIV pandemic, especially in countries that already have limited resources and a higher burden of HIV infection.

Figure 21: Forecasts for spending on HIV services in Africa (2015-2030)



Source: UNAIDS, 2015

2.5 HIV testing and counselling

2.5.1 Introduction

HIV testing is the critical first step in accessing HIV treatment and care, and presents an ideal opportunity to facilitate timely access to HIV prevention and treatment services. HIV testing and counselling (HTC) is where an individual who wants to learn their HIV status is offered counselling before and after undergoing HIV testing. The counselling informs individuals of the risks and benefits of undergoing HIV testing, and about HIV treatment and prevention services available to them. There is some evidence to suggest amongst those who subsequently test HIV positive, HTC has a beneficial effect on reducing high-risk sexual behaviours; this benefit is not evident amongst those who subsequently test HIV negative (Fonner et al., 2012).

However, HTC has grown in importance with the recent publication of several studies supporting the efficacy of biomedical HIV prevention strategies (Gray et al., 2007a, Abdool Karim et al., 2010, Granich et al., 2009, Grant et al., 2010, Cohen et al., 2011). The evidence suggests that HIV infected individuals who are well managed on ART are unlikely to transmit HIV to their uninfected sexual partners (Cohen et al., 2011). Additionally, HIV negative individuals who undergo male circumcision or the use of ARV drugs as pre-exposure prophylaxis (either orally or as a topical vaginal microbicide) are at reduced risk of acquiring HIV infection (Grant et al., 2010, Gray et al., 2007a).

At the population level, using a combination of these strategies, or though providing all HIV infected individuals with ART as soon as they are known to be HIV positive, may reverse the HIV epidemic (Padian et al., 2011, Granich et al., 2009, Powers et al., 2011a). However, for the majority of these strategies to work, individuals need to know their HIV status, posing significant requirements for not just offering HIV testing, but also for frequent re-testing.

2.5.2 Approaches to HIV testing and counselling

The way in which HIV testing and counselling (HTC) is delivered has evolved over the last 20 years. In sub-Saharan Africa, HTC services were implemented in health facilities in the 1990s primarily through the voluntary counselling and testing (VCT) modality that required individuals to visit facilities and request an HIV test (Cooper et al., 2007).

The increasing availability of affordable anti-retroviral drug regimens in the region, the low uptake of HIV testing and the need to prevent transmission of HIV from mothers to their uninfected children, coupled with the finding that much of the morbidity and mortality associated with HIV was attributable to TB (Connolly et al., 1999, Mukadi et al., 2001), shifted the focus of HIV testing away from VCT to provider-initiated HIV testing and counselling (PITC) (Nash et al., 2011).

PITC puts the emphasis on healthcare providers to offer the option of HTC actively to all their clients. However, uptake of HTC remained low in the region, with only 40% of people living with HIV aware of their HIV status (Staveteig et al., 2013), and only 37% of those eligible for ART receiving treatment (UNAIDS, 2014b).

2.5.3 Community-based HIV testing and counselling

Increasingly, it has been recognised that whilst the majority of people want to test for HIV, the lack of confidentiality, social barriers, and cost and inaccessibility associated with facility-based testing act as deterrents (Kalichman and Simbayi, 2003, Wolff et al., 2005, Morin et al., 2006, Wringe et al., 2009, Angotti et al., 2009). This tension between confidentiality and convenience has led many to investigate the potential role of home-based and mobile HTC services.

Home-based HTC offers promise by bringing HIV testing to individuals in the privacy of their homes (Fylkesnes and Siziya, 2004, Bateganya et al., 2007, Were et al., 2003, Maheswaran et al., 2012, Molesworth et al., 2010). Mobile HTC services take HIV testing from overcrowded health facilities to places near individuals' homes (Maheswaran et al., 2012, Morin et al., 2006, Bassett et al., 2014, Ostermann et al., 2011, Labhardt et al., 2014, Sweat et al., 2011).

Home-based and mobile HTC services have been found to be acceptable, feasible and effective in identifying HIV infected individuals, with increased testing completion rates, different populations reached and increased population coverage compared to facility-based HTC services. (Were et al., 2003, Wolff et al., 2005, Tanser et al., 2008, Menzies et al., 2009, Negin et al., 2009, Amolloh et al., 2011, Tumwesigye et al., 2010, Sabapathy et al., 2012, Maheswaran et al., 2012, Suthar et al., 2013, Bassett et al., 2014). When home-based and mobile HTC services have been provided to communities, overall awareness and disclosure of HIV status is increased and good linkage to ART services achieved (Nuwaha et al., 2009, Sabapathy et al., 2012, Tumwesigye et al., 2010, Amolloh et al., 2011, Labhardt et al., 2014, Sweat et al., 2011, Suthar et al., 2013). Recently they have been found to be potentially cost-effective strategies in Africa (Smith et al., 2015, Bassett et al., 2014).

This has led the WHO to actively encourage the scale-up of home-based and mobile HTC services in sub-Saharan Africa (WHO, 2012). However, provision has been limited, possibly related to concerns about its sustainability and cost-effectiveness (Sabapathy et al., 2012, Suthar et al., 2013).

2.5.4 HIV self-testing

There has been a recent interest in investigating the role of oral HIV self-testing because of the WHO recommendations that most adults living in high HIV prevalent settings should re-test for HIV at regular intervals (UNAIDS, 2012), and the recent US

Food and Drug Administration (FDA) approval of over the counter oral HIV self-test kits (Walensky and Bassett, 2011, Myers et al., 2013).

Oral HIV self-testing involves individuals testing themselves using an oral swab, wiping the inside of their mouth and then waiting fifteen minutes before interpreting their test result. HIV counsellors using rapid finger-prick tests currently do the HIV testing in sub-Saharan Africa. Oral self-testing adds to the confidentiality of the HIV testing process by reducing the involvement of counsellors.

Oral self-testing for HIV has been found to be feasible, acceptable and accurate in sub-Saharan Africa. In Blantyre, Malawi, the provision of HIV self-testing through resident community counsellors achieved annual uptake of HIV testing amongst community residents of approximately 75% for the two years the service was provided (Choko et al., 2015b). Importantly, it achieves high uptake amongst “difficult-to-reach” groups of men, couples and repeat testers (Zachary et al., 2012, Napierala Mavedzenge et al., 2013, Pant Pai et al., 2013, Choko et al., 2011).

The first major study investigating the population uptake and coverage of HIV self-testing services was recently published in *PLOS Medicine*. The peer-reviewed publication, which I co-wrote, is shown in **Appendix III**. In addition, a separate peer-reviewed publication in the *Journal of the American Medical Association* examining

the potential of offering home-assessment and initiation of anti-retroviral therapy after HIV self-testing, for which I undertook the costing component of the study, is shown in **Appendix IV**.

HIVST has the potential of increasing the feasibility of implementing home-based HIV testing programmes at relatively low cost (WHO, 2013b). However, there is a need to better understand the costs and cost-effectiveness associated with its provision (Mavedzenge et al., 2013, Choko et al., 2015b).

2.6 Study sites and study populations

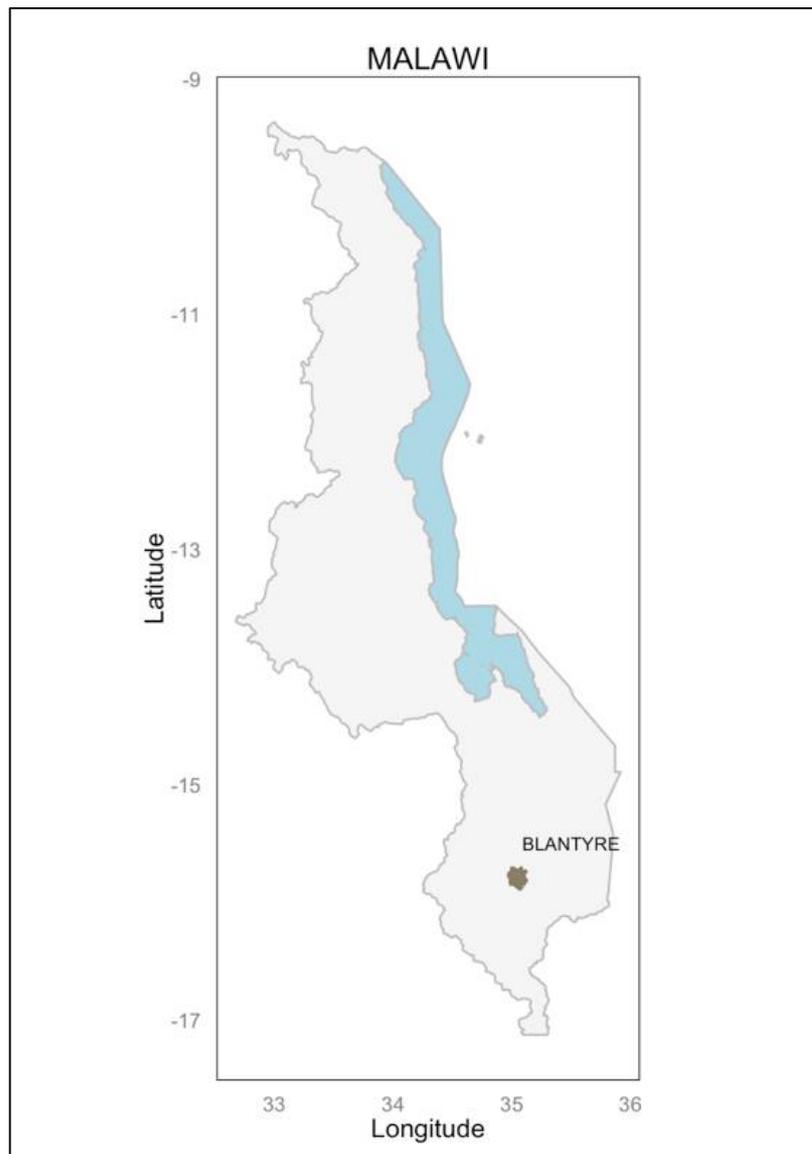
2.6.1 Study site: Blantyre, Malawi

Blantyre is the second city of Malawi, after the capital Lilongwe, and is located in the southern region of Malawi (Figure 22). In 2008, when the last national census in Malawi was conducted, the population of Blantyre City was approximately 660,00, with a total population of just over one million when the suburbs of the city were taken into account (National Statistics Office, 2010).

HIV prevalence amongst adults in Blantyre has recently been estimated to be approximately 18% (Choko et al., 2011). In the city an estimated 10% of adults are in formal full-time employment (Choko et al., 2011), although a large proportion of the population are in informal employment (World Bank, no date).

Residents of Blantyre can access free healthcare at their local primary health clinics, or at the Queen Elizabeth Central Hospital (QECH). Residents also have access to private healthcare through two private hospitals: the Mwaiwanthu Private Hospital and the Seventh-day Adventist Hospital. The primary health clinics provide outpatient care for the local population, including HIV testing and counselling (HTC), and HIV treatment. HTC and HIV treatment are also provided to outpatients at QECH.

Figure 22: Map of Malawi and Location of Blantyre City



2.6.2 HitTB study

2.6.2.1 Introduction to HitTB study

The HitTB study is a community cluster randomised trial of approximately 34,000 adults (ISRCTN02004005). The main objective of the trial is to investigate the impact on adult mortality of provision of intensified HIV and TB prevention services. The trial provides residents of communities randomised to the intervention with access

to home-based HIVST, and with facilitated linkage into HIV and TB treatment and prevention services.

2.6.2.2 HIV self-testing in the HitTB study

In the HitTB study, resident community counsellors provide HIVST to adults aged ≥ 16 years. They advertise the service and distribute the HIV self-test kits. Residents who want to undergo HIVST visit the locally resident counsellors to receive pre-test counselling for HIV, and directions on how to use the HIV self-test kits. Residents who demonstrate they are able to perform the self-test are given a HIV self-test kit to take home and test on their own. Residents are also given generic post-test counselling and referral cards to enable linkage into their local HIV treatment center. The post-test counseling and referral process is not specific to HIV status, and therefore ensures individuals do not have to disclose their test result to the counsellor.

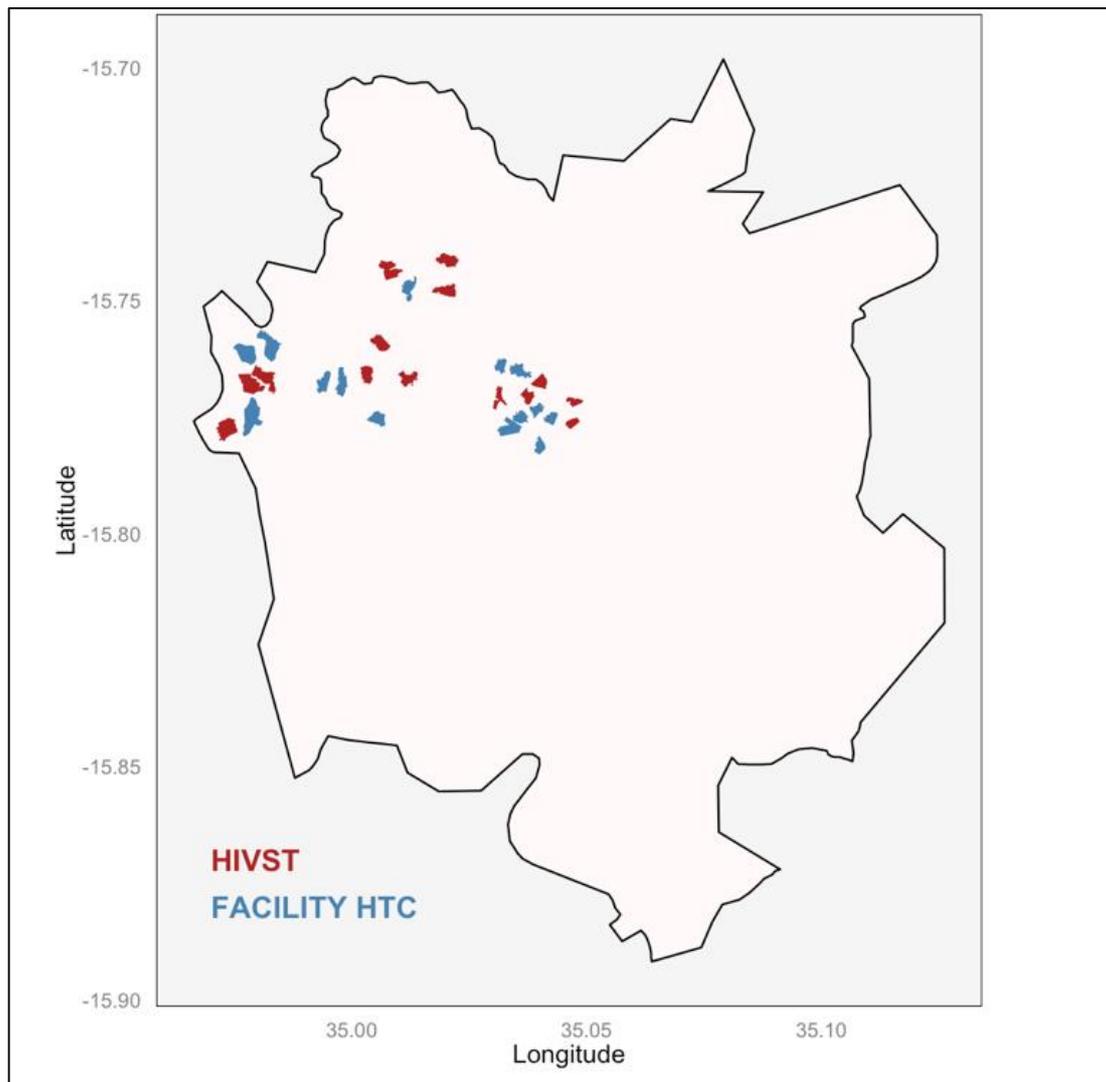
The HIVST is provided using the OraQuick ADVANCE HIV I/II (OraSure Technologies, Bethlehem, USA) test kits. This is the first, and currently the only, HIV self-test kit that has obtained approval from the Federal Drug and Administration in the USA for over the counter sale. The self-testing process involves the individual rubbing the inside of their mouth with the oral test kit, and then waiting for 15 minutes before reading the test result.

2.6.2.3 HitTB cluster-randomised trial

In the trial, neighbourhoods were defined on the basis of existing community catchment areas. The catchment areas are used by local community health services to divide the local population into smaller catchments for their health workers to provide community-based services. In the trial, the communities were enumerated before providing the intervention to determine the age and sex distribution of the population, and total population size. Global position systems (GPS) were used to map the boundaries of the communities.

The resulting trial comprised a total adult population of 34,000 people (≥ 16 year of age), with the population divided into 28 study clusters. On average, clusters were comprised of 1,200 adults. Clusters were randomised on a 1:1 basis, with 14 clusters randomised to receive standard facility HTC, and 14 clusters to HIVST (Figure 23). Individuals residing in the intervention clusters could also access standard facility-based HTC. HIVST was provided for a 2-year period in each of the intervention clusters and the service was gradually introduced from February to May 2012. In the trial, the primary evaluation involves investigating the impact on adult mortality and undiagnosed HIV, all of which are being evaluated at the time of writing, with the findings still blinded. This is being undertaken through a post-intervention surveillance study.

Figure 23: Map of Blantyre City and HitTB Study Clusters



2.6.2.3 Provision of HIV care and treatment in HitTB study

The trial residents could access HIV testing and treatment services at their local primary health clinics (Ndirande or Chilomoni) or through the outpatient clinic at Queen Elizabeth Central Hospital. HIV counsellors provide HIV testing and counselling (HTC) at these outpatient clinics.

Individuals may attend the clinics for the primary purpose of undergoing an HIV test, or they may be at the clinic for a medical reason (e.g Tuberculosis; antenatal care) and be referred to the HIV counsellors for HTC. The HIV counsellors provide counselling, and if the individual consents, HIV testing. Individuals who test HIV negative on the first rapid finger-prick test are informed they are HIV negative. Individuals who test HIV positive on the first finger-prick test have a repeat finger-prick test using an alternative rapid test kit. Individuals who subsequently test HIV positive are informed of their HIV positive test result and asked to return to the HIV treatment clinic at a given appointment date. On this return visit, individuals undergo confirmatory HIV testing and subsequent assessment for eligibility for initiation of ART.

The decision to start ART and which anti-retroviral drug regimen to provide are based on Malawi National ART guidelines (MoH, 2014). The assessment for ART eligibility involves an assessment of their HIV clinical disease stage, this follows the WHO HIV disease staging approach. Those who are found to have advanced HIV disease stage (WHO stage 3 or 4) are immediately started onto ART. All individuals have venous blood taken for assessment of their CD4 count. Individuals who do not have advanced HIV disease (WHO stage 3 or 4) are initiated onto ART if their CD4 count is below 350 cell/ul or if they are pregnant (MoH, 2014).

Individuals who are started onto ART are provided with sufficient anti-retroviral drugs to last until their next appointment date. Individuals who are not found eligible to start ART are entered into pre-ART care. Pre-ART care involves provision of cotrimoxazole preventative (CPT) and Isoniazid preventative therapy (IPT). They undergo repeat CD4 measurements every 6 months for re-assessment of eligibility to start ART. The nurse sees individuals who are started onto ART on each and every repeat visit for HIV clinical assessment and ART drug adherence. If any clinical problems manifest they are referred to the clinical officer or medical doctor at the clinic for further assessment. If no problems are found they are provided with their next supply of anti-retroviral drugs. The interval between each subsequent visit to the clinic may be gradually extended if the patient has good adherence to therapy and no HIV clinical disease progression.

2.6.3 Queen Elizabeth Central Hospital

Queen Elizabeth Central Hospital (QECH) is the largest hospital in Malawi. The hospital is based in the centre of Blantyre and provides a combination of primary, secondary and tertiary level medical care. QECH has approximately 1,500 beds, and admits approximately 25,000 adult patients per year. The hospital serves a population of approximately 1 million in the Blantyre District, with many of its tertiary referrals coming from further afield. The HIV prevalence among inpatients in QECH has previously been reported as high as 70% in patients admitted to medical wards and 36% in patients admitted to surgical wards (Lewis et al., 2003, SanJoaquin et al., 2013).

2.6.4 Primary health clinics: Ndirande and Chilomoni

Ndirande and Chilomoni health centers are both located in the city of Blantyre, and are the two clinics that serve residents of the HitTB trial. Both are primary health centers where local residents visit for initial medical assessment and to access a range of outpatient based medical care. The clinics provide HIV testing and HIV treatment, as well as other primary health services including: immunizations; maternal and child services; family planning; and care for patients with Tuberculosis. The HIV testing services acts as stand-alone HIV testing facilities, with individuals able to visit the testing center without medical referral, or visit the center after being referred by medical personnel. Individuals who test HIV positive are then referred to the HIV treatment center at the respective health facility.

2.7 Summary of Chapter 2

In this chapter I provided an overview of the country of Malawi, and highlighted the economic constraints the country faces, including the low levels of funding available to fund its health services and dependency on the international community to sustain the health of its population. I provided an overview of HIV and its impact on an individual's health. I highlighted the range of HIV associated illnesses that HIV positive individuals suffer from and how providing ART can improve their health. I also described the HIV epidemic in Africa and Malawi, and the current response to the epidemic in the region. I highlighted that despite the major efforts made in tackling the HIV epidemic in the region, millions continue to die. I highlighted that despite the major advances in the provision of HIV care a major limitation has been the poor uptake of HIV testing.

I provided a description of HIV testing and its evolution over the last few decades, including the emergence of HIV self-testing as a potential solution to meeting the current and future demands on increasing awareness of HIV status and subsequent uptake of increasingly efficacious interventions that could potentially end the epidemic in the region. I ended by providing a description of the HIV self-testing study and study sites that I am utilising to collect primary economic data to answer my primary research question. In the next chapter I will provide a detailed overview around economic evaluations targeted at HIV and HIV testing in sub-Saharan Africa.

CHAPTER 3: Methodological Issues around Economic Evaluations of HIV interventions in sub-Saharan Africa

3. Overview of Chapter 3

There have been several recent systematic reviews of economic evaluations of HIV interventions related to sub-Saharan Africa. In this Chapter I review the findings from these systematic reviews, and specific economic evaluations of HIV prevention and treatment interventions in order to highlight potential issues relating to undertaken them. I also provide a targeted review of previous approaches to undertaking decision-analytical modelling of HIV interventions. The findings from this appraisal were then used to develop the methods that address my primary research question.

3.1 Economic evaluations in resource-poor sub-Saharan settings

3.1.1 Introduction

There has been a significant increase in the number of economic evaluations of HIV-related interventions in sub-Saharan Africa (Creese et al., 2002, Walker, 2003, Scotland et al., 2003b, Uthman et al., 2010, Galarraga et al., 2009, Gomez et al., 2013, Sweeney et al., 2012, Johri and Ako-Arrey, 2011, Remme et al., 2014, Santa-Ana-Tellez et al., 2011).

One of the earliest reviews in this field examined economic evaluations of HIV treatment and prevention interventions undertaken in Africa from 1984-2000 (Creese et al., 2002). Further systematic reviews were undertaken to examine the cost-effectiveness of HIV prevention strategies in resource-poor strategies (Walker, 2003, Galarraga et al., 2009), including the cost-effectiveness of interventions to prevent mother to child transmission of HIV (PMTCT) (Scotland et al., 2003a, Johri and Ako-Arrey, 2011).

More recently, reviews have focussed on components of HIV treatment and prevention including examining the cost-effectiveness of providing voluntary male circumcision (Uthman et al., 2010), pre-exposure prophylaxis for HIV prevention (Gomez et al., 2013), interventions to improve outcomes amongst AIDS orphans and vulnerable children (Santa-Ana-Tellez et al., 2011) and gender-responsive interventions for HIV (Remme et al., 2014).

3.1.2 Findings from previous reviews

A common finding of many reviews around economic evaluations in HIV has been the lack of relevant health outcomes and cost data available for such evaluations (Galarraga et al., 2009, Kahn et al., 2011, Creese et al., 2002, Beck et al., 2010, Meyer-Rath and Over, 2012). Additionally, there has been concern around the lack of transparent, comparable and standardised methods for evaluations in the region (Galarraga et al., 2009, Walensky et al., 2010a, Loubiere et al., 2010, Uthman et al., 2010, Beck et al., 2010). Several evaluations have not captured the long-term consequences of interventions (Simpson, 2010) (Weatherly et al., 2009, Kelly et al., 2005), the real world costs of implementing interventions (Creese et al., 2002, Beck et al., 2010) or the uptake/performance of the intervention at the population level (Kahn et al., 2011, Schwartlander et al., 2011, Uthman et al., 2010).

This has led to concerns about potential bias in findings and in the ability to make comparisons across interventions and settings, and these (largely valid) criticisms have reduced the desired impact on rational decision-making (Beck et al., 2010). In addition, the lack of routinely collected cost data by healthcare providers necessitates the collection of ad hoc data which may be inaccurate or applicable only to specific settings, thus reducing generalisability and potentially introducing inaccuracies (Beck et al., 2010). Another factor is that notwithstanding the problems of generalising between settings, this is often necessary because of the scarcity of local cost-effectiveness data.

Finally, the human and financial resources needed to undertake evaluations in a resource-constrained setting may deter such analyses. A common theme from previous reviews has been the predominant use of decision-analytic modelling to undertake economic evaluations (Creese et al., 2002, Johri and Ako-Arrey, 2011, Uthman et al., 2010). Many of these issues are common to economic evaluations in general; however, appropriate solutions may differ depending on context, resources and setting (Kelly et al., 2005).

3.2 Economic evaluations of HIV testing strategies

3.2.1 Introduction

The benefits of timely initiation of ART and continued low uptake of HIV testing through traditional facility-based approaches in Africa highlights the need to investigate modalities and strategies to increase uptake of HIV testing (Labhardt et al., 2014, Suthar et al., 2013, Sabapathy et al., 2012, Lugada et al., 2010). However, policy makers need to be aware of the potential value for money from investing in these different approaches so that the limited resources they have available to provide these services can be optimised (WHO, 2015).

3.2.2 Comparing costs of different HIV testing strategies

Table 2 shows the findings from two costing studies that compared the cost of providing home-based or mobile HIV testing to facility-based provision of HTC (Menzies et al., 2009, Grabbe et al., 2010). In both studies, facility-based provision of HTC was associated with higher costs than provision of HIV testing through home-based or mobile services as a consequence of the higher capital costs associated with managing a health facility (Menzies et al., 2009, Grabbe et al., 2010). However, the higher HIV prevalence amongst health facility testers results in HIV infected individuals, unaware of their status, being identified at a lower cost than through home-based or mobile HTC services (Menzies et al., 2009, Grabbe et al., 2010).

Table 2: Comparison of costs of HIV testing through different modalities

	Grabbe et al., 2010 Kenya		Menzies et al., 2010 Uganda			
	2007 US Dollars		2007 US Dollars			
	Stand-alone testing facility	Mobile testing service	Stand-alone testing facility	Hospital-based	Household-member (contact tracing)	Home-based
Cost per HTC client	\$26.75	\$14.91	\$19.26	\$11.68	\$13.85	\$8.29
Cost per new HTC client	\$43.69	\$16.58	\$29.70	\$14.73	\$14.54	\$9.21
Cost per HIV positive individual identified	\$189.14	\$157.21	\$100.59	\$43.10	\$231.65	\$163.93

3.2.3 Community-based HIV testing strategies

Community-based HTC services have been found to be popular. (Were et al., 2003, Wolff et al., 2005, Tanser et al., 2008, Menzies et al., 2009, Negin et al., 2009, Amolloh et al., 2011, Tumwesigye et al., 2010). Table 3 highlights the different estimates for the costs of providing HIV testing in the communities, with costs ranging from US\$2.45 to US\$33.54 (in 2012 prices) (Suthar et al., 2013). The approaches to quantifying the costs of community-based HIV testing strategies have also differed, with many analyses not taking into account the costs of all resources used in the provision of the service (Table 3).

These analyses only provide estimates of the costs of getting individuals tested (Table 3) (Suthar et al., 2013). As will be highlighted in Chapter 4 of the PhD (Figure 24), this type of economic analysis would be considered a partial evaluation.

The cost of providing community-based HIV testing services may be lower than facility-based HTC, whilst the cost to detect HIV positive individuals through community-based HTC may be higher (Table 2). This information alone can be misleading as it fails to take into account the consequences of HIV testing, namely of the costs and health outcomes after learning ones HIV status.

Table 3: Comparison of costs of community-based HIV testing strategies

Study	Modality of HTC	Country	Resources included in cost estimates	Cost per HTC Client (2012 US dollars)
Molesworth et al., 2010	Home-based	Malawi	Testing supplies	\$2.45
Tumwesigye et al., 2010	Home-based	Uganda	Testing supplies, personnel, and transportation	\$7.77
Menzies et al., 2009	Home-based	Uganda	Testing supplies, personnel, transportation, vehicles, buildings, utilities, training, and equipment	\$9.16
Negin et al., 2009	Home-based	Kenya	Testing supplies, personnel, and transportation	\$9.43
Helleringer et al., 2009	Home-based	Malawi	Testing supplies, personnel, transportation, buildings, utilities, and training	\$14.37
Menzies et al., 2009	Contact tracing	Uganda	Testing supplies, personnel, transportation, vehicles, buildings, utilities, training, and equipment	\$15.30
Edgil et al., 2011	Mobile	Swaziland	Testing supplies	\$3.26
Chamie et al., 2014	Mobile	Uganda	Testing supplies, personnel, and buildings	\$8.27
Kahn et al., 2011	Mobile	Kenya	Testing supplies, personnel, training, and contingency expenses	\$10.55
Grabbe et al., 2010	Mobile	Kenya	Testing supplies, personnel, vehicles, buildings, utilities, and equipment	\$16.47
Terris-Prestholt et al., 2006	Mobile	Uganda	Testing supplies, personnel, vehicles, buildings, and equipment	\$33.54

Adapted from Suthar et al., 2013

HIV infected individuals only tend to access facility-based HTC services in the later stages of their HIV infection, when they have low CD4 counts (Nash et al., 2011, Kigozi et al., 2009) and when they may be suffering from HIV-related co-morbidities

(Lawn et al., 2010b). Consequently, the beneficial effect of ART on improving survival is limited (May et al., 2010a). This is compounded by the poor uptake of HIV care subsequent to a positive test through facility-based services (Rosen and Fox, 2011). Community-based HIV testers have been found to have higher CD4 counts than facility-based testers at the time of accessing the HIV testing service (Dalal et al., 2013, Wachira et al., 2012b). They will have experienced a shorter time period during which they may have suffered HIV associated illnesses or infected others (Dalal et al., 2013, Wachira et al., 2012b).

These factors suggest that HIV positive individuals identified through community-based HIV testing strategies will have better health outcomes and be associated with lower future costs. In addition, economic evaluations of HTC strategies in high-income settings increasingly take into account future HIV related costs and consequences (Brennan and Akehurst, 2000, Beck et al., 2012, Shroufi et al., 2013), and the impact of increased anti-retroviral treatment coverage on HIV transmission (Brennan and Akehurst, 2000, Shroufi et al., 2013, Safren et al., 2012, Lipscomb et al., 2009). Taking these factors into account in an economic evaluation is therefore important.

3.2.4 Cost of providing HIV treatment

Economic evidence from high-income settings suggests that as clinical care for HIV infected individuals has improved, so has the costs of providing HIV treatment

(Schackman et al., 2006, Mandalia et al., 2010). Until recently there was limited data around the costs of providing HIV treatment to inform policy makers (Levy et al., 2006, Beck et al., 2010). Even now the majority of the economic data comes from South Africa (Harling and Wood, 2007, Rosen et al., 2008, Martinson et al., 2009, Long et al., 2010), or from estimates based on international donor supported services (Menzies et al., 2011, Larson et al., 2013, Menzies et al., 2012, Marseille et al., 2012). The cost of providing HIV treatment may to be higher in these settings where care is frequently provided by doctors or in well-resourced health facilities. The costs of providing HIV treatment by health professional other than doctors have been found to be significantly lower (Johns et al., 2014, Babigumira et al., 2009).

The cost of providing HIV treatment has been found to be higher for those with more advanced HIV disease (Leisegang et al., 2009). Additionally, estimates for the costs of providing HIV treatment vary depending on the setting where care is provided, with costs generally being higher in decentralised primary care clinics than in central referral hospitals (Rosen et al., 2008), and falling with time as HIV treatment sites either mature or increase in populations served by the treatment site (Menzies et al., 2011, Menzies et al., 2012, Marseille et al., 2012).

3.2.5 Impact of HIV treatment on health-related quality of life

HIV infection affects the health-related quality of life (HRQoL), with those with more advanced HIV infection generally having poorer HRQoL (Bajunirwe et al., 2009,

Peltzer and Phaswana-Mafuya, 2008). Anti-retroviral therapy has been found to have a beneficial impact on the HRQoL of individuals with HIV infection (Mutabazi-Mwesigire et al., 2014, Stangl et al., 2007, Rosen et al., 2014, Beard et al., 2009). Studies that have used the EuroQol EQ-5D (EuroQol, 1990) measure to examine HRQoL in HIV infected individuals have shown comparable findings. Their findings suggest people with late stage HIV infection have poorer EQ-5D utility scores (Hughes et al., 2004), whilst those on anti-retroviral therapy have higher EQ-5D utility scores (Louwagie et al., 2007), and HRQoL improves over the course of time on anti-retroviral therapy (Jelsma et al., 2005).

3.2.6 Economic evaluation of HIV testing strategies

Early economic evaluations of HIV testing strategies found that providing free HIV testing and counselling services at fixed health facilities was a cost-effective intervention in sub-Saharan Africa (Sweat et al., 2000, Thielman et al., 2006). In these evaluations the provision of free HTC at health facilities was compared to no provision of HTC, and was undertaken at a time when anti-retroviral therapy was not available to those who tested HIV positive (Sweat et al., 2000, Thielman et al., 2006). The analysis suggested that providing free HTC services would cost below US\$50 per disability-adjusted life year (DALY) saved (Sweat et al., 2000, Thielman et al., 2006).

Prior to starting the PhD no full economic evaluation had been undertaken of community-based HIV testing or HIV self-testing strategies in sub-Saharan Africa.

Recently, two full economic evaluations have been undertaken of home-based HIV testing (Smith et al., 2015) and mobile HIV testing (Bassett et al., 2014). Implementing home-based and mobile HIV testing services were found to be a cost-effective strategy in South Africa (ICER < 3 X GDP per capita) (Bassett et al., 2014, Smith et al., 2015).

In South Africa the estimated incremental cost-effectiveness ratio (ICER) for providing home-based HIV testing in addition to facility-based HTC was 2012 US\$1,090 per DALY averted (Smith et al., 2015). In their analysis the ICER estimate was sensitive to the cost of providing anti-retroviral therapy to HIV positive individuals (Smith et al., 2015). In South Africa the estimated ICER for providing mobile HIV testing in addition to facility-based HTC was 2012 US\$2,400 per life year saved (Bassett et al., 2014). In the analysis the ICER estimates were sensitive to the prevalence of undiagnosed HIV in the population and likelihood of linking into HIV treatment amongst those who test HIV positive (Bassett et al., 2014). The model of mobile HIV testing investigated also included provision of on site CD4 measurement and ART assessment, which have been found to be associated with increasing linkage into HIV treatment services (Jani et al., 2011).

A recent cost-effectiveness analysis investigated the potential impact of implementing HIVST in addition to facility-based HTC in Zimbabwe (Cambiano et al., 2015). This modelling study investigated a range of hypothetical scenarios relating to

the effects of the cost of implementing HIVST, uptake of HIVST, linkage into HIV treatment services, and ART eligibility criteria on the incremental cost-effectiveness of implementing HIVST. Table 4 shows the scenarios modelled and the cost-effectiveness findings from the analysis. In their primary analysis the authors assumed the cost of an HIV self-test episode to be 2015 US\$3 (a third of the cost of an HTC episode through health facilities), with ART initiated once an individual's CD4 count fell below 500 cells/ul (Cambiano et al., 2015). The ICER was found to be sensitive to the cost of an HIVST episode, with implementation not cost-effective if the cost was comparable to that of a facility-based HTC episode. Additionally, the authors found that the ICER was sensitive to the likelihood of linking into HIV treatment amongst HIV self-testers who tested HIV positive.

Table 4: Cost-effectiveness of HIV self-testing from Cambiano et al., 2015

Scenario and input parameters	Cost-effectiveness findings
<p><u>Base case</u> Cost of HIVST: US\$3 Cost of facility HTC: US\$9 ART Initiation CD4 <=500 cells/ul Annual proportion tested in facility scenario: 50% Annual proportion tested in HIVST + Facility HTC Scenario: 57% Linkage into HIV treatment after HIVST: 60% CD4 measurement: US\$10 Annual cost of ART: US\$97 Cost of managing WHO stage IV illness: US\$200</p>	<p>Cost saving and more effective</p>
<p><u>Alternative Scenario 1</u> Cost of HIVST: US\$9 Otherwise same as base case</p>	<p>Not cost-effective up to ICER of 2015 US\$10,000/DALY averted</p>
<p><u>Alternative scenario 2</u> ART initiation at CD4 <350 cells/ul Otherwise same as base case</p>	<p>Cost saving and less effective</p>

Economic evaluations of HTC strategies in resource-rich and resource-poor settings have found that the main drivers of cost-effectiveness are the underlying HIV prevalence in the population, the CD4 count of HIV infected individuals at diagnosis, the proportion of testers linking into HIV treatment, the cost of providing HIV treatment, and the cost per person reached (Safren et al., 2012, Shroufi et al., 2013, Brennan and Akehurst, 2000, Kigozi et al., 2009, Beck et al., 2012, Fox-Rushby and Hanson, 2001, Beard et al., 2009, Venkatesh et al., 2013, Smith et al., 2015, Cambiano et al., 2015, Bassett et al., 2014).

3.3 Decision-analytic modelling of HIV interventions

3.3.1 Overview

Decision-analytic modelling in HIV has gradually evolved over the last few years as more information has become available on the progression of HIV infection with and without treatment, the drivers of costs and health outcomes of interventions, the population impact of interventions and on modelling techniques (Simpson, 2010, Anderson and Garnett, 2000, Weinstein, 2006, Marseille et al., 2012, Menzies et al., 2012).

However, there are concerns over the methodological quality of many HIV modelling-based evaluations (Simpson, 2010), including poor reflection of actual treatment pathways, use of input parameters which do not reflect current epidemiological knowledge, and a lack of consideration of adverse consequences of interventions (Johnson and White, 2011, Simpson, 2010).

Table 5, Table 6 **and** Table 7 provide an informal review of model-based economic evaluations undertaken in sub-Saharan Africa. **Appendix V** shows the literature search strategy utilised to find these studies. Some studies are not included because they have used the same model to investigate the cost-effectiveness of a range of different HIV interventions (Losina et al., 2009, Walensky et al., 2012, Walensky et al., 2009, Walensky et al., 2010b, Walensky et al., 2011, Goldie et al., 2006).

3.3.2 Modelling HIV prevention strategies

Models used to investigate the cost-effectiveness of prevention of mother to child transmission (PMTCT) interventions have traditionally used simple decision trees and modelled impact on HIV transmission to uninfected infants using constant rates of transmission, obtained from published literature or primary studies (Table 5) (Sweat et al., 2004, Binagwaho et al., 2013).

These have recently increased in complexity with investigators modelling HIV disease progression in mothers and infants using mutually exclusive health states represented by CD4 count categories (Fasawe et al., 2013, Ciaranello et al., 2013). This change has come about as a consequence of changes in the management of HIV positive pregnant women.

In the early stages of PMTCT, the role of ART was to prevent HIV transmission to uninfected infants, and mothers and infants were given short course anti-retroviral drugs to achieve this (WHO, 2003b). Currently the WHO recommends that all HIV infected pregnant women should initiate HAART and remain on it life-long (WHO, 2010a). This reduces the risk of transmission during breast-feeding and improves health outcomes in mothers (Tudor Car et al., 2011). In order to evaluate the cost-effectiveness of these different strategies, investigators have rightly added complexity to their models to incorporate long-term costs and consequences of providing or not providing mothers with life-long ART (Ciaranello et al., 2013).

Transmission of HIV from mothers to their uninfected children can occur during pregnancy, during delivery or through breastfeeding. These are relatively definable and constant risks that can be obtained through primary clinical trials (Parazzini et al., 1999, Guay et al., 1999), and therefore modellers have not needed to explicitly model the indirect impact of HIV care on HIV incidence. However, for most other HIV prevention strategies, incorporating this indirect effect has driven modelling approaches. Dynamic transmission models provide a powerful mathematical approach to incorporating these effects (Pitman et al., 2012).

As Table 6 highlights, the investigation of cost-effectiveness of HIV prevention interventions have often used these compartmental dynamic transmission models (Pretorius et al., 2010, Nichols et al., 2013, Cremin et al., 2013). Dynamic transmission models represent the impact of the intervention on risk of HIV transmission by altering the flow of individuals from higher infectious compartments to lower infectious compartments, thereby modelling the reduced risk of a susceptible uninfected individual acquiring HIV infection when they come into contact with an HIV infected individual. These interactions between categories of individuals enable the quantification of the indirect effects of an intervention.

As Table 6 shows, for HIV prevention interventions modellers have predominantly used stage of HIV infection to define compartments. This has been based on the scientific literature (Hollingsworth et al., 2008) which has shown that HIV infected

individuals are most infectious and that the risk of sexual transmission is highest during the first few months after acquiring HIV infection. Individuals quickly suppress the HIV viral load and become significantly less infectious, until the late stages of HIV infection when their HIV viral load increases considerably again as does their infectiousness.

Interestingly, several economic evaluations of HIV prevention strategies have also used models that do not explicitly model changing risk of HIV transmission (Kahn et al., 2006, Gray et al., 2007b, Hallett et al., 2011, Walensky et al., 2012, van Hulst et al., 2008). In these analyses, investigators have followed common approaches used in modelling HIV treatment strategies, with HIV incidence assumed to remain constant over time.

3.3.3 Modelling HIV treatment strategies

In decision-analytical modelling, static Markov models are commonly used, with compartments used to define mutually independent health states which cohorts transition through (Cleary et al., 2006, Bachmann, 2006, Marseille et al., 2009, Athan et al., 2010, Rutstein et al., 2013, Pitter et al., 2007, Jarvis et al., 2013).

Markov models differ in the defining characteristics of these compartments or health states, and in the fact that there is no interaction between compartments. In

dynamic transmission models, the compartments represent the infectiousness or non-infectiousness of the average population in that compartment, whilst in Markov models they are used to define the health-related quality of life (HRQoL) and costs associated with a cohort in a particular health state.

Modellers using Markov models to investigate the cost-effectiveness of HIV treatment interventions in sub-Saharan Africa have predominantly used CD4 counts to define health states (Table 7). This has also been driven by the scientific literature, which highlights that the CD4 count of an individual influences their HRQoL (Hughes et al., 2004, Jelsma et al., 2005), the costs for caring for them (Leisegang et al., 2009), their risks of HIV-associated mortality (Brinkhof et al., 2009) and likelihood of comorbidities (Brinkhof et al., 2007).

Over the last few years there has been a change in the number of health states and in the CD4 count ranges which each compartment represents. This has mainly been in response to changes in the clinical management of HIV infected individuals and to increasing knowledge about the epidemiology of HIV disease progression. Recommendations increasingly indicate initiation of HAART earlier in HIV disease (WHO, 2014), with recent findings from randomised trials suggesting that this trend will continue (Group, 2015a, Group, 2015b).

Whilst there are similarities between Cohort Markov models and dynamic transmission models, many differences between them exist; of most importance has been differences in the capture of the indirect effects of an intervention. Recent findings from South Africa demonstrated that even initiating ART at current CD4 count thresholds and achieving relatively low population ART coverage can achieve significant reductions in HIV incidence (Tanser et al., 2013). This has highlighted the need to incorporate the indirect population effects of HIV treatment strategies. Whilst dynamic transmission models allow us to do this, they fail to represent the uncertainty in the decision-making process (Brennan et al., 2006). Decision-analytic models estimate outcomes based on the data used to parameterise the model. Data used to parameterise models could be obtained through primary data collection from a sample of individuals representative of the population of interest, through synthesising secondary data, or as is the case for certain parameters used in dynamic transmission models, by fitting models to observed data. There will always be some degree of uncertainty in these estimates. This uncertainty is taken into account in Markov models by undertaking probabilistic sensitivity analysis, running the model several thousands of times and varying parameters across the range of possible values (Petrou and Gray, 2011b, Briggs et al., 2008).

Representing uncertainty is essential for policy makers, who need to understand the robustness of findings of cost-effectiveness (Briggs et al., 2012a). Probabilistic sensitivity analysis provides the optimal approach to representing this uncertainty in decision-analytic modelling (Briggs et al., 2012a). However, of the studies described

in Table 7 only five studies (Bachmann, 2006, Cleary et al., 2006, Marseille et al., 2009, Bendavid et al., 2011, van Hulst et al., 2008) undertook such analysis.

A shortcoming of both cohort Markov models and dynamic transmission models is that they fail to take into account the random nature of events at the individual level. The increasing computational power available over the last decade has enabled modellers to incorporate this issue into HIV cost-effectiveness models using individual sampling models, where costs and outcomes are simulated at an individual level (Losina et al., 2009, Walensky et al., 2012, Walensky et al., 2009, Walensky et al., 2010b, Walensky et al., 2011, Goldie et al., 2006, Bendavid et al., 2008, Bendavid et al., 2011, Hallett et al., 2011, Gray et al., 2007b). An important advantage of this approach has been the ability to make parameters conditional on attributes of an individual, thereby adding both memory and legitimate heterogeneity to the modelling process (Barton et al., 2004, O'Hagan et al., 2007).

In HIV cost-effectiveness modelling this has allowed modellers to make transitions between health states, costs and health outcomes conditional on individual attributes, including whether an individual has had previous TB, the duration of time on ART, CD4 count at initiation and HIV RNA viral load response to treatment (Losina et al., 2009, Walensky et al., 2012, Walensky et al., 2009, Walensky et al., 2010b, Walensky et al., 2011, Goldie et al., 2006, Bendavid et al., 2008, Bendavid et al., 2011, Hallett et al., 2011, Gray et al., 2007b). The need for incorporation of these factors is

evident as from the current literature that highlights that these events influence subsequent response to treatment, disease progression and costs of care (Lawn et al., 2010a, Martinson et al., 2009, Leisegang et al., 2009, Harling and Wood, 2007).

The three published cost-effectiveness analysis of community-based HIV testing strategies have used either dynamic transmission modelling (Cambiano et al., 2015, Smith et al., 2015) or individual sampling models (Bassett et al., 2014). The differences in modelling approaches suggest there is no agreed consensus of the optimal approach.

Table 5: Overview of Models evaluating cost-effectiveness of Prevention of Mother-To-Child Transmission (PMTCT) of HIV

Study	Objective	Modelling approach	How was HIV disease progression modelled?	Approach to HIV transmission?
Sweat et al., 2004	Investigate cost-effectiveness of nevirapine in the PMTCT in eight Africa countries.	No Interaction Decision Tree	Decision tree with single HIV state	Constant risk determined by maternal/infant HIV treatment given
Binagwaho et al., 2012	Investigate cost-effectiveness of a range of PMTCT strategies in Rwanda.	No interaction Markov Model	Decision tree with single HIV state	Constant risk determined by maternal/infant HIV treatment given
Fasawe et al., 2013	Investigate cost-effectiveness of a range of PMTCT strategies in Malawi	No interaction Markov Model	Health states defined by CD4 stratum (>350; 350-200; 199-0).	Constant risk determined by maternal/infant HIV treatment given
Ciaranello et al., 2013	Investigate cost-effectiveness of a range of PMTCT strategies in Zimbabwe	No interaction Markov Model	Health states defined by CD4 stratum (>350; 350-200; 199-0) HIV associated co-morbidities	Constant risk of HIV transmission determined by maternal/infant HIV treatment given

Table 6: Overview of Models evaluating cost-effectiveness of interventions to tackle transmission and acquisition of HIV infection

Study	Objective	Modelling approach	How was HIV disease progression modelled?	Approach to HIV transmission?
Kahn et al., 2006	Investigate cost-effectiveness of adult male circumcision in South Africa.	No interaction Decision Tree	Decision tree with single HIV state	Constant risk of HIV transmission determined by circumcision status
Gray et al., 2007	Investigate cost-effectiveness and impact on HIV incidence of male circumcision in Uganda	No interaction Individual simulation	Health states defined by stage of HIV infection (Acute; Latent; AIDS)	Constant risk of HIV transmission determined by stage of HIV infection
Pretorius et al., 2010	Investigate cost-effectiveness and impact on HIV transmission of PreP in South Africa.	Interaction System dynamics	Did not model HIV progression	Compartmental model with additional risk heterogeneity determined by Age; Sex; HAART; PreP; Condom use
Hallet et al., 2011	Investigate cost-effectiveness and impact on HIV transmission of PreP and HAART amongst serodiscordant heterosexual couples in South Africa.	No Interaction Individual simulation	Health states defined by CD4 stratum (>500; 350-500; 350-200; <200)	Constant risk of HIV transmission determined by HIV health state
Walensky et al., 2012	Investigate cost-effectiveness of PreP in South Africa	No interaction Individual simulation	Health states defined by stage of HIV infection (Acute; Chronic) HIV-associated comorbidities.	Impact on HIV transmission not incorporated
Nichols et al., 2013	Investigate cost-effectiveness of PreP in Zambia	Interaction System dynamics	Health states defined by stage of HIV infection (Acute; Chronic; Early AIDS; Late AIDS)	Compartmental model with additional risk heterogeneity determined by sexual activity
Cremin et al., 2013	Investigate cost-effectiveness and impact on HIV transmission of PreP, HAART and Male Circumcision in high HIV prevalent settings.	Interaction System dynamics	Health states defined by a combination of stage of HIV infection + CD4 stratum (Acute infection >350; 350-200; Early AIDS; Advanced AIDS; Severe AIDS)	Compartmental model with additional risk heterogeneity determined by Age; Sex; HAART; PreP; Condom use; Sexual activity
van Hulst et al., 2008	Investigate cost-effectiveness of different screening strategies for blood donations in Ghana.	No interaction Markov Model	Health states defined by WHO HIV Stages (Stage 1, 2, 3 & 4)	Constant risk of HIV transmission determined by blood transfusion

Table 7: Modelling approaches to evaluating cost-effectiveness of HIV treatment interventions

Study	Objective	Modelling approach	How was HIV disease progression modelled?	Approach to HIV transmission?
Goldie et al., 2006	Investigate cost-effectiveness of providing HAART in the Ivory Coast.	No interaction Individual simulation	Health states defined by stage of HIV infection (Acute; Chronic) + HIV-associated comorbidities.	Impact on HIV transmission not incorporated
Bachmann, 2006	Investigate cost-effectiveness of providing HAART, TB treatment and HIV prophylaxis in Southern Africa.	No interaction Markov Model	Health states defined by CD4 stratum (350-200; <200) + HIV associated comorbidities	Impact on HIV transmission not incorporated
Cleary et al., 2006	Investigate cost-effectiveness of providing HAART in South Africa.	No interaction Markov Model	Health states defined by CD4 stratum (199-50; <50)	Impact on HIV transmission not incorporated
Bendavid et al., 2008	Investigate cost-effectiveness of clinical and laboratory monitoring strategies for those on HAART in South Africa	No interaction Individual simulation	Health states defined by CD4 stratum (>350; 350-201; 200-51; <50) + HIV associated co-morbidities	Impact on HIV transmission not incorporated
Marseille et al., 2009	Investigate cost-effectiveness of providing home-based HAART to HIV infected individuals in Uganda.	No interaction Markov Model	Health states defined by WHO HIV Stages (Stage 1, 2, 3 & 4)	Impact on HIV transmission not incorporated
Athan et al., 2010	Investigate cost-effectiveness of using routine CD4 count monitoring to guide initiation of HAART in resource-limited settings.	No interaction Markov Model	Health states defined by CD4 stratum (>350; 350-200; AIDS) + HIV associated comorbidities	Impact on HIV transmission not incorporated
Kahn et al., 2011	Investigate cost-effectiveness of clinical and laboratory monitoring strategies for those on HAART in Uganda.	No interaction Decision Tree	Used a decision tree but with separate health states for HIV-associated co-morbidities. HIV infected health state was not subdivided.	Impact on HIV transmission not incorporated
Bendavid et al., 2011	Investigate cost-effectiveness of different first line HAART regimens in Southern Africa.	No interaction Individual simulation	Health states defined by CD4 stratum (>500; 500-351; 350-201; <200) + HIV associated co-morbidities	Impact on HIV transmission not incorporated
Rutstein et al., 2012	Investigate cost-effectiveness of different contact tracing approaches to identifying HIV infected sexual partners of those already in care in Malawi	No interaction Markov Model	Health states defined by stage of HIV infection and treatment eligibility (Acute; Chronic; HAART Eligible)	Impact on HIV transmission not incorporated
Pitter et al., 2007	Investigate cost-effectiveness of providing cotrimoxazole prophylaxis among persons infected with HIV in Uganda.	No interaction Markov Model	Health states defined by CD4 stratum (>500; <500) + HIV associated co-morbidities	Impact on HIV transmission not incorporated
Jarvis et al., 2013	Investigate cost-effectiveness of cryptococcal antigen screening in HIV infected individuals in South Africa with CD4 counts less than 100 cell/ul.	No interaction Markov Model	Health states defined by CD4 stratum (100-50; <50) + HIV associated co-morbidities	Impact on HIV transmission not incorporated

3.4 Summary of Chapter 3

In this chapter I provided an overview of previous economic evaluations undertaken in HIV testing and approaches to performing economic evaluations of HIV interventions. I also provided a discussion of modelling approaches to performing economic evaluations of HIV interventions. The modelling approaches utilised have to an extent been driven by whether the objective of the analysis was to investigate strategies to prevent HIV transmission or to treat those infected with HIV. I highlighted the complexity of trying to incorporate the impact of HIV treatment on both HIV disease progression and HIV transmission.

This chapter highlights the importance of considering the long terms costs of providing care and health outcomes of HIV positive individuals identified through HIV testing services. This supports the rationale for undertaking the primary observational studies described in Chapters 5, 6 and 7 of the PhD.

As will become apparent in Chapter 8 of the PhD, I utilise a decision-analytical approach that primarily considers the impact of HIV treatment on HIV disease progression, without explicitly taking into account the changing impact on HIV transmission through higher population coverage of ART.

CHAPTER 4: Overview of PhD Research Methods

4. Overview of Chapter 4

In this chapter I will discuss the broad research, epidemiological and health economic methods used in the studies presented in my PhD. I will begin by introducing the primary research question, and the aims and objectives of the PhD. I will provide an overview of how the research studies undertaken in chapter 5 to 8 aim to meet the objectives of the PhD and thereby answer my primary research question.

I will provide an overview of the methods of health economic evaluation and the approach I use to investigate the cost-effectiveness of HIVST. I will describe the rationale for using decision-analytic modelling to undertake my primary economic evaluation, and provide a review of how modelling can be performed. I will also provide a description of the methods used in the three primary observational studies undertaken in chapters 5, 6 and 7. In addition, I will describe the approaches to collecting and estimating the costs and health related quality of life data that will be used to parameterise the models.

4.1 Overview of PhD research

4.1.1 Primary research question

The primary research question of my PhD is: “How cost-effective is home-based HIV self-testing in Blantyre, Malawi?” In order to answer my research question, I needed to decide on the appropriate methods. As the research was being undertaken in the context of a larger cluster-randomised trial, it provided an opportunity to collect primary data from participants of the trial who have been randomised to receive or not receive the exposure of interest (HIV self-testing). This was also necessary because of the lack of relevant data to answer this question.

A recent publication by Cambiano and colleagues highlights 18 issues with regards to lack of data they encountered when trying to evaluate the cost-effectiveness of HIVST (Cambiano et al., 2014, Cambiano et al., 2015). As highlighted in the previous and preceding chapters of this thesis, there are probably even more data needs than that. Of note, the authors only mention two issues with regards to costs and health-related quality of life (highlighted below) (Cambiano et al., 2014).

“What is the cost of implementing HIVST in resource-limited settings?”

“What is the quality of life following a positive or a negative HIVST as compared to the same result communicated by a provider?”

These two issues are likely to play an important role in the investigation of the cost-effectiveness of HIVST. However, other issues regarding costs and quality of life need to be considered also. An economic evaluation is a comparative analysis of the costs and consequences of an intervention, and consequently will also require the investigation of the costs and quality of life consequences of HIVST and current approaches to providing HIV testing and counselling. For example, does it cost the same to manage someone on ART who self-tested as someone who accessed HIV testing at the health facility? Do those who self-tested have the same health-related quality of life as facility testers after they access HIV treatment? In addition, HIV testing is the entry point into accessing HIV treatment, and when someone starts ART has an impact on their subsequent risk of developing HIV associated diseases. If offering HIVST results in more timely initiation of ART amongst those who test positive, many of these HIV associated diseases could be averted.

4.1.2 Rationale of overall study design

In answering my main research question I used decision-analytic modeling to undertake a cost-utility analysis (CUA). The on-going study (HitTB study) is a cluster-randomised trial. Undertaking an economic evaluation alongside a randomised clinical trial potentially provides the least biased estimates for economic and health outcomes data.

HIV testing strategies reach different populations and at differing stages in their disease progression. As this impacts on subsequent health outcomes and cost of providing care, there is a need to incorporate the long-term costs and health outcomes subsequent to entering HIV care. Whilst it may have been possible to follow-up Hit-TB trial participants, the large sample sizes and long follow-up suggested a decision-analytical modelling approach would be more efficient, and enabled the incorporation of other relevant evidence from secondary sources (Petrou and Gray, 2011b, Buxton et al., 1997).

In addition, whilst there is a lack of primary economic data with regards to HIV, there is a large amount of research undertaken to investigate outcomes amongst HIV positive individuals who have and have not started anti-retroviral therapy. Decision-analytic models allows us to synthesize this data, analogous to performing a meta-analysis, so that estimates of cost-effectiveness are potentially based on all the available evidence rather than from evidence from a single randomised trial (Drummond et al., 2005b, Briggs et al., 2008, Briggs et al., 2012b).

4.1.3 Aims and objectives

The broad aim is to investigate the costs and health benefits of providing residents in Blantyre, Malawi access to HIV self-testing (HIVST) in addition to facility-based HIV testing and counselling (HTC) services, thereby allowing estimation of its value for

money within an economic evaluation framework. The specific primary and secondary objectives of the PhD are listed below.

Primary objective:

To undertake a decision-analytic modelling based cost-utility analysis to estimate the incremental cost per quality-adjusted life year (QALY) gained from the provision of HIV self-testing in conjunction with traditional facility-based HIV testing and counselling services in Blantyre, Malawi.

-> Investigated in Chapter 8 of PhD

Secondary objectives:

To compare and contrast the costs to individuals and to healthcare providers, and health-related quality of life outcomes, amongst individuals who access facility-based or HIV self-testing services in Blantyre, Malawi.

-> Investigated in Chapter 5 of PhD

To compare and contrast the costs to individuals and to healthcare providers, and health-related quality of life outcomes, amongst HIV positive individuals who access HIV care and treatment services subsequent to testing at facility-based or through HIV self-testing services in Blantyre, Malawi.

-> Investigated in Chapter 6 of PhD

To estimate the costs, to individuals and to healthcare providers, and health-related quality of life of adults who are admitted to the medical wards in Queen Elizabeth Central Hospital, Blantyre, Malawi, for the management of medical illnesses.

->Investigated in Chapter 7 of PhD

To investigate the relative impact of HIV infection on costs and health-related quality of life of adults who are admitted to the medical wards in Queen Elizabeth Central Hospital, Blantyre, Malawi, for the management of medical illnesses.

->Investigated in Chapter 7 of PhD

4.2 Economic evaluation

4.2.1 Overview

Economic evaluations are a relatively new research tool in healthcare research, and over the last few decades the findings of evaluations are playing an increasing role in decision-making in healthcare. Their basic premise is that resources are scarce, and there is potentially an infinite number of alternative ways to use these resources. In addition, health is an important good that all members of society should have access to. Therefore decisions have to be made on how to allocate finite resources. Economic evaluations provide an approach to aid this process. They build on clinical effectiveness research by relating relevant costs associated with providing an intervention to the consequences of its provision, and by comparing the costs and consequences of alternative approaches to providing healthcare interventions to their alternatives, thereby aiding decisions about whether implementing a new intervention represents an efficient use of resources (Drummond et al., 2005b).

4.2.2 Why undertake an economic evaluation

Health and healthcare research rapidly evolve. The burden of an illness can change over time, and new illnesses emerge. In addition, the approaches to treating illness change over time as new health technologies are found. In this rapidly evolving environment, decisions have to be made on how to use the finite resources available. Economic evaluation is an analytical tool that allows the systematic appraisal of the costs and consequences of diseases and health technologies to provide policy

makers with additional information on which to make decisions (Drummond et al., 2005b). The primary reason to undertake them is to provide information, additional to clinical effectiveness, for decision makers, thereby helping them reduce the uncertainty around their decision.

Economic evaluations can vary in the scope of the analysis undertaken. Figure 24 provides a description of the evaluations undertaken by the scope of the costs and consequences considered in the analysis. The different types of analysis provide different types of information that may be useful for a policy maker who needs to make the decision.

Figure 24: Approaches to performing an economic evaluation

		Are both costs and consequences of alternatives compared?		
		No	Yes	
Is there comparison of two or more alternatives?	No	Examines only consequences	Examines only costs	Partial Evaluation Cost-Outcome Description
	Partial Evaluation Outcome description	Partial Evaluation Cost Description		
Yes	Efficacy or Effectiveness evaluation	Cost Analysis	Full Economic Evaluation Cost-Effectiveness Analysis Cost-Utility Analysis Cost-Benefit Analysis	

Courtesy of Drummond et al., 2005

Economic evaluations help reduce the uncertainty that policy makers face when they are making a decision (Brennan and Akehurst, 2000). They can make comparisons between two or more interventions to inform the relative costs and consequences incurred through each intervention. They can link the costs of providing an intervention to the health outcomes of receiving the intervention. Whilst a new intervention may be more effective than current practice, it may also be significantly more costly than current practice. Therefore funding the new intervention may not be affordable for the policy maker, or funding it may result in other interventions not being funded.

However there have been concerns that decision makers often find that economic evaluations have a very narrow focus, whilst diseases are complex and unpredictable, making their findings potentially less useful (Lessard, 2007). There are concerns that economic evaluations place far too much emphasis on efficiency and fail to consider issues of equity, an issue that is of importance for policy makers (Coast, 2004, Nord et al., 1999, Stolk et al., 2004). There is uncertainty amongst decision makers on the value of findings from analyses undertaken in other settings, where costs of healthcare and approaches to delivering health services differ from their settings (Hoffmann et al., 2002, Drummond et al., 2005a). There are also concerns that the methods utilised are complex and lack transparency, making it difficult for policy makers to evaluate the quality of findings generated (Hoffmann et al., 2002, Brousselle and Lessard, 2011, Eddama and Coast, 2008).

4.2.3 Why undertake economic evaluations in resource-poor sub-Saharan settings

Resource-poor countries in sub-Saharan Africa face even more challenges when it comes to ensuring the health of their population. Health providers have less financial and human resources available to provide healthcare to their population. In addition, the burden of illness is usually higher in these countries, with lower life expectancy and higher levels of morbidity (Murray et al., 2012, Lozano et al., 2012). In resource-poor settings the challenges are not always what health interventions to provide, but whether there are sufficient resources to provide them. The optimal medical management of HIV in sub-Saharan Africa is not limited by knowledge of what interventions improve the health of those affected, but by what resources are available.

The problem often facing resource-rich countries is the too rapid uptake of new health technologies, driving up the costs for healthcare providers. In resource-poor settings the concern is different, where new health technologies take time before they are utilised, and are utilised without an evidence base or driven by international donor preferences (Kriza et al., 2014, Chalkidou et al., 2010). There is an opportunity cost to this. If the new technology proves to be effective, affordable and offers good value for money for health providers, delays in introduction reduces potential health benefits to the population. Conversely, if new health technologies are introduced without an evidence base that includes an assessment of cost-effectiveness, healthcare providers in the country risk wasting what limited financial and human

resources they have, and what could be better spent providing alternative health technologies.

The financial climate and limited resources in the region has led to increasing demand for economic evaluations from local and international policy makers, and international donors (Walensky and Kuritzkes, 2010, Denny and Emanuel, 2008, WHO, 2001, WHO, 2003a, Kahn and Marseille, 2000, Schwartlander et al., 2011). The scientific literature reflects the long-standing interest of economic evaluations in resource-poor settings. Economic evaluations and reviews of cost-effectiveness studies have been undertaken for HIV (Creese et al., 2002), Malaria (Morel et al., 2005), Tuberculosis (Baltussen et al., 2005), mental health (Chisholm and Saxena, 2012), maternal and child health (Ginsberg et al., 2012), cancer care (Ginsberg et al., 2012, Goldie et al., 2005), cardiovascular and other non-communicable diseases (Ortegon et al., 2012, Anderson et al., 2009, Gaziano, 2008). Their use will become ever more vital if concerted efforts are to be made to optimise the provision of basic and novel health technologies in the region.

4.2.4 Types of economic evaluation

The three main types of full economic evaluations are cost-effectiveness analysis (CEA), cost-utility analysis (CUA) and cost-benefit analysis (CBA) (Palmer et al., 1999, Drummond et al., 2005b). Table 8 provides a brief overview of the main types of full economic evaluations.

Table 8: Approaches to performing an economic evaluation

Cost-Effectiveness Analysis	Cost-Benefit Analysis	Cost-Utility Analysis
Costs measured in monetary units	Costs measured in monetary units	Costs measured in monetary units
Consequences measures in the most appropriate natural or physical units <ul style="list-style-type: none"> • Life years • HIV tests performed 	Consequences measured using same units as costs <ul style="list-style-type: none"> • Monetary units 	Consequences measured using a utility based measure <ul style="list-style-type: none"> • Quality adjusted life years (QALYs) • Disability adjust life years (DALYs)
Can only be used to compare within a comparable treatment/illness	Can be used to compare across a range of treatment areas	Can be used to compare across a range of treatment areas
	Concern and methodological challenges over valuing health in monetary terms	Concerns over the optimal approaches to value QALYs/DALYs
	Provides a simple decision rule based on net benefit, where positive net benefit implies adoption of intervention	Requires an explicit decision rule to determine threshold for willingness to pay

Source: Drummond et al., 2005b

A cost-effective analysis (CEA) relates the costs of providing an intervention to the health effects from receiving the intervention, with the health effect quantified in natural units. The natural units can range from procedures or tests performed, to life years saved. Their use is primarily limited by the lack of a standardised measure of health effect that can then allow fair and legitimate comparisons to be made across interventions targeting different aspects of health. This contrasts with cost-utility

analysis (CUA) where the use of a universal preference-based measure of health, allows comparisons to be made across a diverse range of interventions. For example the findings of a CUA of cancer treatments can be directly compared to that of an HIV intervention. This allows decisions to be made on allocative efficiency and therefore more useful for policy makers (Drummond et al., 2005b). Cost-benefit analysis (CBA) offers, but differs in that the health effects are quantified in monetary values. CBA are not commonly used in health economic evaluations, a major barrier has been the issue of valuing health benefits in monetary terms (Drummond et al., 2005b). CUAs and CEAs remain the most common types of full economic evaluations undertaken by the academic research community, and in previous evaluations of HIV interventions (Galarraga et al., 2009, Kahn et al., 2011, Creese et al., 2002, Beck et al., 2010, Meyer-Rath and Over, 2012).

4.2.5 Rationale for undertaking a cost-utility analysis in this PHD

There is an increasing volume of economic evaluations in resource-poor settings, with analysis being undertaken in other disease areas as well as in HIV (Creese et al., 2002, Ortegon et al., 2012, Ginsberg et al., 2012, Goldie et al., 2005). The findings from a CUA will be of more value for policy makers who may wish to compare findings across a range of disease areas to inform decisions on allocative efficiency. Consequently in this PhD I undertook a CUA to answer the primary research question. The description and findings of the analysis are presented in Chapter 8 of the PhD.

4.3 Decision-analytic models

4.3.1 Introduction

Economic evaluations can be undertaken using patient-level data obtained alongside clinical trials, using decision-analytic models, or using a combination with decision-analytic models extrapolating findings beyond the period of the clinical trial (Drummond et al., 2005b).

Clinical trials are designed to answer clinical effectiveness questions. Undertaking economic evaluations alongside clinical trials has the benefit of obtaining timely evidence on cost-effectiveness, with the evidence obtained at low cost, and with findings potentially robust to concerns over validity (Petrou and Gray, 2011a). Whilst clinical trials provide high quality evidence of clinical effectiveness, their use for 'piggy backing' an economic evaluation can be challenging (Glick et al., 2014, Gray et al., 1997). Clinical trials are costly and may only evaluate a limited number of comparators (Sculpher et al., 2006b). The time period of the evaluation may be too short to incorporate all consequences relevant to investigate cost-effectiveness. The sample size may be too small to detect differences in cost-effectiveness between comparators, and the findings may not be transferable to a setting other than where the trial was undertaken (Sculpher et al., 2006a, Sculpher et al., 2006b).

Decision-analytic modeling offers an explicit, quantitative, and systematic approach to combining all relevant information to provide estimates of cost-effectiveness and

the uncertainty surrounding the estimates. Whilst its use has come under scrutiny (Campbell et al., 2007, Sheldon, 1996, Cooper et al., 2005), it may be unavoidable in several circumstances (Buxton et al., 1997). Decision-analytic models have the advantage of being flexible to the time period of analysis, comparators considered and populations investigated (Petrou and Gray, 2011b, Sun and Faunce, 2008, Barton et al., 2004, Briggs et al., 2008, Brennan and Akehurst, 2000). They are able to combine evidence from a range of primary and/or secondary sources, thereby allowing evaluations of comparators that may not have been compared directly (Buxton et al., 1997). They can extrapolate beyond the observed end-point in a clinical study to an end-point relevant to the economic evaluation (Brennan and Akehurst, 2000). Unlike clinical trials which may require large numbers of participants, long periods of follow-up and considerable investment of human and financial resources, they can be a low cost option to the estimation of cost-effectiveness (Royston, 1999). Consequently, their role may be of greater significance in resource-poor settings, where the opportunity costs of research are considerable.

4.3.2 Approaches to decision-analytic modeling

A decision-analytic model is a tool to evaluate the impact of a decision, thereby allowing comparisons between two or more alternative decision options. A range of terminology is used to describe decision-analytic models, and often these can be conflicting or inconsistent (Brennan et al., 2006, Barton et al., 2004, Briggs et al., 2008). A common approach to describing model structures has been to consider

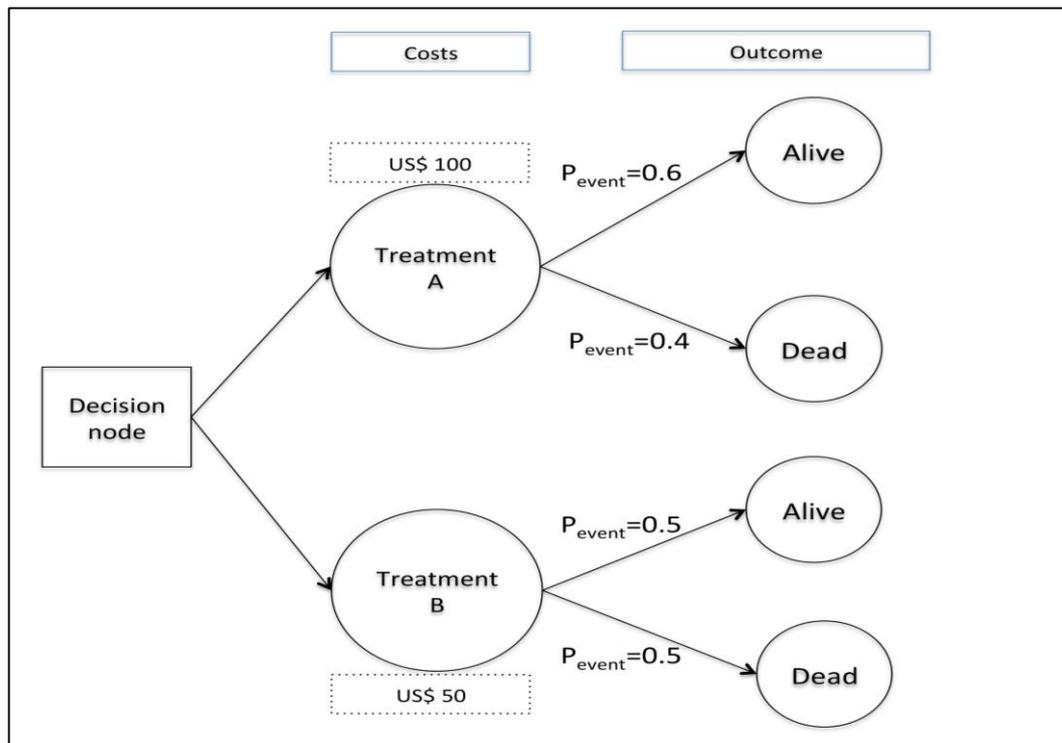
three factors: (1) who is being modelled; (2) is there interaction between those being modelled; (3) what is the time between events being modeled (Brennan et al., 2006, Barton et al., 2004, Briggs et al., 2008). However, the increasing use of decision-analytic modeling in healthcare decision-making has resulted in the development of a range of guidelines for the undertaking, presentation and validation of decision-analytic models (Briggs et al., 2012b, Eddy et al., 2012, Siebert et al., 2012, Briggs et al., 2008). The International Society for Pharmacoeconomics and Outcomes Research (ISPOR) provides a range of good practice guidelines for the undertaking of decision-analytic modelling in cost-effectiveness research (Briggs et al., 2012b, Eddy et al., 2012, Siebert et al., 2012). In the PhD, I adhered to these good practices and used their guidelines for the development and undertaking of the cost-effectiveness analysis.

4.3.3 Decision trees

A decision tree is the simplest model structure used in decision-analytic modeling. A decision tree comprises the possible pathways resulting from the two or more potential decisions being evaluated. The pathways represent all the possible clinical outcomes, with probabilities attached to the likelihood of these outcomes occurring and values attached to quantify each outcome (Brennan et al., 2006, Barton et al., 2004, Briggs et al., 2008). The values attached to these outcomes in health economic evaluations are comprised of costs and health outcomes (e.g. quality-adjusted life years). Decision trees predominantly model cohorts of individuals, thereby allowing mean values to be estimated, and assume there is no interaction within or between

the groups being modeled (Brennan et al., 2006). In addition, decision trees model the event over a predefined time period dependent on decision is being evaluated. Figure 25 shows a simple decision tree modeling the impact of providing two alternative treatments options. In this example the incremental cost-effectiveness ratio is estimated by dividing the difference in the total cost of providing the treatment by the total difference in health outcomes (i.e. US\$500/Life saved).

Figure 25: Simple Decision trees



Decision trees are a useful to model relatively simple decisions and can allow for multiple outcomes to be evaluated. However, as the potential outcomes increase in number, or if there is a need to model outcomes that may recur over time, the number of branches will increase and their structure can become complicated. In

addition, decision trees are not able to consider outcomes that may vary over time, or that recur over time (e.g. side effects from drug therapy).

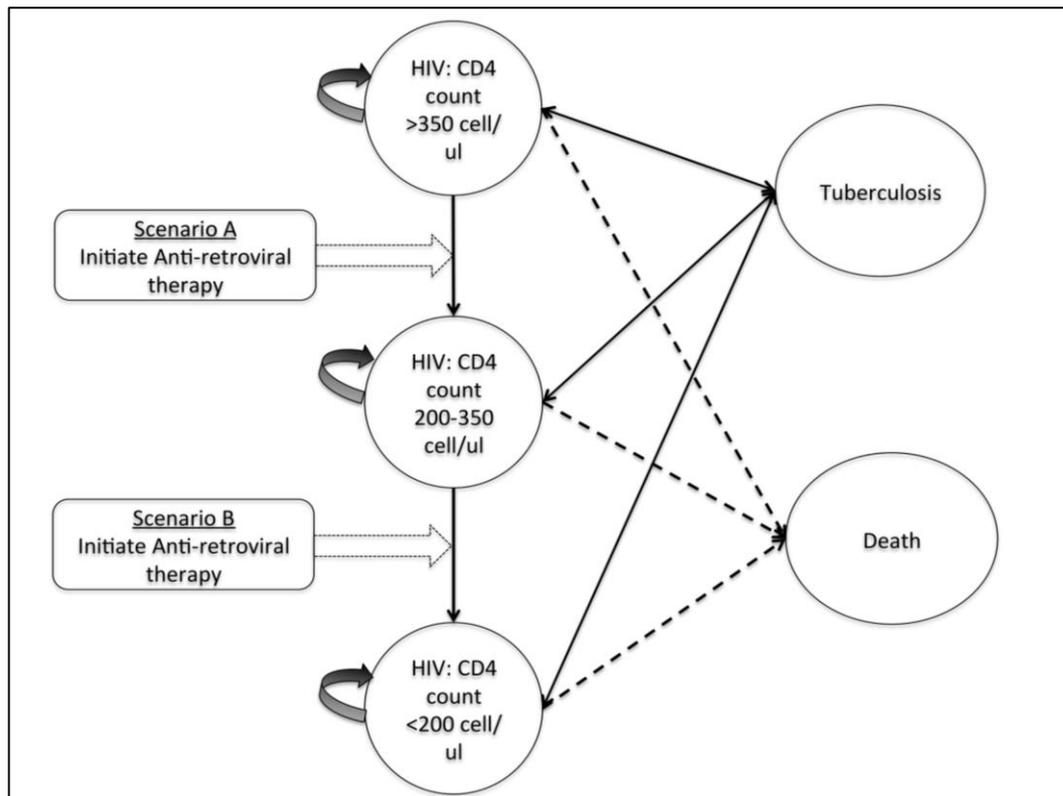
4.3.4 Markov models

Markov models are more complex than decision trees, and provide a possible solution to some of the limitations of decision trees. In a Markov model, we simulate a cohort of individuals transitioning through the health states, with probabilities determining the proportion of the cohort who transition from one to another health state (Briggs and Sculpher, 1998, Briggs et al., 2006).

Figure 26 shows an example of a Markov model that examines the impact of initiating anti-retroviral therapy at different CD4 counts in HIV positive individuals. The model provides a more simplistic approach to represent HIV disease progression than a decision tree would. The Markov model uses mutually exclusive health states that in a decision tree would need to be represented by a multitude of branches (Briggs and Sculpher, 1998). In this example, the health states represent mutually exclusive and distinct stages of HIV disease progression. Individuals enter a health state, if their HIV disease progresses they transition into another health state, whilst if their HIV disease remains stable they remain in the same health state. The likelihood of transitioning to another health state is modeled over time by applying a fixed time interval between each potential transition. In addition, the modeller can

determine the exact time interval between each potential transition to another health state.

Figure 26: Markov models



In the Markov model, a transition probability is assigned to model the likelihood of movement between health states or remaining in the same health state, with all probabilities emanating from one health state adding up to a total of one (Briggs and Sculpher, 1998). Each health state is then assigned a cost and health outcome (e.g. a utility score). In the final analysis the total costs and health outcomes are estimated by multiplying the time spent in each health state by the cost and health outcome assigned to the health state. An advantage of Markov models is their ability to

model events that may recur over time (Brennan et al., 2006, Barton et al., 2004). In the example in Figure 26 there is an additional health state to represent the development of TB amongst HIV positive individuals. HIV positive individuals may acquire TB and have their disease treated. However, they may still be at risk of re-acquiring TB, and the Markov model can provide a simplified approach to representing this continued risk.

Markov models do have several limitations. Markov models simulate the transition of cohorts of individuals and consequently cannot take into account individual-level characteristics (Barton et al., 2004). This assumption, called the “Markovian assumption” does not allow the model to record past events or allow transition probabilities, costs or health outcomes to be dependent on individual-level characteristics (Briggs and Sculpher, 1998, Barton et al., 2004). For example, in the model shown in Figure 26, individuals who acquire TB could be eligible to start anti-retroviral therapy (irrespective of their CD4 count). As the model lacks memory, it cannot differentiate between those who have had a history of TB and those who have not. This limitation can be resolved by adding an additional health state for those who are HIV positive and had a history of past TB disease. However, with increasing complexity and past events occurring, the number of health states will need to increase to allow transition probabilities (and potentially costs and health outcomes) to be dependent on past events. If there is a need to model events on a large number of past events or individual-level characteristics, the model may have too many health states.

4.3.5 Individual sampling models (ISM)

An individual sampling model (sometimes referred as Monte Carlo simulation or microsimulation) overcomes the 'memoryless' feature of Markov models (O'Hagan et al., 2007, Barton et al., 2004, Brennan et al., 2006). ISM simulates the transition of an individual through the model as they accumulate costs, and record their health outcomes. The model then repeats the analysis for a large enough number of individuals to estimate the mean costs and health outcomes. As the model simulates an individual it can vary its parameters based on the characteristics of the individual (Brennan et al., 2006, Barton et al., 2004). For example, the risk of mortality in an HIV positive individuals could be simulated as two different values based on whether the individual has had TB disease in the past or not. An advantage of this approach is that the number of health states can be minimised, making it easier to describe the model structure to the reader (Brennan et al., 2006, Barton et al., 2004).

4.3.6 Decision models that allow interaction

A limitation of decision trees, Markov models and ISMs is that they do not allow for interaction between the individuals being modeled. One situation where this may be important is in modeling infectious diseases, where the risk of acquiring the infectious disease will be dependent on the number of individuals who already have the infection. For example in the treatment of TB, getting individuals onto TB treatment reduces their risk of transmitting the infection to un-infected individuals.

Not taking this into account would bias against interventions that reduce the infectious period.

Health economists have increasingly used transmission dynamic modeling (sometimes referred to as system dynamic models) to take into account the interaction between individuals (Jit and Brisson, 2011). However, transmission dynamic models simulate groups of individuals and therefore have comparable limitations to Markov models with regards to the issue being 'memoryless' and the inability to take into account individual-level characteristics (Barton et al., 2004). An alternative approach to enable both consideration of interaction between individuals and individual-level characteristics is to use discrete event simulation (DES) (Barton et al., 2004). DES provides the greatest flexibility in decision-analytic modeling, but also the greatest needs in terms of model parameters and computational time (Karnon, 2003, Barton et al., 2004, Brennan et al., 2006). They allow interaction between individuals, and allow events to be conditional on individual-level characteristics or to vary over time (Karnon, 2003).

4.3.7 Summary of modeling approaches

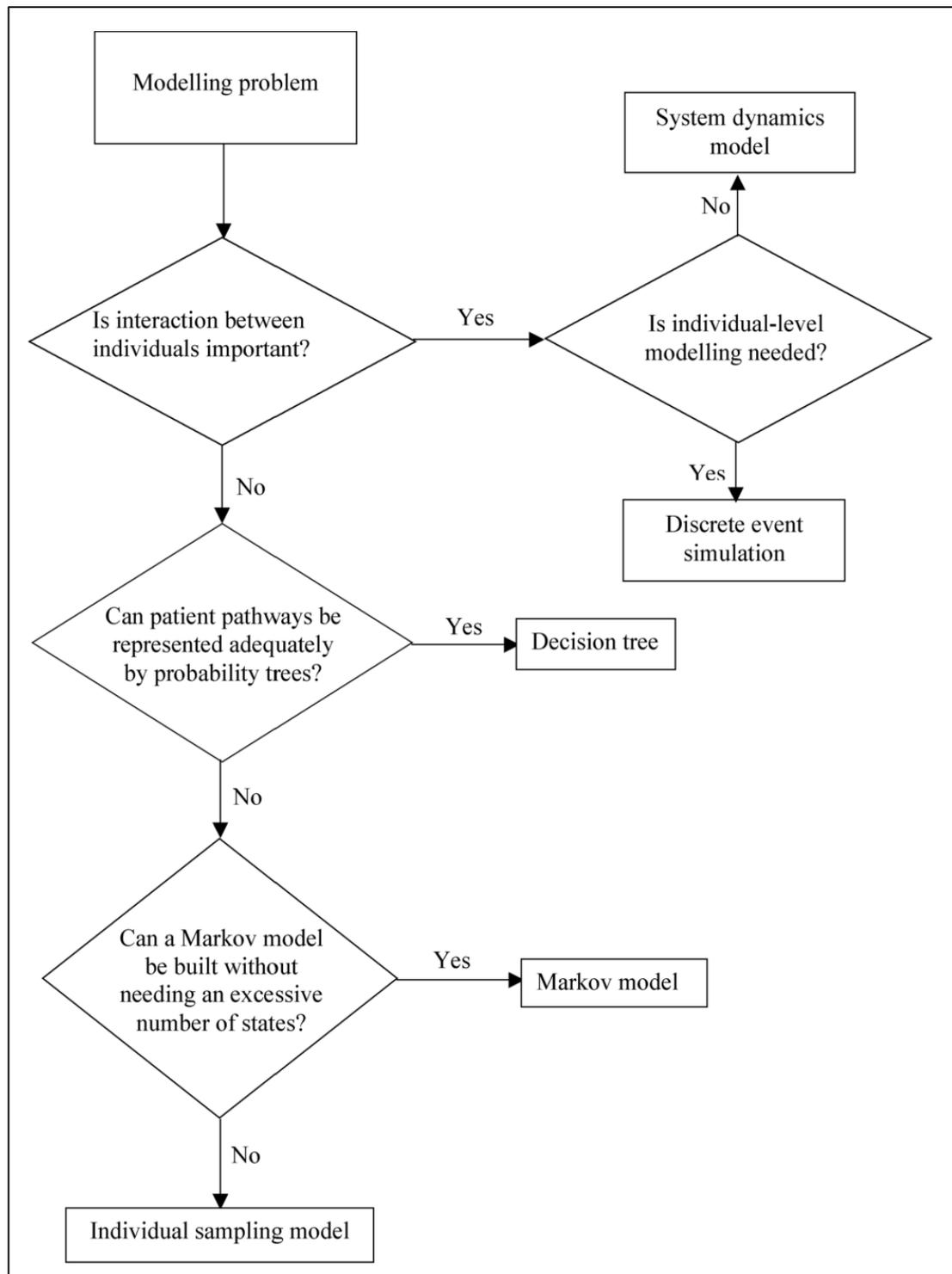
A range of different modelling approaches exists for undertaking decision analytical modelling. Each will have its associated advantage and disadvantage, and it is up to the modeller with input from clinical experts in the field to determine the most suitable strategy (Sun and Faunce, 2008). Barton and colleagues provide a simplified

approach to deciding a suitable modelling approach for undertaking decision-analytic modelling (Figure 27) (Barton et al., 2004).

In Chapter 8 of the PhD I undertake decision-analytic modelling to answer my primary research question. In Chapter 8 I highlight why I used an individual simulation model (ISM) to investigate my primary objective:

“To undertake a decision-analytic modelling based cost-utility analysis to estimate the incremental cost per quality-adjusted life year (QALY) gained from the provision of HIV self testing in conjunction with traditional facility-based HIV testing and counselling services in Blantyre, Malawi”

Figure 27: An approach to determining the appropriate model structure



Source: Barton et al., 2004

4.4 Cross-sectional and longitudinal studies

4.4.1 Introduction

In the collection of primary economic and health-related quality of life data, decisions need to be made on how and from whom the data is to be collected. The main trial in the HitTB Study was a cluster-randomised trial, with communities being the unit of randomisation, with the study using a post-intervention prevalence survey to investigate the primary outcomes. This necessitated design of my own studies, undertaken in the trial population, to investigate the primary research question of the thesis.

4.4.2 Cross-sectional studies

Cross-sectional studies are observational studies that allow us to describe an exposure or outcome of interest, although they can be used to investigate associations between the two (Rothman et al., 2008). Their use is not just limited to investigating aetiology of diseases (Rothman et al., 2008), and they play a major role in both public health and health economics research. In these areas, the objective may be limited to only understanding or measuring the prevalence of a risk factor or health outcome; use of health services; or measuring the HRQoL of a population.

They have the advantage that they are relatively inexpensive and quick to perform, can be used to investigate multiple factors, and not affected by issues of loss to follow-up (Rothman et al., 2008, Feldman and McKinlay, 1994). However, these

studies do not allow us to investigate a causal relationship between an exposure and outcome (Rothman et al., 2008, Feldman and McKinlay, 1994).

In Chapter 5 of the PhD I investigate one of the objectives of my thesis:

“To compare and contrast the costs to individuals and to healthcare providers, and health-related quality of life outcomes, amongst individuals who access facility-based or home-based HIV testing services in the HitTB study population.”

In investigating this objective, I deemed a cross-sectional study an appropriate study design. The benefit was that it allowed me to investigate a range of issues, namely HRQoL, direct non-medical costs and indirect non-medical costs of HIV self-testers and facility testers at the same time. Additionally, it allowed me compare and contrast between the two populations by the modality of HIV testing received. The objective was not to investigate whether offering HIV self-testing would improve the quality of life of HIV testers, or reduce costs.

4.4.3 Longitudinal studies

A cohort, or longitudinal, study is an observational study where several observations are undertaken on participants over a period of time. In epidemiology, the objective is to investigate a causal relationship between an exposure and health outcome

(Feldman and McKinlay, 1994, Rothman et al., 2008). Through undertaking the study prospectively, the investigator is also able to investigate whether there are changes in outcomes of interest over time, and compare changes in outcomes between two or more groups (Goldstein and Goldstein, 1979, Feldman and McKinlay, 1994, Diehr et al., 1995). The advantages of longitudinal studies come at a cost. Following up participants in low-income settings, where participants may not have a fixed abode, postal address or telephone contact number, may be difficult and bias findings.

In Chapter 6 of my PhD I investigate one of the objectives of my thesis:

“To compare and contrast the costs to individuals and to healthcare providers, and health-related quality of life outcomes, amongst HIV positive individuals who access HIV care and treatment services subsequent to testing at facility-based or home-based testing services in the HitTB study population.”

For the purposes of the research described in Chapter 6 a longitudinal study design was optimal. A longitudinal study would provide me with an unbiased estimate of treatment effect. I wanted to examine the costs and health outcomes of receiving HIV treatment and compare between those who had received HIVST to those who had received facility-based HTC. Individuals access HIV treatment after learning their HIV status, and therefore the exposure I was interested in, modality of HIV testing received, occurred before the outcomes I was examining.

In Chapter 7 of my PhD I investigate two further objectives of my thesis:

“To estimate the costs, to individuals and to healthcare providers, and health-related quality of life of adults who are admitted to the medical wards in Queen Elizabeth Central Hospital, Blantyre, Malawi, for the management of medical illnesses.”

“To investigate the relative impact of HIV infection on costs and health-related quality of life of adults who are admitted to the medical wards in Queen Elizabeth Central Hospital, Blantyre, Malawi, for the management of medical illnesses.”

A longitudinal study design was again deemed appropriate as it allowed unbiased estimation of economic variables, to investigate whether HIV status, the exposure, had an independent effect on the total direct health provider costs, direct non-medical costs and indirect costs during hospitalisation.

4.5 Cost analysis

4.5.1 Introduction

In undertaking an economic evaluation one needs to estimate the impact of the current treatment and the alternative treatment options on economic costs. To do this requires consideration of a range of methodological issues ranging from the

viewpoint of the cost analysis, the time period over which the costs are to be considered and the methods used to estimate the costs (Drummond et al., 2005b).

4.5.2 Costing perspective

An economic evaluation can be undertaken from either the health provider or societal perspective. The choice of perspective will determine which costs are to be estimated.

The health provider perspective is often considered the primary perspective in economic analysis, especially where the Government incurs the majority of costs of healthcare provision in a country. The rationale for using the health provider perspective stems from the use of CUA in determining budget allocation decisions to maximise utility (in this case QALYs). The budget that is being maximised is the budget available to the healthcare provider (or payee), and therefore it argued that only these costs should be considered in the analysis (Edelson et al., 1990, Johannesson and O'Connor, 1997b, Williams, 1985). In Malawi, HIV services and hospital care are provided free of user fees, and the cost is incurred by the Ministry of Health (MoH). The MoH is the decision maker and primarily responsible for determining which services are to be provided.

However, diseases and their treatment not only incur a cost to the health provider, but also to those affected. It is therefore considered important in some circumstances to incorporate the economic constraints of those affected into the analysis, and therefore undertake costing from the societal perspective (Jonsson, 2009). It has been argued that allocation decisions are based on implementing interventions that are classified as cost-effective, i.e. below a threshold of willingness to pay for a gain in QALY, as international organisations like the World Health Organisation advocate (WHO, 2003a). If a fixed threshold is used in the decision-making, then incorporating all costs, and therefore taking the societal perspective, may ensure that the analysis reflect the optimal decision for society (Jonsson, 2009, Johannesson and O'Conor, 1997b). To estimate the cost from the societal perspective requires estimating both the costs incurred by the health provider and the costs incurred by those affected by the disease or through accessing care for the treatment of the disease.

4.5.3 Health provider costing

The health provider perspective requires estimating the costs incurred by the healthcare provider, the Malawi MoH, in providing the relevant health services. Often this cost is termed the **direct health provider cost** and refers to the costs of resources that are directly used in the provision of healthcare (Johannesson, 1994, Drummond et al., 2005b).

In many countries like the UK, the health provider publishes reference costs that inform health economic evaluations. These reference costs are grouped into healthcare resource groups and are provided to analysts undertaking economic evaluations. In Malawi, and the majority of countries in sub-Saharan Africa, comparable reference cost estimates are not available. It is therefore often necessary to collect primary cost data, which ideally requires both the assessment of resource inputs used in care provision, and the subsequent valuation of those resource inputs (Drummond et al., 2005b).

In this PhD, observational studies were undertaken prospectively to collect data on the healthcare resources used by individuals in accessing the relevant health services. A more detailed description of the observational studies undertaken and data collection process is provided in the relevant Chapters (Chapter 5, Chapter 6 and Chapter 7). The healthcare resources quantified in these studies were then costed following standard guidelines (UNAIDS, 2011, Drummond et al., 2005b).

Costing resource-use items can be complex and time-consuming, often necessitating some compromise in the methodological approach. Costing approaches can either take a 'top-down' or 'bottom-up' form, although in many cases a combination of approaches may be utilised (Drummond et al., 2005b, Lipscomb et al., 2009). The top-down method is less resource-intensive but may provide less accuracy in estimates and potentially reduces ability to detect cost differences (Drummond et al.,

2005b, Lipscomb et al., 2009). The approach involves assigning aggregate level cost data to service outputs, where service output units may range from hospital admission days to outpatient visits. Whilst the approach is simpler, it may not be appropriate in many cases because of the heterogeneous nature of care provided in hospitals (Carey and Burgess, 2000).

The bottom-up approach involves quantifying all the resources used in providing care and costing each resource input to determine the total cost. The bottom-up approach allows total costs of a service output to be more closely related to the actual resources used, and is often felt to be more accurate than the top-down approach (Berlin and Smith, 2004, Negrini et al., 2004). Whilst there is no consensus on the correct approach, it is widely accepted that the choice needs to take into account the objective of the analysis and understanding of the relative costs of different inputs and their likely impact on total cost (Drummond et al., 2005b). Often it may be optimal to use a combination of the two approaches (Baker, 1995, Carey and Burgess, 2000), which may be determined by regulatory or advisory boards (NICE, 2008, UNAIDS, 2011).

In Chapters 5, 6 and 7 I provide more detailed description of the methods used in estimating the costs for resource-use items. The exact methods used varied depending on the healthcare resources that were being costed. Broadly, this involved first examining the healthcare service and determining the outputs of the

service (e.g. outpatient visit; day of hospital admission; investigations performed). Second, interviews were undertaken with senior staff members working at the healthcare organisation to quantify the inputs used in providing the healthcare resource-use item (e.g. staff inputs; consumables; equipment; etc.). Third the unit costs of the inputs used in providing the healthcare resource-use items were obtained. Fourth the unit costs were applied to the resource-use inputs to determine the total cost of the resource-use items. Where the healthcare service (e.g. HIV testing clinic) being costed only had one output (e.g. HIV test performed), all costs were summed and divided by the total number of outputs from the services. Where the healthcare service (e.g. hospital) being costed had more than one output (e.g. days of admission; investigations performed), a proportion of some costs (e.g. overhead; central administrative; utility bills) were allocated to the relevant resource-use item based on services delivered.

4.5.4 Patient incurred costs

Patients, or those who use healthcare services, may incur two types of costs. They may incur costs when they access the healthcare service, referred to as **direct non-medical costs**, and as a consequence of their illness, referred to as **indirect costs** (Drummond et al., 2005b). In addition, the family member or friend who is providing informal care for the patient could also incur these costs. Collectively these costs are referred to as **patient and family resource use** (Drummond et al., 2005b).

The costs that constitute direct non-medical costs are relatively simple to quantify and measure, as these are the resources used in accessing medical care that are not classified as healthcare resources (Drummond et al., 2005b). For example a patient (or their care giver) may spend money on transport to attend a health facility that they would not have otherwise spent if they (or the patient they were caring for) were well or not seeking medical care. However, determining the extent of the non-medical resources used in accessing medical care will depend on the type of medical care they access. For example, patients who are admitted to hospital will spend more money on non-medical resources (e.g. soap; clothes) than someone who attends an outpatient clinic would. In the studies undertaken in the PhD (Chapter 5, 6, and 7), I undertook pilot studies to determine the range of non-medical resources that patients (and their care giver) could potentially spend their own money on.

The issues around indirect costs are slightly more complicated with different views on what constitutes an indirect cost and how to quantify it (Koopmanschap et al., 1995, Koopmanschap and van Ineveld, 1992, Ernst, 2006). The broadest approach to estimating the indirect cost involves valuing the loss to society from absenteeism, disability and premature mortality (Van Roijen et al., 1996). However, previous studies have used different time horizons over which to measure indirect costs, differed in what activities (e.g. employment; informal care; leisure time) constitute as loss to society and used different tools used to measure these costs (Jacobs and Fassbender, 1998, Posnett and Jan, 1996, Merkesdal et al., 2005, Liljas, 1998). For the purposes of the PhD, I equate the indirect cost to the cost of absenteeism that

resulted directly from accessing healthcare services and use the human capital approach to estimate this cost (Glied, 1996, Weisbrod, 1961).

4.5.5 Adjusting and communicating costs

In undertaking primary costing studies, the resources measured need to be valued to provide quantitative values for use in the analysis. The valuation of healthcare resources often necessitates the collection of unit cost data from a range of sources, the costs may have been obtained from different time periods or denominated in different currencies. To ensure that the different input costs used to determine the final estimates are comparable, and the findings can be generalised to different settings (e.g. to another country) from which the primary analysis was undertaken, adjustments are often required (Drummond et al., 2005b, Drummond et al., 2009). Costs need to be converted to the same currency and year of currency in the final analysis and presentation of findings. In addition, the input costs used to make the final estimates have to reflect the true opportunity cost of the resource item.

In resource-constrained settings like Malawi, this poses some challenges. As previously highlighted in Chapter 2, Malawi has experienced high levels of inflation and receives a large amount of its healthcare funding from International donors. In addition, healthcare providers purchase a significant proportion of goods used in the production of health (e.g. drugs, medical consumables and equipment) from

overseas sources, whilst others resources (e.g. staff salaries) are paid locally. This requires a rigorous and repeatable approach to adjusting and communicating costs.

The World Health Organisation (WHO) provides guidance on how to adjust and communicate costs in economic evaluations (Johns et al., 2003, WHO, 2003a). In the studies undertaken in Chapters 5, 6, and 7 their guidance was followed. Broadly, this involves firstly adjusting from the year of cost to the year of analysis using the World Bank Gross Domestic Product (GDP) deflators and, secondly, converting the currency of the costs to International dollars (Johns et al., 2003, WHO, 2003a). As the primary objective of the economic analysis is to inform policy makers in Malawi, and the Malawian currency has been unstable and often devalued over the last few years, I present all costs in 2014 US and International dollars in the PhD. All costs were inflated to the year 2014 using the GDP deflators, and currencies were converted into 2014 US dollars using the market exchange rate, and then into 2014 International dollars by applying the relevant purchasing power parity conversion factor (Shemilt et al., 2010, Taylor, 2003).

4.6 Health outcomes and health-related quality of life

4.6.1 Introduction

A CUA involves quantifying the health consequences of health interventions. An advantage of CUA is that the health consequences are quantified in comparable preference-based units thereby allowing comparisons to be made between interventions targeting different diseases. In CUA the consequences on health outcomes take into account both the impact on mortality and morbidity. For interventions targeting HIV this is becoming increasingly important. There are now an increasing number of approaches to improve the health of HIV infected individuals, with the disease now considered a chronic manageable infectious disease. Therefore, more attention has been given to improving the HRQoL of those affected as well as improving their survival.

4.6.2 Measuring health-related quality of life

Quality of life is a broad term that aims to describe the physical, mental, social, and environmental aspects of an individual's life (WHO, 1995), whilst health-related quality of life focuses on the health domains relating to an individual's life (Guyatt et al., 1993). In healthcare research the objective is to provide a quantitative measure of an individual's HRQoL, as a sphygmomanometer does for blood pressure, so that the impact of diseases and treatments on an individual can be monitored, or in health economics, used to inform inputs into economic evaluations.

In health economics two primary metrics exist for quantifying HRQoL, the quality-adjusted life year weight and the disability-adjusted life year weight. These metrics are used to multiply the time an individual spends in that health state and thereby allows calculation of quality-adjusted life years (QALYs), or disability-adjusted life years (DALYs). Whilst there are differences in their meaning, measurement and use, the weights used in calculating QALY broadly equate to the one minus the weights used in calculating DALYs (Murray and Acharya, 1997).

There has been considerable debate over the relative merits of the use of DALYs and QALYs, and other measures, in economic evaluations (Airoldi and Morton, 2009, Anand and Hanson, 1997, Arnesen and Nord, 1999, McAlearney et al., 1999, Murray and Acharya, 1997, Gold et al., 2002, Sassi, 2006). Whilst both are preference-based measures of HRQoL, the DALY was designed to measure the burden of disease (Murray and Acharya, 1997, Murray et al., 2012, Sassi, 2006), whilst the QALY for primary use in economic evaluations (Gerard, 1992). Unlike QALYs, DALYs apply an additional weight depending on the age of individuals, thereby incorporating equity issues into an efficiency calculation (Sassi, 2006). Cost-utility analysis aims to provide objective assessments of efficiency, and not normative views of equity, consequently incorporating equity into a quantitative evaluation impacts on policy makers and societal views on equity (Arnesen and Nord, 1999, Gold et al., 2002).

Importantly in HIV there are only 4 possible weights in the calculation of DALYs, whilst the tools used to estimate QALYs can discriminate a significantly greater number of potential HIV-related health states (Sassi, 2006). As the evidence suggests that the impact of HIV and HIV treatment on HRQoL is complex (Alibhai et al., 2010, Beard et al., 2009, Louwagie et al., 2007, Peltzer and Phaswana-Mafuya, 2008), using QALYs as the health outcome measure in the PhD will allow me to better measure the impact of more timely entry into HIV care on HRQoL.

4.6.3 Quality-adjusted life weights and QALY estimation

The weights used to estimate QALYs represent an assessment of an individual's health state on a scale ranging from zero, equating to death, to one, equating to perfect health. Although the scale can extend to negative values, representing health states worse than death (Dolan, 1997, Dolan et al., 1996a). A range of tools exists to determine these weights (Brazier et al., 1999). One common approach is to ask individuals to describe their own health status or health-related quality of life across a range of health domains (e.g. pain, mobility, mental health). The responses are then converted to a utility score (the QALY weight). A tariff is commonly used to convert the responses to the corresponding utility score (the QALY weight). The tariff is generally derived from a separate study undertaken in the general population of a country. In this study healthy volunteers representative of the general population are recruited and then asked to value a selection of health states derived from the relevant tool. The process of valuing these health states is based on the theory of preferences where individuals are asked to make a choice based on two different

health states, the exact method (e.g. standard gamble; time trade off) varies depending on the tool used (Brazier et al., 1999, Dolan et al., 1996b, Bleichrodt and Johannesson, 1997). In choosing healthy volunteers the study ensures that the preference-based values reflect decision-making under uncertainty (Bleichrodt and Gafni, 1996, Dolan and Kahneman, 2008), and reflect the methodological underpinnings on which cost-utility analysis is based (Brouwer et al., 2008).

The utility weights (or QALY weights) derived are then converted to QALYs by multiplying the time spent in the relevant health state by the quality-adjusted weight for that health state (Drummond et al., 2005b). Therefore by asking patients about their HRQoL at regular intervals, using one of these measures, one can estimate their total quality-adjusted years lived during the time period of the analysis.

4.6.4 The EuroQol EQ-5D measure

The EQ-5D measure is an example of a tool that is commonly used to capture health outcomes in QALYs (Dolan, 1997) with the values utilised in cost-utility analysis (Drummond et al., 2005b). It is a preference-based generic measure of HRQoL. It has been used in over 50 countries, and translated into more than 40 languages, several in sub-Saharan Africa. It has been found to have construct validity (good agreement with disease specific measures) and is a reliable (high test-retest agreement) measure of HRQoL in sub-Saharan Africa and in HIV infected individuals (Jelsma et al., 2005, Jelsma et al., 2003).

The EQ-5D-3L measure comprises two components, the EQ-descriptive component and the EQ visual analogue scale (Dolan, 1997). The descriptive component defines HRQoL in terms of five dimensions: 'mobility', 'self care', 'usual activities', 'pain/discomfort' and 'anxiety/depression' (Brooks, 1996). Responses in each dimension are divided into three ordinal levels, coded: (1) no problems; (2) some or moderate problems; and (3) severe or extreme problems. The potential responses to the descriptive system can theoretically generate 243 (3^5) different health states. More recently the EQ-5D-5L measure has been developed that is comparable to the EQ-5D-3L but each of the five dimensions are now divided into five ordinal levels.

The responses to the descriptive component of the EQ-5D-3L are converted to an EQ-5D utility score (QALY weight) using a tariff. The tariff sets are derived from national surveys of the general population, with a subset of the 243 health states being valued, most commonly using the time trade-off method (Dolan et al., 1996a). The remainder of the EQ-5D health states are subsequently valued through the estimation of a multivariable model.

There is currently no Malawian EQ-5D tariff, and for the studies undertaken in the PhD the Zimbabwean EQ-5D tariff set (Jelsma et al., 2003) was used to derive an EQ-5D utility score for each participant at each relevant time point. The health economic literature highlights that it is accepted practice to use tariffs from another country

where none exists for the country of interest, provided the investigator believes the two populations would value health comparably (Drummond et al., 2005b). Whilst the populations of Zimbabwe and Malawi are different, the underlying health issues, the population demographics and economics in the country are sufficiently comparable to suggest that the two populations would value health comparably.

In accordance with the EuroQol Group's guidelines the EQ-5D was translated by a specialist agency employed for the PhD purposes into Chichewa, the local language in the study population in Blantyre, Malawi. The agency used a standardised translation protocol that conforms to internationally recognised guidelines (EuroQol, no date). Briefly, this involved 2 forward translations by two bilingual translators. Then 2 bilingual translators undertook two back translations into English. Finally a pilot study with approximately thirty lay persons was used to evaluate the semantics and the linguistic adaptations. The EuroQol Group provided feedback to the agency at each stage to ensure the EQ-5D concepts have been translated correctly. The EuroQoL group approved the final Chichewa version of the EQ-5D-3L for use in Malawi.

4.7 Summary of Chapter 4

In this chapter I have provided an overview of my research question and the primary and secondary objectives of my PhD. I described why economic evaluations are an important tool in public health research and the different approaches to undertaking them. I provided a description and rationale for using a cost-utility analysis to investigate the cost-effectiveness of providing HIVST in Blantyre, Malawi. I also provided an overview of the methods and the economic data reported in the next three Chapters (Chapter 5, 6 and 7). In addition, I described how the economic data collected would allow me to answer the primary research question (contained in Chapter 8).

The following four chapters (Chapters 5, 6, 7 and 8) will provide a more detailed description of the relevant methods used in the four studies undertaken, and present the findings from them. The Chapters (5, 6, 7 and 8) have been written in the format of a manuscript for submission for publication in peer-reviewed journals, although the contents of the Chapters are more detailed than required for the final manuscripts that have been or will be submitted. Therefore, these Chapters have a brief introduction into the specific topic being investigated, a detailed description of the methods used, and presentation of the results. In these Chapters I will also provide a discussion of the relevant findings, with a more detailed overall discussion in Chapter 9.

**CHAPTER 5: A comparison of the
costs and consequences of Facility
HIV testing and Home HIV self-
testing**

5 Overview of Chapter 5

In this chapter I will aim to investigate one of the secondary objectives of my PhD.

To compare and contrast the costs to individuals and to healthcare providers, and health-related quality of life outcomes, amongst individuals who access facility-based or HIV self-testing services in Blantyre, Malawi

As previously mentioned, the chapter has been written in the format of a manuscript for publication in a peer-reviewed journal. The manuscript from this chapter has been submitted and is currently under review.

In this Chapter I investigate the costs of providing HIV self-testing and facility-based HIV testing and counselling. I estimate the costs for the health providers and those who used the service. I also compare the health-related quality of life amongst users of both services. The study was undertaken by recruiting only individuals who resided in the HiTTB study communities and the services that were costed were the ones that were available to the study participants. The economic data collected in this chapter will inform the decision-analytic modeling (Chapter 8) to estimate the cost-effectiveness of offering HIVST in addition to standard facility-based HTC services.

5.1 Introduction

In sub-Saharan Africa, HIV testing and counseling (HTC) remains one of the main barriers to timely access to effective HIV treatment and prevention interventions (Cohen et al., 2011, Gray et al., 2007a, Grant et al., 2010). The region currently accounts for three quarters of all new infections and HIV-related deaths (UNAIDS, 2014b). Despite increases in investments to scale-up HIV testing services, only half of Africans living with HIV know their HIV status (Staveteig et al., 2013, UNAIDS, 2014b).

Facility-based HTC is not popular amongst Africans (Morin et al., 2006, Angotti et al., 2009, MacPherson et al., 2012a), with evidence suggesting many of barriers could be overcome through community-based HTC services, including home-based and mobile HTC (Sabapathy et al., 2012). These HTC modalities reach HIV infected individuals earlier in their disease progression (Wachira et al., 2012a), reducing subsequent healthcare costs of providing HIV care (Leisegang et al., 2009). The high cost of delivering community HTC services (Suthar et al., 2013) may explain why few National HIV programs have implemented these services (Staveteig et al., 2013). In addition, the need for trained healthcare workers, restrictions of service operating times, fear of status disclosure and stigma, and concerns over linkage into HIV treatment have raised concerns over their long-term sustainability, and usage by hard-to-reach groups (Ostermann et al., 2011, Negin et al., 2009, Dolan, 1997, Sabapathy et al., 2012). HIV self-testing (HIVST) is highly acceptable, safe and effective at achieving high coverage rates in communities, with comparable levels of

linkage into HIV services as seen with facility-based HTC services (Choko et al., 2011, Choko et al., 2015b, MacPherson et al., 2014).

In this study, I investigated the economic impact on users and healthcare providers offering a semi-supervised semi-restricted community distribution model of HIVST. I collected individual-level economic data from users of both services, and undertook primary costing studies of the two approaches, within the context of a large cluster-randomised study investigating the health impact of offering HIVST in addition to facility-based HTC in Blantyre, Malawi.

5.2 Methods

5.2.1 Ethical statement

I obtained ethical approval from the College of Medicine Ethics Review Committee, University of Malawi; and the University of Warwick Biomedical Research Ethics Committee (**Appendix I**). All participants received an information leaflet in their local language (**Appendix VI and VII**), which explained the study, and all provided informed consent (**Appendix VIII and IX**).

5.2.2 Study setting and study population

The participants in the cluster-randomised trial (and therefore the population on which this study is based) live in three high-density urban suburbs of Blantyre (Ndirande, Chilomoni and Likabhula) (Choko et al., 2015b). These communities were demarcated into 28 clusters of approximately 1,200 adults using global-positioning satellites (GPS) mapping. Residents in 14 clusters were randomised to the intervention arm and received community-based access to HIVST and routine facility-based HTC. The remaining 14 clusters were allocated to the control arm and received access to routine facility-based HTC alone.

Residents who were trained as community HIV counsellors provided HIVST. These community counsellors advertised the service at regular intervals, encouraging residents to attend the counsellor's home to receive counselling, directions on how to use the self-test kits, and the self-test kits themselves. Residents self-tested in the

privacy of their own homes. People in the control arm had their usual continuing access to standard facility-based HTC. In all clusters, people had access to HIV testing and care services through Queen Elizabeth Central Hospital, or the two primary health clinics (Ndirande Health Centre and Chilomoni Health Centre).

HIVST was provided for a 2-year period during the trial, with the service introduced into intervention clusters from February to May 2012. In this study I recruited participants from February 2013 to April 2014. Recruitment was restricted to residents of the main trial clusters and to those who had not already started anti-retroviral therapy. A previously validated “Map Book” approach designed for the main trial (MacPherson et al., 2013) was used to determine whether participants were resident in one of the intervention or control clusters of the main trial.

I recruited participants who accessed HIVST consecutively using the Quality Assurance (QA) cohort of the main trial (Choko et al., 2015b). In the QA component HIVST participants were sampled for checking of compliance with the trial protocol, with a minimum 5% randomly selected for home-visit by one of the trial’s study nurses. I recruited facility-based HTC participants consecutively from the three local health facilities (Queen Elizabeth Central Hospital; Ndirande Health Centre; and Chilomoni Health Centre). **Appendixes X and XI** show the case report form (CRF) used to elicit the relevant data form all participants.

5.2.3 Cost analysis

5.2.3.1 Direct health provider costs

I undertook economic costing of both the HIVST service and facility HTC services using a health provider perspective (UNAIDS, 2011, Drummond et al., 2005b). For the HIVST service, I interviewed community counsellors to determine resources used in providing the service, and programme managers and accounting staff to estimate costs of identified resources and other service delivery costs. All research-related costs were excluded. **Appendix XII** shows the data extraction tool used to record the resources used at each of the clinics during interviews with staff.

I obtained the HIVST service output records to find out the number of HIV self-testing episodes for each community counsellor, and total numbers for the service. I interviewed counsellors working at the facility HTC services, and administrative staff at the Blantyre District Health Office (which manages the two health facilities at Ndirande and Chilomoni), and at the Queen Elizabeth Central Hospital. I obtained programme output data to determine numbers of individuals tested and number of HIV positive individuals identified. I divided resources used in providing HIV testing into: (1) staff salaries; (2) staff training; (3) monitoring and evaluation; (4) consumables and equipment; and (4) capital/overheads.

Staff salaries included employer contributions and fringe benefits. For staff training, I included all training provided to staff that related specifically to service provision.

For facility-based HTC, I included the cost of HTC refresher training, but did not include the cost of the initial HIV counseling training course. For HIVST, I included the cost of the initial HIV counseling training course, as the community workers were not previously trained as HIV counselors. I also included the cost of all other training provided to the community counselors providing HIVST, but excluded all training for research related activities. The cost of staff training was annuitized over their useful life with an annual discount rate of 3% (WHO, 2003a), and with the useful life based on how often the training would be repeated.

The costs of consumables and equipment's were obtained from the Malawi Ministry of Health (MoH) price catalogue, which includes the cost of shipping for imported goods. For items not supplied by the MoH, I used the on-land costs obtained from local suppliers. I used the international price for items bought internationally (e.g. HIV self-test kits), and included the cost of shipping and insurance. Equipment costs were likewise annuitized over their useful life with an annual discount rate of 3% (WHO, 2003a). As the majority of the equipment was office equipment, I assumed the useful life to be 3 years.

The cost of monitoring and evaluation (M+E) was estimated based on activities undertaken locally and centrally. For facility-based HTC, I asked all staff working at the facilities about time spent doing M+E activities or providing local supervision, and allocated this cost to M+E. In addition, I included the costs of M+E visits from

the HIV teams at the Blantyre District Health Office and the Malawi Ministry of Health. For the HIVST service, I included all M+E activities undertaken centrally by staff working on the main trial, but excluded research-related M+E activities. The M+E costs were based on the proportion of total working hours spent by personnel at the sites of interest.

Overhead and capital costs included the costs of utilities, security and building maintenance. I obtained these costs from the Blantyre District Health office which manages the Ndirande and Chilomoni health facilities. The HTC clinic at Queen Elizabeth Central hospital (QECH) is managed by the hospital administration. As QECH provides both inpatient and outpatient care, I allocated all capital and overhead costs based on the ratio of clinical personnel working in the HTC clinic to the total number of clinical personnel working at the hospital, and only included costs relevant to the outpatient HTC service. The costs of buildings were estimated from rental costs for equivalent space. The HIVST service did not incur any capital or overhead costs as it is provided in the community counselors' homes at no additional cost.

5.2.3.2 Direct non-medical and indirect costs

I developed a questionnaire (**Appendix XI**), administered by an interviewer, which asked all participants about direct non-medical costs that they or accompanying

family member or carers incurred in accessing HIV testing services, and their associated work losses. User fees were not charged for either modality of testing.

The direct non-medical costs included cost of transportation, food and drinks whilst waiting, and other costs incurred as a consequence of getting an HIV test. Indirect costs were estimated by recording whether participants, or accompanying family member or carers, had taken time off work and multiplying work losses by self-reported income (Pritchard and Sculpher, 2000). In addition, total time taken to access the testing service, including travel and waiting time, was recorded. The questionnaire eliciting direct non-medical and indirect costs was translated into Chichewa, the local language of the study population, and back translated by two independent bilingual Malawians to ensure accuracy. The final version of the questionnaire was developed following pilot testing and discussions with senior Malawian staff working at the Malawi-Liverpool Wellcome Trust Clinical Research Programme.

5.2.3.3 Cost conversions

All costs were converted into 2014 US Dollars and International Dollars (Drummond et al., 2005b) using data reported by the World Bank (Evans et al., 2005). For all unit costs, the currency, price year and country were recorded. A Gross Domestic Product (GDP) deflator index, provided by the World Bank, was used to adjust the cost from the price year to the year of reporting (2014). As some prices were for goods

purchased, all costs were then converted to 2014 US Dollars using the market exchange rate, and to 2014 International dollars using purchasing power parity conversion factor (Krijnse Locker and Faerber, 1984, Shemilt et al., 2010).

5.2.4 Health-related quality of life

All participants recruited into the study were asked about their HIV test result and their health-related quality of life (HRQoL) at the time of interview about economic costs. I used a self-assessed health (SAH) measure to ask individuals to rate their general health on a five-point Likert scale, with responses coded as: very good; good; fair; poor; or very poor. The SAH measure has been found to be a strong predictor of future health outcomes in high-income settings (Idler and Benyamini, 1997), and has also been used in resource-constrained settings (Gilbert and Soskolne, 2003, WHO, 2002).

The EuroQoL EQ-5D-3L (Dolan, 1997) measure was used to estimate the HRQoL of all study participants, a detailed description of the tool is provided in Chapter 4. Briefly, the EQ-5D-3L is a generic HRQoL measure, and was translated into Chichewa following international and EuroQoL guidelines (EuroQol, no date). The Chichewa version of the EQ-5D-3L used for this component of the study is shown in **Appendix XI**. The EQ-5D-3L measure consists of two principal measure components, a descriptive system and a visual analogue scale (EuroQol, 1990). The descriptive system defines HRQoL in terms of five dimensions: 'mobility', 'self care', 'usual

activities', 'pain/discomfort' and 'anxiety/depression' (Brooks, 1996). Responses in each dimension are divided into three ordinal levels, coded: (1) no problems; (2) some or moderate problems; and (3) severe or extreme problems. Responses to the descriptive component are then converted into an EQ-5D utility score using a tariff set that is derived from national surveys of the general population. As no Malawian EQ-5D tariff exists, and the Zimbabwean EQ-5D tariff (Jelsma et al., 2003) was used to derive EQ-5D utility scores for each study participant.

The visual analogue scale (VAS), similar to a thermometer, ranges from 100 (best imaginable health state) to 0 (worst imaginable health state). Participants are asked to indicate how good or bad their health was on the day of response by drawing a line on the scale.

5.2.5 Statistical analysis

All analysis was undertaken in Stata version 13.0 (Stata Corporation, Texas, USA). Socio-demographic data was collected on all participants recruited into the study. This included sex, age, marital status, educational attainment, employment status, and self-reported income. For socio-economic position, I collected data on household assets, nine in total, and information on home environment, for example distance to toilet. I undertook principal component analysis to classify an individual's socio-economic position based on wealth quintiles (Filmer and Pritchett, 2001). **Appendix X** shows the final case report forms used to collect individual-level socio-

demographic and economic data. Comparisons of socio-demographic characteristics were made between participants resident in control clusters and intervention clusters using the chi-squared test.

I estimated the direct health provider cost per individual tested, and the cost per HIV positive individual identified by dividing the total annual provider cost by the number of individuals tested, and the number of HIV positive individuals identified. For the HIVST service, I used the HIV prevalence reported in the main study to inform the cost per HIV positive individual identified (Choko et al., 2015b). I made comparisons between the mean direct non-medical and indirect costs for HIV self-testers and facility testers, and for facility-testers who resided in control clusters and intervention clusters. As the cost data was skewed, I used non-parametric bootstrap methods, with 1000 bootstrap replications, to derive 95% confidence intervals (CI) for mean cost differences for relevant cost categories (Thompson and Barber, 2000).

I undertook multivariable analysis to investigate the independent effect of the mode of HIV testing and HIV test result on the total societal costs associated with HIV testing. I estimated the mean total societal cost of HIV testing amongst the participants by summing direct and indirect costs. For the HIV self-testers, I estimated direct health provider cost per individual tested at the counsellor level. This was possible because the HIVST service records the total number of individuals tested by each of the community counsellors. For facility-based HIV testers, I used

the estimated direct health provider cost per individual tested for the clinic attended for testing. This component of the analysis excluded participants who had their HIV test at QECH. As all participants incurred a cost, and the cost data was skewed, I used generalized linear models (GLM) for multivariable analyses of cost data (Barber and Thompson, 2004). I ran model diagnostics to determine the optimal choices for the distributional family and link function (Manning and Mullahy, 2001). For this, I used a combination of the Park test, linktest, Akaike information criterion and visual inspection of plots of the deviance residuals to determine the optimal choice for the link function and the distributional family (Harrell, 2013).

I compared the responses to the self-assessed health (SAH) and EQ-5D measures between facility-based HIV testers residing in the intervention clusters to those residing in control clusters. For the descriptive component of the EQ-5D, few respondents reported severe or extreme problems. Responses were therefore dichotomized into reporting: no problems; or moderate/severe problems. I used chi-squared test for categorical variables, and student's t-test for continuous variables.

I undertook multivariable analysis to investigate the independent effect of the mode of HIV testing and HIV test result on the EQ-5D utility score. EQ-5D utility scores were non-normally distributed, skewed and truncated at 1.0. I evaluated four commonly used estimators to analyse these data: ordinary least squares (OLS) regression; Tobit regression, Fractional logit regression (Flogit), and censored least

absolute deviations (CLAD) regression (Powell, 1984, Austin et al., 2000, Papke and Wooldridge, 1996). I compared the mean squared error (MSE) and mean absolute error (MAE) statistics between the observed EQ-5D utility score and the estimated scores for the whole sample, and for sub-groups of the sample based on observed EQ-5D utility scores to determine the choice of estimator.

For all multivariable analyses, I ran two alternative models, the first adjusted for modality of HIV testing received, HIV test result and age and sex, and the second additionally adjusted for marital status, educational attainment, income and socio-economic position (Stangl et al., 2007). I accounted for clustering using the cluster of residence for the participants to produce robust variance estimators.

5.2.6 Sensitivity analysis

I undertook sensitivity analysis to investigate the impact of using an alternative tariff set to determine EQ-5D utility scores. I used the UK York A1 tariff (Dolan et al., 1996a), which has been found to translate health states with 'severe' problems in one or more of the five dimensions to a lower EQ-5D utility scores than the Zimbabwean tariff (Jelsma et al., 2003). For the multivariable analysis of total societal costs, I performed additional sensitivity analyses that (i) used the median wage of the sample, and (ii) the total HIV testing time to value income loss.

5.3 Results

5.3.1 Participant characteristics

1,241 participants were recruited; 775 who self-tested and 466 who had facility-based testing (253/466 were from the intervention clusters and 213/466 from the control clusters) (Figure 28).

Figure 28: Recruitment of HIV testing participants

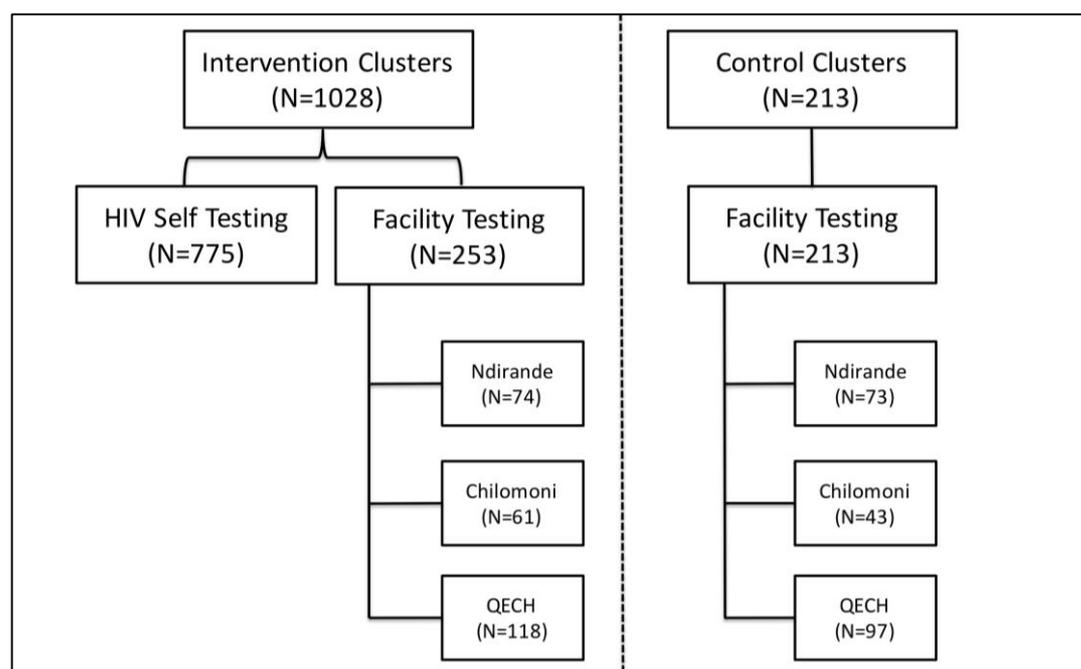


Table 9 shows the characteristics of the participants, by residence status within the main trial and modality of HIV testing received. Individuals accessing facility-based HTC who were resident in the intervention clusters were not statistically significantly different in terms of sex, age, marital status, educational attainment, employment or wealth, to those who accessed facility-based testing who were resident in the control clusters.

Table 9: Characteristics of HIV testers

		Intervention Clusters		Control Clusters	*p-value
		HIVST	Facility HTC	Facility HTC	
All		775	253	213	
Sex	Male	288 (37.2%)	90 (35.6%)	76 (35.7%)	0.981
	Female	487 (62.8%)	162 (64.3%)	137 (64.3%)	
Age (years)	18-24	316 (40.8%)	64 (25.3%)	64 (30.0%)	0.335
	25-39	379 (48.9%)	149 (58.9%)	111 (52.1%)	
	40+	80 (10.3%)	40 (15.8%)	28 (17.8%)	
Marital status	Single (never-married)	227 (29.3%)	40 (15.8%)	26 (12.2%)	0.606
	Married/Cohabiting	455 (58.7%)	175 (69.2%)	148 (69.5%)	
	Separated/Divorced	78 (10.1%)	24 (9.5%)	24 (11.3%)	
	Widower/Widow	15 (1.9%)	14 (5.5%)	15 (7.0%)	
Educational attainment	Up to standard 8	300 (38.7%)	132 (52.2%)	124 (58.2%)	0.402
	Up to form 6	442 (57.0%)	113 (44.7%)	82 (38.5%)	
	University or training college	32 (4.1%)	8 (3.2%)	7 (3.3%)	
	Missing	1 (0.1%)	0 (0%)	0 (0%)	
Income	Not working	400 (51.6%)	93 (36.8%)	86 (40.4%)	0.752
	Up to 4,000 Kwacha/week	162 (20.9%)	79 (31.2%)	56 (36.3%)	
	4,000 to 8,000 kwacha/week	108 (13.9%)	42 (16.6%)	34 (16.0%)	
	8,000 to 12,000 kwacha/week	48 (6.2%)	18 (7.1%)	15 (7.0%)	
	Over 12,000 kwacha/week	57 (7.4%)	21 (8.3%)	22 (10.3%)	
Employment status	Formal employment	139 (17.9%)	75 (29.6%)	62 (29.1%)	0.801
	Informal employment/Unemployed	234 (30.2%)	85 (33.6%)	67 (31.5%)	
	School/University	159 (20.5%)	18 (7.1%)	15 (7.0%)	
	Retired	2 (0.4%)	1 (0.4%)	1 (0.5%)	
	Housework	238 (30.7%)	72 (28.5%)	68 (31.9%)	
	Sick leave	2 (0.3%)	2 (0.8%)	0 (0%)	
Socio-economic position[¶]	Highest quintile	172 (22.2%)	32 (12.6%)	43 (20.2%)	0.239
	2nd highest quintile	154 (19.9%)	55 (21.7%)	39 (18.3%)	
	Middle quintile	148 (19.1%)	58 (22.9%)	42 (19.7%)	
	2nd lowest quintile	145 (18.7%)	55 (21.7%)	48 (22.5%)	
	Lowest quintile	154 (19.9%)	53 (20.95%)	41 (19.2%)	
	Missing	2 (0.3%)	0 (0%)	0 (0%)	
Had HIV testing in last year	Not tested	127 (16.4%)	96 (38.0%)	97 (45.5%)	0.048
	Tested once	260 (33.5%)	69 (27.3%)	64 (30.0%)	
	Tested >1	388 (50.1%)	88 (34.8%)	52 (24.4%)	

*Comparison between facility testers in control and Intervention clusters

[¶]Socio-economic position estimated through principal component analysis of responses to assets and housing environment questions

5.3.2 Direct health provider costs of HTC service

The direct health provider costs of facility-HTC and HIVST are shown in Table 10. The mean costs per individual tested at the three health facilities were US\$7.53 (INT\$20.25), US\$10.57 (INT\$25.18), and US\$8.90 (INT\$20.44), whilst the costs of providing HIVST were US\$8.78 (INT\$17.25) per-participant. The mean costs per HIV positive individual identified at the three health facilities were US\$67.33 (INT\$181.05), US\$76.39 (INT\$182.03), US\$28.30 (INT\$65.00), whilst the mean cost per HIV positive individual identified through HIVST was US\$97.50 (INT\$191.70).

At the three health facilities, staff salaries accounted for between 11.1% and 17.9%, staff training between 0.5% and 1.1%, monitoring and evaluation between 4.2% and 11.9%, and consumables and equipment between 65.5% and 70.5% of the total International Dollar costs. In comparison, for the HIVST service staff salaries accounted for 30.3%, staff training for 13.0%, monitoring and evaluation for 20.8%, and consumables and equipment accounted for 35.9% of the total International Dollar cost.

5.3.3 Direct non-medical and indirect costs for HTC participants

Table 11 shows the time, and direct non-medical and indirect costs associated with accessing either modality of HTC. Most individuals who self-tested did not incur any costs, require a family member or carer to accompany them, or need to take time off work. Approximately 27% (124/466) of all facility testers reported taking time off

work to get tested, and 27% (126/466) needed a family member or carer to accompany them for testing. In comparison to HIVST, facility-based HTC participants incurred a mean additional direct non-medical cost of US\$0.84 (bootstrap 95%CI: US\$0.73-US\$0.95), whilst indirect costs averaged \$1.41 (bootstrap 95%CI: US\$0.86-US\$1.96), with the testing process taking an additional 176.5 minutes (95%CI: 166.1-186.9). The mean combined direct non-medical and indirect cost of facility-HTC was US\$2.93 (bootstrap 95%CI: US\$1.92-US\$3.94) higher than for HIVST.

5.3.4 Total societal costs of HTC

The societal cost for facility-HTC was US\$11.84 (95%CI: US\$10.81-12.86) and for HIVST was US\$9.23 (95%CI: US\$9.14-US\$9.32). In the multivariable analysis (Table 12), after adjusting for individual characteristics and HIV test result, the societal costs was US\$2.38 (95%CI: US\$0.87-US\$3.89) less for HIVST than for facility-based HTC.

Table 10: Annual Direct Health Provider costs of HIV testing and counselling

Cost category	Ndirande clinic			Chilomoni Clinic			QECH HTC Clinic [¶]			HIVST service		
	US	INT	% of	US	INT	% of	US	INT	% of	US	INT	% of
	Dollars (2014)	Dollars (2014)	Total*	Dollars (2014)	Dollars (2014)	Total*	Dollars (2014)	Dollars (2014)	Total*	Dollars (2014)	Dollars (2014)	Total*
Staff salaries	6,738	24,545	17.9%	6,433	15,019	11.1%	8,710	24,195	12.5%	23,066	79,431	30.3%
Staff training	353	982	0.7%	530	1,472	1.1%	353	982	0.5%	12,268	34,077	13.0%
Monitoring + Evaluation	2,098	5,828	4.3%	5,785	16,069	11.9%	2,920	8,111	4.2%	15,833	54,521	20.8%
Consumables + Equipment	38,453	96,475	70.5%	40,910	94,070	69.6%	60,324	126,995	65.5%	82,133	94,051	35.9%
Capital/Overheads	3,257	9,047	6.6%	3,102	8,618	6.4%	12,129	33,691	17.4%	0	0	0
Total annual health provider cost	50,899	136,876		56,760	135,248		84,436	193,973		133,300	262,080	
Direct cost per individual tested	7.53	20.25		10.57	25.18		8.90	20.44		8.78	17.25	
Direct cost per HIV positive identified	67.33	181.05		76.39	182.03		28.30	65.00		97.50	191.70	

[¶]Outpatient HIV Testing and counseling clinic at Queen Elizabeth Central Hospital

*Percentages based on costs estimated in International Dollars

Table 11: Direct non-medical and indirect costs and time

	Intervention Clusters		Control Clusters		Mean Differences (95% CI)***	
	HIVST (n=775)	Facility HTC (n=253)	Facility HTC (n=213)	HIVST v All Facility HTC	Intervention Facility HTC v Control Facility HTC	
Patient direct non-medical costs						
2014 US Dollars (Mean/SE)	0 (0, 0)*	0.90 (0.09)	0.78 (0.06)	-0.84 (-0.95, -0.73)	0.12 (-0.10, 0.33)	
2014 INT Dollars (Mean/SE)	0 (0, 0)*	2.49 (0.25)	2.17 (0.16)	-2.32 (-2.63, -2.01)	0.32 (-0.28, 0.92)	
Time to get tested (Mean/SE)**	30.2 (1.8)	215.2 (7.0)	196.5 (6.9)	-176.5 (-186.9, -166.1)	18.7 (-0.9, 38.3)	
Patient Time off work						
No	762 (98.3%)	190 (75.1%)	152 (71.4%)	-	-	
Yes	13 (1.7%)	63 (24.9%)	61 (28.6%)			
Indirect costs						
2014 US Dollars (Mean/SE)	0 (0, 0)*	1.07 (0.24)	1.93 (0.56)	-1.41 (-1.96, -0.86)	-0.87 (-2.11, 0.38)	
2014 INT Dollars (Mean/SE)	0 (0, 0)*	2.97 (0.67)	5.37 (1.55)	-3.91 (-5.44, -2.38)	-2.41 (-5.87, 1.05)	
Family or Carer accompanied						
No	762 (98.3%)	188 (74.3%)	152 (71.4%)	-	-	
Yes	13 (1.7%)	65 (25.7%)	61 (28.6%)			
Family/Carer direct non-medical costs						
2014 US Dollars (Mean/SE)	0 (0, 0)*	0.24 (0.04)	0.26 (0.04)	-0.25 (-0.31, -0.19)	-0.02 (-0.13, 0.10)	
2014 INT Dollars (Mean/SE)	0 (0, 0)*	0.68 (0.11)	0.72 (0.11)	-0.70 (-0.86, -0.54)	-0.04 (-0.36, 0.27)	
Family/Carer Time (Mean/SE)**	0 (0, 0)*	54.3 (6.8)	51.8 (6.4)	-52.4 (-43.3, -61.5)	2.5 (-16.5, 21.5)	
Family/Carer Loss of income						
2014 US Dollars (Mean/SE)	0 (0, 0)*	0.03 (0.02)	1.29 (0.95)	-0.59 (-1.43, 0.25)	-1.25 (-3.16, 0.65)	
2014 INT Dollars (Mean/SE)	0 (0, 0)*	0.09 (0.05)	3.57 (2.65)	-1.64 (-3.97, 0.69)	-3.48 (-8.70, 1.72)	
Total direct medical and indirect costs						
2014 US Dollars (Mean/SE)	0 (0, 0)*	2.22 (0.27)	3.91 (1.09)	-2.93 (-3.94, -1.92)	-1.69 (-3.88, 0.51)	
2014 INT Dollars (Mean/SE)	0 (0, 0)*	6.18 (0.74)	10.87 (3.02)	-8.14 (-10.94, -5.35)	-4.69 (-10.73, 1.36)	

*Median and IQR reported because of low numbers incurring costs/taking time

** Time measured in Minutes and includes travel to and from testing site, waiting time and counseling and testing time

***Bootstrapped estimates of Mean differences and 95%CI

Table 12: Multivariable analysis exploring relationship between modality of HIV testing and total Societal cost of testing*

		Total Societal cost			
		Model 1 (n=1240)		Model 2 (n=1237)	
		2014 US Dollars Coef (95% CI)	2014 INT Dollars Coef (95% CI)	2014 US Dollars Coef (95% CI)	2014 INT Dollars Coef (95% CI)
Exposure	Control Clusters: Facility HTC	Ref	Ref	Ref	Ref
	Intervention Clusters: Facility HTC	-1.45 (-3.62, 0.73)	-4.24 (-9.99, 1.52)	-0.98 (-2.59, 0.63)	-2.97 (-7.07, 1.13)
	Intervention Clusters: HIVST	-3.01** (-5.14, -0.88)	-12.52** (-18.23, -6.82)	-2.38** (-3.89, -0.87)	-10.82** (-14.79, -6.87)
HIV Test Result	HIV Negative	Ref	Ref	Ref	Ref
	HIV Positive	1.19 (-0.04, 2.41)	2.76 (-0.29, 5.81)	1.11** (0.24, 1.99)	2.57** (0.41, 4.72)

Model 1: adjusted for exposure, HIV test result, age and sex

Model 2: additionally adjusted for marital status, educational attainment, income and wealth quintile

Missing data for HIV test result: 1; missing data for educational attainment: 1; missing data for socio-economic position: 2

*Findings from Generalized Linear Model with Poisson distribution and Identity link function

** $p < 0.05$

5.3.5 Health-related quality of life of HTC participants

Figure 29 compares the reported EQ-5D utility scores to the reported visual analogue scores. The Pearson's correlation coefficient between the two different self-reported HRQoL measures was 0.448.

Figure 30 shows the EQ-5D utility scores of participants by their response to their self-assessed health. There were no participants who reported very poor health in response to being asked about their SAH.

Figure 29: Comparison of EQ-5D utility scores to Visual Analogue Scale scores

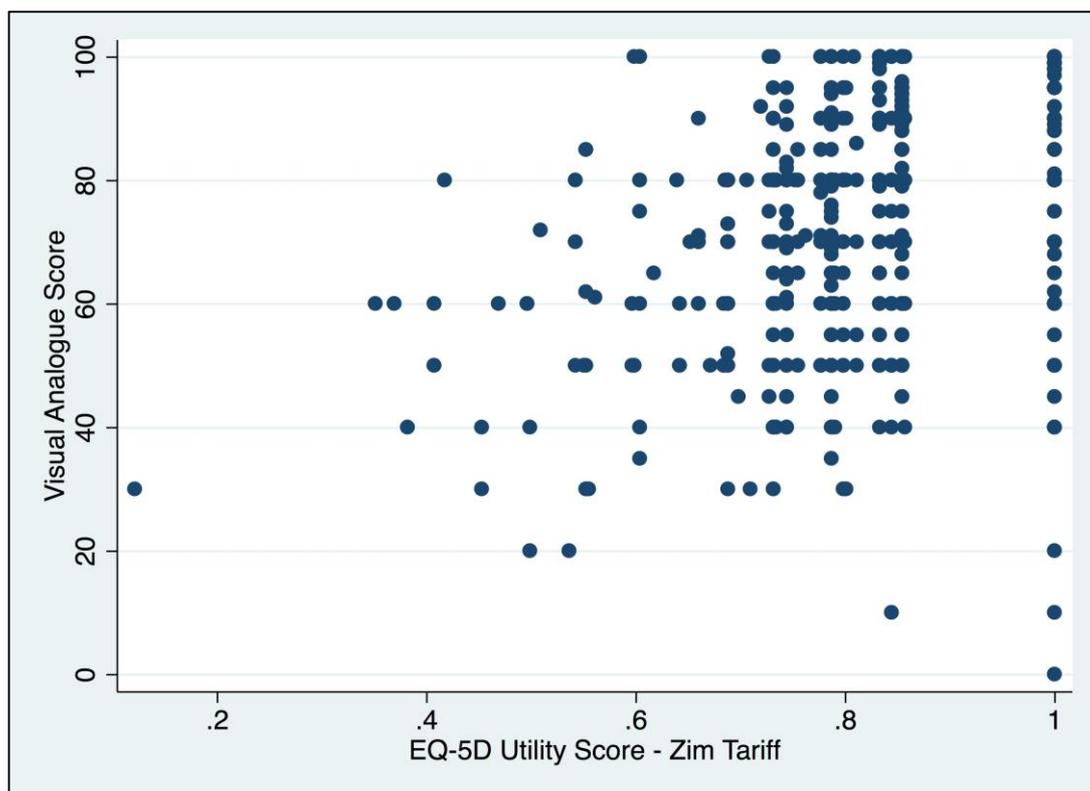
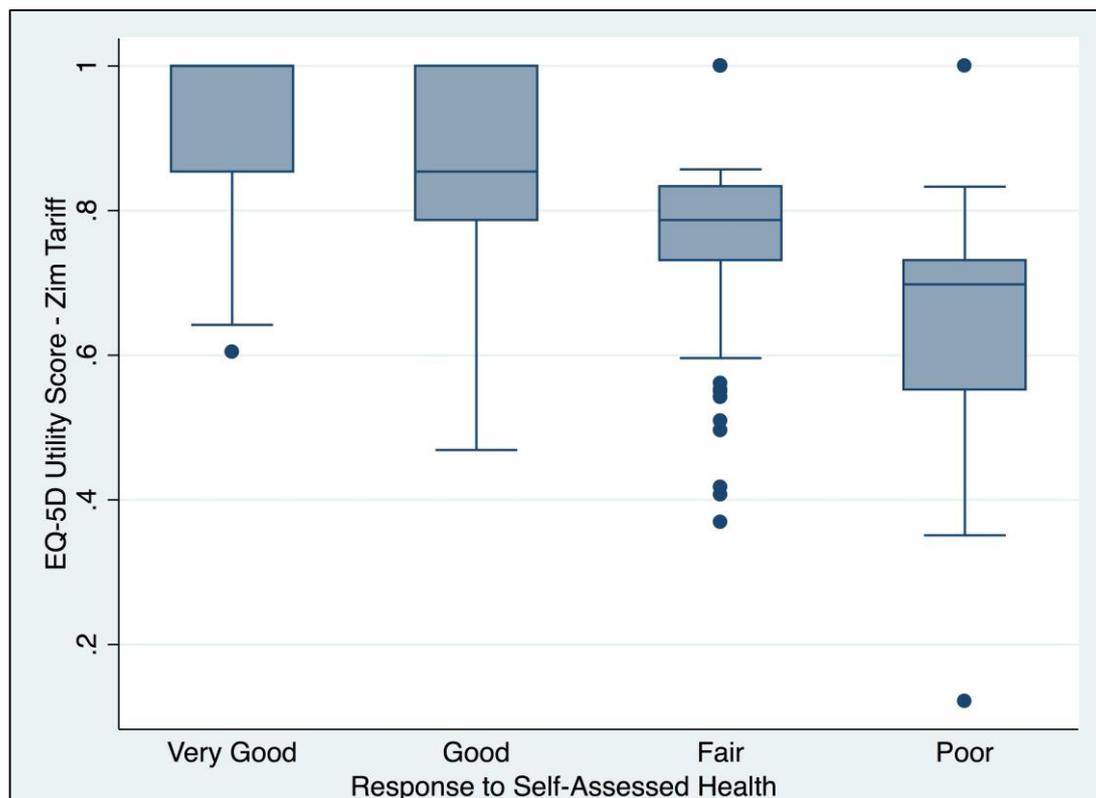


Figure 30: EQ-5D utility scores by response to Self-assessed health



The HIV test result and HRQoL outcomes are shown in Table 13. There was no significant difference between facility testers who resided in the intervention and control clusters with regards to the mean EQ-5D utility score, the mean VAS score, the descriptive components of the EQ-5D measure or their responses to the SAH measure. A smaller proportion of HIVST participants reported problems in all five EQ-5D dimensions, with the mean EQ-5D utility score amongst them higher (0.905, 95%CI: 0.897-0.913) than in facility testers residing in the intervention (0.828, 95%CI: 0.812-0.844) or control (0.839, 95%CI: 0.821-0.857) clusters.

The mean VAS score amongst HIVST participants was also higher (82.1, 95%CI: 81.0-83.3) than amongst facility-HTC participants residing in the intervention (74.5, 95%CI: 72.2-76.8) or control clusters (75.4, 95%CI: 72.9-78.0). The majority of HIVST participants reported being in very good or good health (676/775, 87%), whilst 69% of all facility testers reported very good or good health (323/466).

Table 13: Health-related quality of life of HIV testers

		Intervention Clusters		Control Clusters	p-value
		HIVST (n=775)	Facility HTC (n=253)	Facility HTC (n=213)	
HIV Test Result	HIV negative	670 (86.5%)	146 (57.7%)	115 (54.0%)	0.421
	HIV positive	104 (13.4%)	107 (42.3%)	98 (46.0%)	
	Not reported	1 (0.1%)	0 (0%)	0 (0%)	
EQ-5D: Utility Score	All	0.905 (0.897, 0.913)	0.828 (0.812, 0.844)	0.839 (0.821, 0.857)	0.359
	HIV negative	0.916 (0.908, 0.924)	0.853 (0.834, 0.873)	0.862 (0.839, 0.884)	0.591
	HIV positive	0.842 (0.814, 0.870)	0.794 (0.768, 0.819)	0.813 (0.786, 0.840)	0.306
EQ-5D: VAS Score	All	82.1 (81.0, 83.3)	74.5 (72.2, 76.8)	75.4 (72.9, 78.0)	0.597
	HIV negative	83.7 (82.5, 84.9)	79.4 (76.6, 82.2)	79.5 (76.0, 82.9)	0.966
	HIV positive	72.5 (69.0, 76.0)	67.9 (64.4, 71.3)	70.7 (67.0, 74.4)	0.270
EQ-5D: Mobility	No problems	689 (88.9%)	180 (71.15%)	162 (76.1%)	0.232
	Moderate or severe problems	86 (11.1%)	73 (28.85%)	51 (23.9%)	
EQ-5D: Self-Care	No problems	767 (99.0%)	245 (96.8%)	211 (99.1%)	0.099
	Moderate or severe problems	8 (1.0%)	8 (3.2%)	2 (0.9%)	
EQ-5D: Usual Activities	No problems	730 (94.2%)	209 (82.6%)	174 (81.7%)	0.796
	Moderate or severe problems	45 (5.8%)	44 (17.4%)	39 (18.3%)	
EQ-5D: Pain	No problems	565 (72.9%)	131 (51.8%)	112 (52.6%)	0.863
	Moderate or severe problems	210 (27.1%)	122 (48.2%)	101 (47.4%)	
EQ-5D: Anxiety	No problems	519 (67.0%)	126 (49.8%)	110 (51.6%)	0.692
	Moderate or severe problems	256 (33.0%)	127 (50.2%)	103 (48.4%)	
Self-Assessed Health	Excellent	318 (41.0%)	53 (20.9%)	42 (19.7%)	0.947
	Good	358 (46.2%)	121 (47.8%)	107 (50.2%)	
	Fair	87 (11.2%)	60 (23.7%)	50 (23.5%)	
	Poor	12 (1.5%)	19 (7.5%)	14 (6.6%)	
	Very Poor	0 (0%)	0 (0%)	0 (0%)	

*Comparison between facility testers in control and Intervention clusters

In the multivariable analysis, the model diagnostics revealed the OLS estimator performed as well or better than the other estimators (Table 14 and Table 15). The EQ-5D utility scores predicted by the OLS estimator show close approximation to the observed EQ-5D utility scores in the sample. All estimators performed less optimally in predicting lower EQ-5D utility scores.

Table 14: Estimated predicted values compared to actual utility scores

	Model	Obs	Mean	Min	Max	MSE	MAE
	Observed	1241	0.878	0.121	1.000		
	OLS	1237	0.878	0.736	0.975	0.000	0.094
Model	TOBIT	1237	0.886	0.703	0.970	0.007	0.094
	CLAD	1237	0.891	0.670	1.042	0.012	0.093
	Flogit	1237	0.879	0.701	0.956	0.000	0.096

OLS: Ordinary Least Squares
Flogit: Fractional logit
CLAD: Censored least Absolute deviations

MSE: Mean Squared Error
MAE: Mean Absolute Error

Table 15: MSE and MAE for regression models by utility score range

		Observed EQ-5D utility score												
		<0	0 to <0.2		0.2 to <0.4		0.4 to <0.6		0.6 to <0.8		0.8 to <1		1	
Obs		0	1	2	30	350	310	544						
		MSE	MAE	MSE	MAE	MSE	MAE	MSE	MAE	MSE	MAE	MSE	MAE	
OLS	-	-	0.759	0.759	0.430	0.430	0.302	0.302	0.010	0.102	0.030	0.050	0.101	0.101
TOBIT	-	-	0.784	0.784	0.430	0.430	0.306	0.306	0.106	0.109	0.036	0.057	0.092	0.092
CLAD	-	-	0.775	0.775	0.444	0.444	0.309	0.309	0.105	0.108	0.039	0.066	0.081	0.083
Flogit	-	-	0.771	0.771	0.421	0.421	0.300	0.300	0.100	0.104	0.053	0.031	0.101	0.101

OLS: Ordinary Least Squares
Flogit: Fractional logit
CLAD: Censored least Absolute deviations

MSE: Mean Squared Error
MAE: Mean Absolute Error

In the fully adjusted OLS model (Table 16), individuals who accessed HIVST had a higher adjusted mean EQ-5D utility score of 0.046 (95%CI: 0.022-0.070) than those who accessed facility-HTC. Those who tested HIV positive had a lower adjusted mean EQ-5D utility score of 0.048 (95%CI: 0.024-0.073) than those who tested HIV negative. There were no significant differences in the adjusted mean EQ-5D utility scores between facility testers who resided in the control and intervention clusters.

Table 16: Multivariable analysis exploring relationship between modality of HIV testing and EQ-5D utility scores*

		Sensitivity Analysis			
		EQ-5D Utility Score (Zimbabwean Tariff)		EQ-5D Utility Score (UK Tariff)	
		Model 1 (n=1240) Coef (95% CI)	Model 2 (n=1237) Coef (95% CI)	Model 1 (n=1240) Coef (95% CI)	Model 2 (n=1237) Coef (95% CI)
Exposure	Control Clusters: Facility HTC	Ref	Ref	Ref	Ref
	Intervention Clusters: Facility HTC	-0.012 (-0.038, 0.014)	-0.011 (-0.037, 0.015)	-0.145 (-0.055, 0.026)	-0.012 (-0.053, 0.029)
	Intervention Clusters: HIVST	0.043** (0.018, 0.068)	0.046** (0.022, 0.070)	0.059** (0.026, 0.092)	0.065** (0.031, 0.099)
HIV Test Result	HIV Negative	Ref	Ref	Ref	Ref
	HIV Positive	-0.054** (-0.077, -0.031)	-0.048** (-0.073, -0.024)	-0.076** (-0.112, -0.040)	-0.068** (-0.105, -0.031)

Model 1: adjusted for exposure, HIV test result, age and sex

Model 2: additionally adjusted for marital status, educational attainment, income and wealth quintile

Missing data for HIV test result: 1; missing data for educational attainment: 1; missing data for socio-economic position: 2

*Findings from OLS estimator

** $p < 0.05$

5.3.6 Findings from sensitivity analysis

In the sensitivity analysis, when the UK tariff was used to derive EQ-5D utility scores, the adjusted mean EQ-5D utility score was 0.059 (95%CI: 0.026-0.092) higher amongst HIVST participants than amongst facility testers (Table 16). In addition, those reporting a positive HIV test result had an even lower mean adjusted utility decrement compared to those who reported a negative HIV test result (0.068; 95%CI: 0.031-0.105). Table 17 shows that the total societal cost of HIVST remains lower than facility-based HTC when alternative approaches to valuing loss of income.

Table 17: Sensitivity Analysis for multivariable regression of total societal cost (Model 2)*

		Total Societal cost					
		Sensitivity Analysis A (n=1237)		Sensitivity Analysis B (n=1237)		Sensitivity Analysis C (n=1237)	
		2014 US Dollars Coef (95% CI)	2014 INT Dollars Coef (95% CI)	2014 US Dollars Coef (95% CI)	2014 INT Dollars Coef (95% CI)	2014 US Dollars Coef (95% CI)	2014 INT Dollars Coef (95% CI)
Exposure	Control Clusters: Facility HTC	Ref	Ref	Ref	Ref	Ref	Ref
	Intervention Clusters: Facility HTC	0.19 (-0.76, 1.15)	0.35 (-1.66, 2.35)	-0.32 (-1.66, 1.03)	-1.07 (-4.41, 2.27)	0.36 (-0.47, 1.18)	0.82 (-0.89, 2.53)
	Intervention Clusters: HIVST	-1.12 (-2.02, 0.22)	-7.30** (-9.57, -5.04)	-1.88** (-3.13, -0.62)	-9.38** (-12.69, -6.07)	-1.73** (-2.56, -0.92)	-8.97** (-11.10, -6.84)
HIV Test Result	HIV Negative	Ref	Ref	Ref	Ref	Ref	Ref
	HIV Positive	0.77** (0.45, 1.08)	1.70** (0.97, 2.43)	1.30** (0.63, 1.97)	3.09** (1.44, 4.74)	0.77** (0.47, 1.08)	1.75** (1.02, 2.49)

*Findings from Generalized Linear Model with Poisson distribution and Identity link function

** $p < 0.05$

Sensitivity Analysis A: Using median wage rate and self-reported time off work to value income loss

Sensitivity Analysis B: Using self-reported income and total HIV testing time to value income loss

Sensitivity Analysis C: Using median wage rate and total HIV testing time to value income loss

5.4 Discussion

In this component of the PhD, I found that HIVST reaches a healthier population, with users incurring lower direct non-medical and work absences, whilst the direct health provider costs of offering HIVST were comparable to facility-based HTC. At the societal level, the cost of offering HIVST was found to be significantly lower than the cost of facility-based HTC. Recent work has highlighted the high population uptake, safety and acceptable linkage into HIV treatment services when HIVST has been provided to communities in Blantyre, Malawi (Choko et al., 2015b). Taken together, these data suggest that HIVST is an affordable and potentially highly effective option for national policy makers in Africa wishing to increase uptake of HIV testing.

The main finding of the analysis was the comparable cost of offering HIVST to that of facility-based HTC services. However it must be remembered that at the population level the cost of providing HIVST, in addition to routine facility-based HTC services, will place significant financial burden on healthcare providers. Importantly, the direct health provider costs of HIVST (US\$8.78 in 2014 prices) compares favourably with previous estimates of mobile or home-based HIV testing services (US\$7.77 to US\$33.54 in 2012 prices) (Suthar et al., 2013), suggesting HIVST offers an affordable option for providers wishing to scale-up community-based HIV testing services. The relatively high current cost of the oral fluid RDT kits (2014 US\$4, or US\$4.80 including shipping and insurance), compared to the cost of the standard finger-prick RDT kit used in health facilities (2014 US\$0.69 in my analysis) accounts for much of

the difference in costs between the two modalities of HIV testing examine in this study. The cost of oral fluid RDT kits accounted for approximately one half of the total cost per individual tested through HIVST, whilst the cost of the rapid finger-prick test kit accounted for only one tenth of the cost of facility-based HTC.

Previous research highlights that high direct non-medical and indirect costs act as a deterrent to individuals accessing facility-based HTC services (Wolff et al., 2005, Morin et al., 2006, Wringe et al., 2009). In comparison to HIVST, I found facility testers incurred an additional US\$2.93 to test for HIV in a health facility. In Malawi approximately three-quarters of the population live on less than \$2 a day (Bank). Therefore, it is easily understandable why the high client costs of accessing facility-based HTC may act as a deterrent, and this may partly explain the high levels of uptake of HIVST seen in the main trial (Choko et al., 2015b).

HIV testing and counseling has been provided at health facilities in Africa for nearly a decade. HIV counselors at health facilities are experienced in providing HTC, and monitoring and evaluation systems have evolved. HIVST is still in its infancy, with concerns around potential harms it may cause users (Scott, 2014). Consequently, in the main trial HIVST was provided through a semi-supervised semi-restricted community distribution model. Community counselors providing HIVST needed additional training around delivering HIV self-testing, and had regular visits by supervisors to monitor the service and ensure safety and quality. This is reflected in

the costing's which show that salaries, staff training, and monitoring and evaluation accounted for approximately two-thirds of the cost of delivering HIVST, whilst these costs represented less than a quarter of the cost of delivering facility-based HTC.

I used the average yield from the HIVST service over the two years in operation to estimate the health provider cost per HIV positive individual identified through HIVST, assuming individuals were offered annual HIVST. In the main trial, the HIV prevalence amongst self-testers was found to be higher in the first year than in the second (representing prevalence rather than incidence testing) (Choko et al., 2015b). As the cost per individual tested through HIVST services may vary, it will be important to consider this issue in the main decision-analytical modeling, and investigate the impact on different costs on the final estimates of cost-effectiveness.

I made comparisons between facility testers who were residents of the intervention clusters of the main trial, and therefore had the option of HIV self-testing, and those who lived in control clusters, and who therefore did not have access to HIVST. I found that there were no statistically significant differences between these two populations of facility testers, and that the yield of HIV positive individuals was comparable.

Community-based HTC strategies are a more costly approach to identifying HIV positive individuals (Menzies et al., 2009). I found the cost per HIV positive individual identified was lower at the health facilities than through HIVST, with the lowest cost at the HTC facility at Queen Elizabeth Central Hospital. However, those who self-tested reported better HRQoL than those who accessed facility testing services, even after accounting for differences in HIV test result. In addition, previous work from the main trial found the median CD4 count amongst HIV self-testers who initiated ART to be higher than facility-based testers who initiated ART (Choko et al., 2015b). Evidence from studies examining HRQoL in HIV positive individuals suggests that HRQoL deteriorates with advancing HIV disease (Alibhai et al., 2010, Beard et al., 2009). The finding of HIV self-testers and those identified HIV-positive through HIVST reporting better HRQoL than facility testers is likely to reflect lead time bias, with HIVST detecting individuals earlier in their HIV disease progression (Figure 31). HIVST is offered in the community and therefore will be utilised by individuals who may otherwise be well. Many of those who access facility-based HTC services are attending the health facility because they are unwell and or have more advanced HIV disease, and have been referred for HIV testing by medical personnel. The value of HIVST will partly depend on if HIV-positives individuals initiated onto ART, subsequently experience improvements in their HRQoL (Figure 32). The study undertaken in Chapter 6 further explores this issue by examining the impact of HIV disease stage (and CD4 count) on HRQoL before and after starting anti-retroviral therapy.

Figure 31: Quality of life adjusted survival without ART

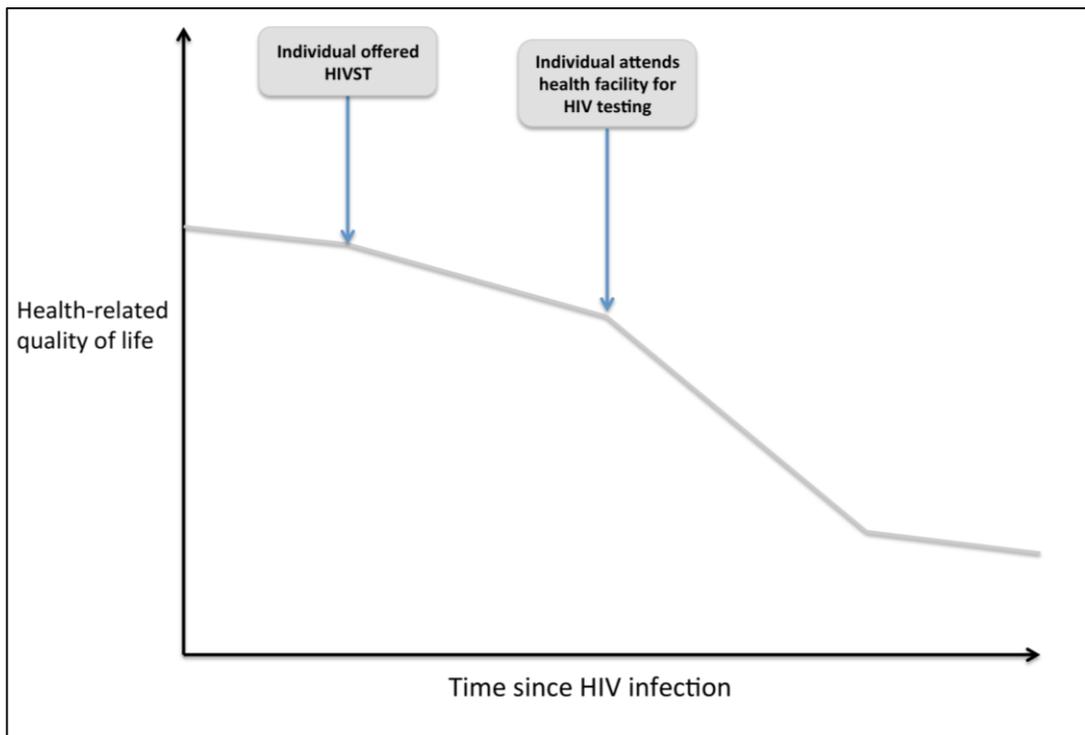
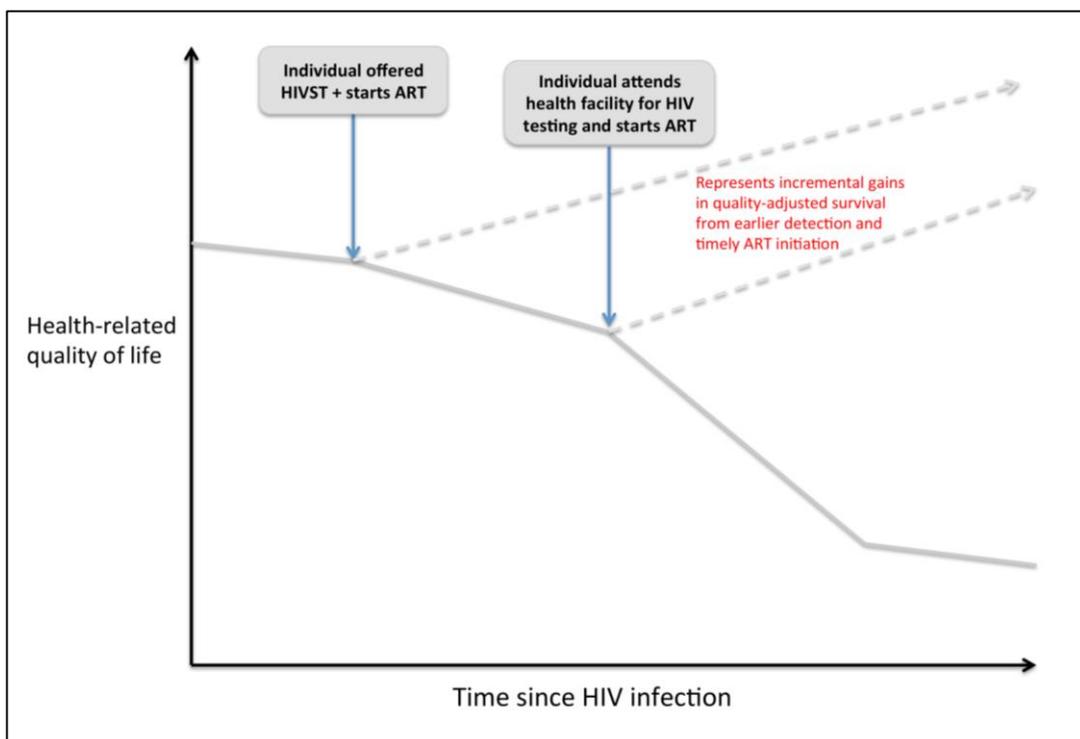


Figure 32: Quality of life adjusted survival with ART



5.5 Summary of Chapter 5

In this chapter I undertook primary data collection from participants of a trial of HIVST in Blantyre, Malawi. I collected data from participants on the costs they incurred in accessing either HIVST or facility-based HTC. I also undertook primary costing studies to estimate the health provider cost of providing each service. I looked at the total societal cost of accessing each modality of HIV testing. In addition, I investigated the health-related quality of life of people who accessed each modality of HIV testing.

The findings suggest that offering HIVST reduces the economic burden on clients and at the societal level is cost saving. The affordability of HIVST would substantially improve if the costs of HIV self-test kits were lower. The economic data collected from this chapter will be used to inform the decision-analytic modeling of the cost-effectiveness of HIVST (Chapter 8). This study provides estimates for the health provider cost of both facility-based HTC and HIVST. In addition, the multivariable analysis provides estimates for the societal costs of providing both facility-based HTC and HIVST whilst controlling for individual level characteristics and HIV test result.

In Chapter 6, I will describe the study I undertook amongst HIV positive individuals who attended the HIV clinic to access HIV care after accessing either facility-based HTC or HIV self-testing.

CHAPTER 6: A comparison of the costs and consequences of Accessing HIV treatment

6 Overview of Chapter 6

In this chapter I will aim to investigate one of the secondary objectives of my PhD.

To compare and contrast the costs to individuals and to healthcare providers, and health-related quality of life outcomes, amongst HIV positive individuals who access HIV care and treatment services subsequent to testing at facility-based or through HIV self-testing services in Blantyre, Malawi

As previously mentioned, the chapter has been written in the format of a manuscript for publication in a peer-reviewed journal. The manuscript from this chapter will be submitted in the coming months.

In this Chapter, I follow-up a cohort of HIV positive individuals as they access HIV care after accessing either HIVST or facility-based HTC. I investigate the costs of providing HIV care, including anti-retroviral therapy, to the population. In addition, I investigate the health outcomes amongst HIV positive individuals and investigate whether their HIV disease stage and starting anti-retroviral therapy impacts on their health-related quality of life. I also investigate whether the modality of HIV testing received prior to entering HIV care independently affects these economic outcomes. The economic data collected in this Chapter will inform the decision-analytic modelling undertaken in Chapter 8 of the PhD.

6.1 Introduction

There are now over 13 million people worldwide living with HIV who are receiving anti-retroviral therapy (ART), with 6 million individuals started onto treatment since 2010 (UNAIDS, 2014b). Sub-Saharan Africa accounts for three quarters of those on anti-retroviral therapy (UNAIDS, 2014b). Providing HIV care and treatment is costly, with limited data around to inform to inform policy makers (Levy et al., 2006, Beck et al., 2010). The existing economic data relates to services provided in South Africa (Harling and Wood, 2007, Rosen et al., 2008, Martinson et al., 2009, Long et al., 2010), or from estimates based on international donor supported services (Menziés et al., 2011, Larson et al., 2013, Menziés et al., 2012, Marseille et al., 2012). These estimates tend to be higher (Johns et al., 2014, Babigumira et al., 2009), or do not reflect current and local approaches to providing HIV services (Menziés et al., 2011, Menziés et al., 2012, Marseille et al., 2012, Rosen et al., 2008). Additionally there is limited data on the impact of ART on preferences-based measures of health-related quality of life (HRQoL) for use in economic evaluations (Robberstad and Olsen, 2010, Beard et al., 2009), or on the costs incurred by those affected when they access HIV services (Chimbindi et al., 2015, Schwartlander et al., 2011).

HIV self-testing (HIVST) offers an opportunity to increase awareness of HIV status at the population-level and potentially reach individuals earlier in their HIV disease stage (Choko et al., 2011). This will result in an increased financial burden on healthcare providers with increased numbers entering HIV treatment services. However, there are likely to be potential cost savings, through prevention of HIV

associated comorbidities, and a beneficial impact on health outcomes of those affected, through timely initiation of ART (Leisegang et al., 2009, Badri et al., 2006a, Jahn et al., 2008, May et al., 2010a). Consequently, to undertake a full economic evaluation of HIVST requires an understanding of the economic and quality of life impact of accessing HIV care, and whether there are differences in these outcomes between those who enter HIV care after HIVST or facility-based HIV testing and counselling (HTC) (Mavedzenge et al., 2013, Pant Pai et al., 2013).

In this component of the PhD I investigate the economic impact associated with HIV infected individuals of accessed HIV treatment, and the cost to healthcare providers providing this care. I recruited a cohort of HIV positive individuals who attended the health facilities in Blantyre, Malawi to access HIV treatment. The main aims were to investigate the HQRoL of HIV infected individuals as they accessed HIV treatment, and to estimate the economic costs of HIV treatment for individuals accessing care and for health providers providing the care. I investigate whether there are differences in economic and HRQoL outcomes between those who entered HIV services after HIVST and after facility-based HTC. Additionally, I aimed to investigate the impact of HIV disease stage on these economic outcomes.

6.2 Methods

6.2.1 Ethical statement

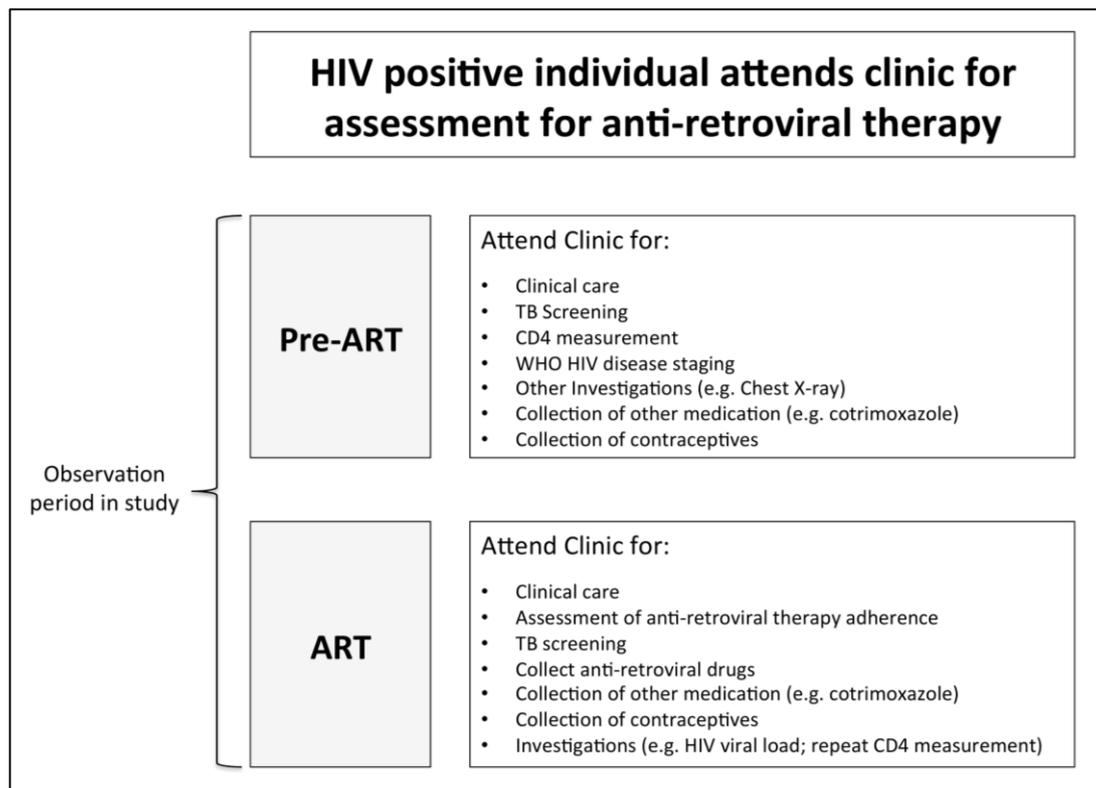
This study follows on from the study described in Chapter 5. Ethical approval for this study was obtained in combination with the previous study comparing HIVST to facility-based HTC. This was to enable data collected from the previous study to be linked to this study, and to obtain information of past HIV testing on those who were recruited into this study but not in the previous study. Ethical approval was obtained from the College of Medicine Ethics Review Committee, University of Malawi; and the University of Warwick Biomedical Research Ethics Committee (**Appendix I**). All participants received the same information leaflets and the same procedures were followed to obtain informed consent (**Appendix VI; VII; VIII; IX**).

6.2.2 Overview

The study compares the economic impact of accessing HIV treatment for those who test HIV positive. The study also examines this in the context of the modality of HIV testing received, aiming to compare the effects of HIVST or standard facility-based HTC. HIV positive participants were recruited into the study if they attended health facilities in Blantyre, Malawi to be assessed for eligibility for ART. Observation of participants was divided into two time periods. The first time period (pre-ART) was from initial visit to the health facility until participants either initiated anti-retroviral therapy or were assessed to be ineligible for ART. The second time period (ART) was from initiation of anti-retroviral therapy until completion of the first on treatment.

Figure 33 provides an overview of these two time periods and how they relate to the clinical care participants received. For each time period, I investigated direct health provider costs, direct non-medical and indirect costs of accessing HIV care, and health-related quality of life (HRQoL) of participants.

Figure 33: Description of observation period for HIV cohort study



6.2.3 Study setting and study population

I recruited a cohort of adults (aged ≥ 18 years) who were participants in a cluster-randomised trial, undertaken in three high-density urban suburbs (Ndirande, Chilomoni and Likabhula) of Blantyre, Malawi (Choko et al., 2015a). The methods used in the trial have been described previously (Chapter 2). Participants were

recruited into this cohort study if they were cluster residents and they attended the health facility to be assessed for eligibility for ART.

For this study eligible participants included those who had been recruited into the previous cross-sectional study comparing HIVST to facility-based HTC and who tested HIV positive (Chapter 5). They were only recruited into this component of the study if they returned to the health facility to be assessed for ART eligibility following testing. In addition, cluster residents who attended the three health facilities to be assessed for ART eligibility and who had accessed either modality of HIV testing after the main cluster-randomised trial had started were also recruited into this cohort study. Recruitment was undertaken at the same three health facilities serving the cluster residents: Queen Elizabeth Central Hospital (QECH); Ndirande Health Centre; and Chilomoni Health Centre. This present study also recruited participants from February 2013 to April 2014. The “Map Book” approach was again used to determine cluster of residence (MacPherson et al., 2013), and consequently whether participants were eligible for recruitment into this study.

In Malawi more broadly and in the study clinics specifically, those who test HIV positive access the HIV treatment clinic at health facilities for subsequent HIV care. At the health facility HIV positive individuals are seen by a health professional for an initial assessment which includes CD4 count measurement, screening for presence of active Tuberculosis, WHO clinical staging and provision of cotrimoxazole. Individuals

may be required to visit the health facility multiple times to complete this assessment. Individuals who meet the Malawi national ART eligibility criteria (CD4 count <350 cells/mm³ or WHO stage 3 or 4, or breastfeeding or pregnant) are subsequently initiated onto ART.

Those who are eligible for ART attend a group counselling session to prepare for initiation onto treatment, and if ready, are given the anti-retroviral (ARV) medications. Individuals are then asked to return to the health facility at regular intervals to see a nurse and obtain further supplies of ARVs and other relevant medications (e.g. Cotrimoxazole). On each return visit to the health facility, the individual is seen by a nurse who assesses them for any problems including ARV drug adherence (or lack of) and side-effects from taking the ARVs, and screens them for other clinical problems including TB. The nurse may refer patients to be seen by a clinical officer or doctor if there are any problems that cannot be managed. At the clinic, individuals may also have investigations or be given medications for treatment of other illnesses. Of note, individuals attending the ART clinic at QECH may be referred by the nurse to either a doctor or clinical officer, whilst at the two health centres (Ndirande Health Centre and Chilomoni Health Centre), only referral to a clinical officer is possible. At each visit to the health facility after ART initiation, the nurse will provide the individual with a date for a return visit to the clinic and sufficient ARV drug supplies until that date. Frequency of visits may be as regular as one per week, or as irregular as six monthly, and will depend on the patients' response to ART.

Participants recruited into this cohort study were seen at their first attendance to the health facility for assessment for ART eligibility. The field worker then saw the participants at each subsequent visit to the health facility. At each visit to the health facility, the field worker asked the participant a series of pre-specified questions about the medical management they received, the direct non-medical and indirect costs that were incurred and their health-related quality of life. For their medical management, the participant was asked about the results of their CD4 measurements, their ART regimen and any side effects experienced from taking the treatment, as well as findings from their screening for TB. In addition, participants were asked about which medical personnel they saw at the clinic, any investigations performed and any other medications given. **Appendix XIII** shows the questionnaires the field worker completed with participants at each visit. Participation follow-up was for a one year from anti-retroviral therapy initiation, with participants censored if they were not eligible for ART or if they were lost to follow-up.

6.2.4 Cost analysis

6.2.4.1 Direct health provider costs

I undertook economic costing of care provision models at the three health facilities (QECH; Ndirande Health Centre; and Chilomoni Health Centre) providing the HIV care and treatment to the study participants. Economic costing was undertaken from the health provider perspective (UNAIDS, 2011, Drummond et al., 2005b), and followed the same macro-costing principles used in Chapter 5 and described in Chapter 4.

I interviewed the senior nurse at each health facility to determine the resources used in providing medical care provided to study participants. I also interviewed central administrative staff at the Blantyre District Health Office that manage the two health facilities (Ndirande and Chilomoni), and central administrative staff at the Queen Elizabeth Central Hospital (QECH) to estimate costs for central support and overheads. All the interviews followed the same procedures described in Chapter 5, and used the same data extraction tool to record resources used (**Appendix XII**).

I estimated the average cost of visiting each of the three health facilities and the *average cost per consultation* for the different types of medical staff. Participants could be seen by: a counsellor, a nurse, a clinical officer or a doctor. I obtained the average annual salaries for each of these and the average time each spent with their patients.

To estimate the *average cost per health facility visit*, I recorded all the staff that worked at the facility and the proportion of their working time they spent not in direct contact with patients. I recorded the consumables and their respective quantities used annually. I also made a list of all equipment at each clinic. I then obtained estimates for central support costs from the central administrative staff. These included the costs for utilities, security and building maintenance. I included the costs of monitoring and evaluation visits by the HIV teams at the Blantyre District Health Office and Malawi Ministry of Health (MoH). There was no cost available for

the purchase or construction of the buildings at the health facilities. However, the rooms at the clinics are often rented for research studies, and therefore the proxy rental costs were used. I took into account the number of clinic rooms and waiting areas at each of the health facilities and multiplied these numbers by their respective rental costs. For the HIV Clinic at QECH, I followed the same principle for estimating the central administrative and overhead costs as in Chapter 5. I estimated the total capital and overhead costs (undertaken in Chapter 7) and allocated a proportion of this cost to the total running cost, based on the ratio of clinical personnel working in the clinic to the total number of clinical personnel working at the hospital, and only included costs relevant to providing the HIV treatment service.

Staff salaries were obtained from the employer, and included employer contributions and fringe benefits. I followed the same process in obtaining unit costs for consumables and equipment's used at the HIV clinics. The costs of consumables and equipment's were obtained from the Malawi Ministry of Health price catalogue, which includes the cost of shipping for imported goods. For items not supplied by the Malawi MoH, I used the on-land costs obtained from local suppliers. For items bought internationally, I included the cost of shipping and insurance provided in the quote. I assumed the useful life of equipment to be 3 years, and annuitized costs at an annual discount rate of 3% (WHO, 2003a).

After estimating the total cost of each clinic, excluding the cost of direct patient contact, I obtained the outputs of the clinic. The clinics record and report to the Blantyre District health office, and Malawi MoH, the total numbers of individuals attending the clinic for HIV care. I divided the total cost by these attendance data to estimate the average health provider cost of a health facility visit.

I used the international market price for the cost of medications, including anti-retroviral medications (Health, 2013). Medications at the clinics are supplied from central pharmacy and dispensed by the nurses at the clinics. I therefore took into account the cost of dispensing the drug by central pharmacy by using the average costs per prescription estimated in Chapter 7. This cost was added to the international market price, and equated to US\$0.0058 (INT\$ 0.0162) per dosage of drug (Chapter 7, Table 46). Investigations undertaken at the health facilities are processed (e.g. HIV viral load) or performed at QECH (e.g. Chest X-Ray). I therefore used the costs of investigations I estimated for QECH (Chapter 7, Table 43 and Table 44). Of note, during the study period HIV viral load was not routinely undertaken.

6.2.4.2 Direct non-medical and indirect costs

HIV treatment is provided free to individuals in Malawi; however, individuals will incur costs when attending the health facility. These costs include the cost of transportation, food and drinks whilst waiting. In addition, they may take time off work or be accompanied by a carer or family member. As these cost categories are

comparable to those estimated in Chapter 5, I followed the same approach in quantifying the direct non-medical and indirect costs incurred by individuals on each visit to the clinic. At each visit, participants were asked about the direct non-medical costs that they or their accompanying family members or carers incurred in accessing HIV treatment services, and the associated work losses (**Appendix XIII**). The questions were adapted from those developed in Chapter 5 and translated into Chichewa, the local language of the study population. The questionnaire was pilot tested and discussions were held with senior Malawian staff working at the Malawi-Liverpool Wellcome Trust Clinical Research Programme, to determine if additional questions should be added to optimise the questionnaire.

6.2.4.3 Cost conversions

All costs were converted into 2014 US Dollars and International Dollars (Drummond et al., 2005b) using data reported by the World Bank (Evans et al., 2005). For all unit costs the currency, price year and country were recorded. A Gross Domestic Product (GDP) deflator index, provided by the World Bank, was used to adjust costs from the price year to the year of reporting (2014). All costs were then converted into 2014 US Dollars using the market exchange rate, and to 2014 International dollars using the purchasing power parity conversion factor (Krijnse Locker and Faerber, 1984, Shemilt et al., 2010).

6.2.5 Health-related quality of life

On each visit to the clinic, participants were asked about their health-related quality of life (HRQoL). The self-assessed health (SAH) measure was used to ask individuals to rate their general health on a five-point Likert scale, with responses coded as: very good; good; fair; poor; or very poor.

The Chichewa EuroQoL EQ-5D-3L (Dolan, 1997) was used to estimate the HRQoL of all study participants (**Appendix XIII**). Participants completed both the descriptive EQ-5D-3L system and a visual analogue scale (EuroQol, 1990). A more detailed description of the EQ-5D tool is provided in Chapter 4 of the PhD. Briefly, the responses to the five dimensions in the EQ-5D-3L descriptive system are converted into an EQ-5D utility score using a tariff. Tariff sets have been derived from national surveys of the general population, with a subset of the 243 health states being valued, most commonly using the time trade-off method (EuroQol 1990). The remainder of the EQ-5D health states are subsequently valued through the estimation of a multivariable model. As there is no Malawian EQ-5D tariff, I used the Zimbabwean EQ-5D tariff set (Jelsma et al., 2003) to derive an EQ-5D utility score for each study participant. The other component of the EQ-5D tool is the visual analogue scale (VAS), similar to a thermometer, and ranges from 100 (best imaginable health state) to 0 (worst imaginable health state). Participants record how good or bad their health is on that day by drawing a line on the scale.

6.2.6 Statistical analysis

All analyses were undertaken in Stata version 13.0 (Stata Corporation, Texas, USA). Socio-demographic data was collected on all participants recruited into the study. For this I used the same questionnaire as used in Chapter 5 (**Appendix X**). The questionnaires recorded the sex, age, marital status, educational attainment, employment status, and self-reported income of participants. For socio-economic position, I undertook principal component analysis (described in Chapter 5) to classify an individual's socio-economic position based on wealth quintiles (Filmer and Pritchett, 2001).

I estimated the total direct health provider cost for each clinic visit recorded. The total direct health provider cost was estimated by adding the: (1) *average cost per health facility visit*; (2) *average cost per consultation*; (3) cost of all medications given; and (4) cost of all investigations performed. I then allocated each clinic visit cost to one of the two main observation periods: (1) pre-ART observation period; or (2) ART observation period (Figure 33). The pre-ART observation period included all the costs that were incurred before the participant started anti-retroviral therapy. The ART observation period included all the costs that were incurred after the participant started anti-retroviral therapy. To determine the observation period to which the costs were to be allocated I used the date of initiation of anti-retroviral therapy. I followed the same processes for the allocation of the direct non-medical and indirect costs to the relevant observation period.

I estimated the total societal cost per study participant by adding the total health provider cost to the total direct non-medical and indirect costs. I estimated the mean costs for each cost category (total health provider; total direct non-medical and indirect; total societal) and used non-parametric bootstrap methods, with 1000 bootstrap replications, to derive 95% confidence intervals (CIs) for the mean cost estimates.

I undertook multivariable analysis to investigate the association between the total direct health provider cost and total societal cost during the two observation periods and the; (1) modality of HIV testing received prior to entry into HIV care; and (2) baseline CD4 count on entry into HIV care. For the costs incurred in the pre-ART observation period, I also adjusted for the number of CD4 counts done to take into account that some participants were not eligible to initiate anti-retroviral therapy and were asked to return at approximately 6 monthly intervals for re-assessment of eligibility. For the ART observation period, I also adjusted for the month from starting ART (as a categorical variable). For these multivariable analysis I ran two alternative models, the first was additionally adjusted for age and sex (model 1); the second was additionally adjusted for age, sex, marital status, educational attainment, income and socio-economic position (model 2) (Stangl et al., 2007). For the multivariable analysis, I used generalized linear models (GLM) as the cost data was skewed (Barber and Thompson, 2004). I ran the same set of model diagnostics applied in Chapter 5 to determine the optimal choices for the distributional family and link function (Manning and Mullahy, 2001).

For the analysis of HRQoL, I estimated the mean EQ-5D utility score and VAS score, and used non-parametric bootstrap methods, with 1000 bootstrap replications, to derive 95% confidence intervals (CI) for the mean scores. I undertook multivariable analysis to investigate the independent effect of the CD4 count (pre-starting ART) and modality of HIV testing received on the EQ-5D utility score before starting ART. For this I followed the same approach as described in Chapter 5 and evaluated four commonly used estimators: ordinary least squares (OLS) regression; Tobit regression, Fractional logit regression (Flogit), and censored least absolute deviations (CLAD) regression (Powell, 1984, Austin et al., 2000, Papke and Wooldridge, 1996). For these multivariable analysis I ran two alternative models, the first was additionally adjusted for age and sex (model 1); the second was additionally adjusted for age, sex, marital status, educational attainment, income and socio-economic position (model 2) (Stangl et al., 2007).

For those who initiated antiretroviral therapy, I also undertook multivariable analysis to investigate the independent effect of the baseline CD4 count, modality of HIV testing received and time on anti-retroviral therapy on the EQ-5D utility score. I used generalised estimating equation (GEE) model to account for correlation of utility scores within individuals (Zeger et al., 1988, Zorn, 2001). For these multivariable analysis I ran two alternative models, the first was additionally adjusted for age and sex (model 1); the second was additionally adjusted for age, sex, marital status, educational attainment, income and socio-economic position (model 2) (Stangl et al.,

2007). In addition, I also ran a third model that additionally adjusted for the baseline EQ-5D utility score (model 3) (Manca et al., 2005).

6.2.7 Sensitivity analysis

I undertook sensitivity analysis to investigate the impact of using an alternative tariff set to determine EQ-5D utility scores. I used the UK York A1 tariff (Dolan et al., 1996a), which has been found to translate health states with 'severe' problems in one or more of the five dimensions to a lower EQ-5D utility scores than the Zimbabwean tariff (Jelsma et al., 2003).

6.3 Results

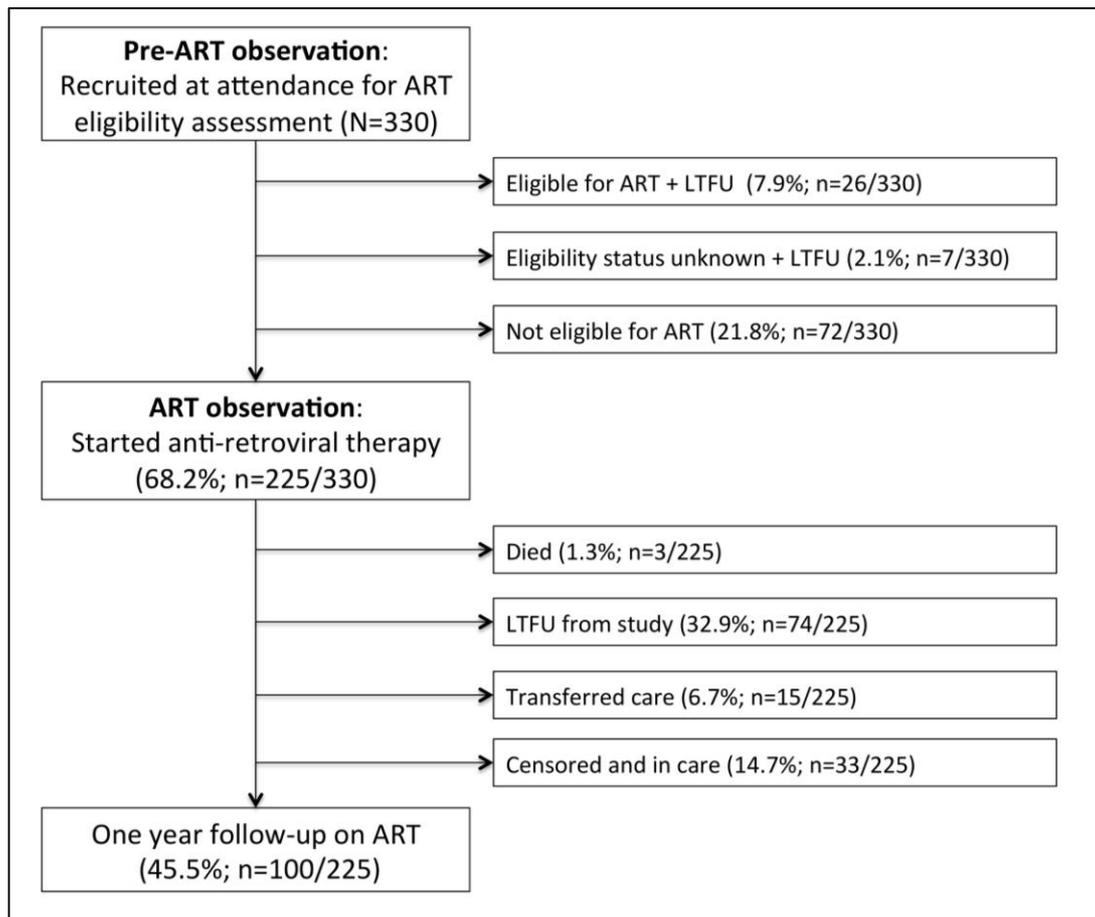
6.3.1 Participant characteristics

Figure 34 shows the recruitment and follow-up of participants in the study. In total, 330 participants were recruited and observed during their attendance at the health facilities for assessment of eligibility for anti-retroviral therapy (pre-ART observations). 21.8% (72/330) were found not to be eligible to start ART, 7.9% (29/330) were found to be eligible for ART but did not start, and 2.1% were lost to follow-up before a decision had been made on whether they were eligible for anti-retroviral therapy.

In total, 68.2% (225/330) participants started ART and were followed-up in the study (ART observations). Of those who did start ART, 45.5% (100/225) had been on ART for one year when the study finished, whilst 14.7% (33/225) had been on treatment for less than one year. In addition, of those who did start ART, 1.3% (3/225) were known to have died by the end of the observation period, 32.9% (74/225) were lost to follow-up and 6.7% (15/225) had transferred their care to a non-study clinic.

Table 18 shows the characteristics of participants who were observed for the two time periods of the study.

Figure 34: Recruitment and follow-up of participants



LTFU: Lost to follow-up

Table 18: Characteristics of recruited participants

		Pre-ART Observation	ART Observation
		n (%)	n (%)
All		330	225
Sex	Male	131 (39.7%)	90 (40.0%)
	Female	199 (60.3%)	135 (60.0%)
Age (years)	18-24	44 (13.3%)	29 (12.9%)
	25-39	208 (63.0%)	141 (62.7%)
	40+	78 (23.6%)	55 (24.4%)
Marital status	Single (never-married)	24 (7.3%)	18 (8.0%)
	Married/Cohabiting	224 (67.9%)	157 (69.8%)
	Separated/Divorced	55 (16.7%)	30 (13.3%)
	Widower/Widow	27 (8.2%)	20 (8.9%)
Educational attainment	Up to standard 8	211 (63.9%)	138 (61.3%)
	Up to form 6	117 (35.5%)	85 (37.8%)
	University or training college	2 (0.6%)	2 (0.9%)
Income	0 Kwacha/week	110 (33.3%)	77 (34.2%)
	Up to 4,000 Kwacha/week	943(28.2%)	59 (26.2%)
	4,000 to 8,000 kwacha/week	55 (16.7%)	34 (15.1%)
	8,000 to 12,000 kwacha/week	28 (8.5%)	23 (10.2%)
	Over 12,000 kwacha/week	44 (13.3%)	32 (14.2%)
Employment status	Formal employment	83 (25.2%)	55 (24.4%)
	Informal employment/Unemployed	139 (42.1%)	96 (42.7%)
	School/University	9 (2.7%)	7 (3.1%)
	Retired	2 (0.6%)	1 (0.4%)
	Housework	95 (28.8%)	65 (28.9%)
	Sick leave	2 (0.6%)	1 (0.4%)
Socio-economic position[¶]	Highest quintile	63 (19.1%)	39 (17.3%)
	2nd highest quintile	71 (20.9%)	52 (23.1%)
	Middle quintile	67 (20.3%)	49 (21.8%)
	2nd lowest quintile	65 (19.7%)	44 (19.6%)
	Lowest quintile	64 (19.4%)	41 (18.2%)
HIV Testing Location	Facility-based HIV testing	269 (81.5%)	186 (82.7%)
	HIV self-testing	61 (18.5%)	39 (17.3%)
CD4 Count	CD4 count >=350	107 (32.4%)	34 (15.1%)
	CD4 count 200-350	82 (24.8%)	71 (31.6%)
	CD4 count 50-200	89 (27.0%)	80 (35.6%)
	CD4 count <50	15 (4.5%)	10 (4.4%)
	Not done or missing	37 (11.2%)	30 (13.3%)

[¶]Socio-economic position estimated though undertaking principal component analysis of responses to assets and housing environment

6.3.2 Direct health provider costs of HIV treatment clinics

Table 19 shows the direct health provider cost of a single consultation with the different health professionals working at the HIV clinics. The estimated direct health provider cost per consultation was estimated at US\$0.18 (INT\$0.49) for a HIV counsellor, US\$0.59 (INT\$1.64) for a nurse, US\$0.89 (INT\$2.46) for a clinical officer and US\$5.51 (INT\$15.31) for a doctor.

Table 19: Direct Health Provider costs of consultation with health professional

Health Professional	Average time (Minutes)	Health provider cost	
		2014 US Dollars	2014 INT Dollars
Consultation with HIV Counsellor	10	0.18	0.49
Consultation with Nurse	20	0.59	1.64
Consultation with Clinical Officer	30	0.89	2.46
Consultation with Doctor*	30	5.51	15.31

*Consultation with Doctors only at HIV clinic at Queens Elizabeth Central Hospital.

Table 20 shows the annual cost of the three health facilities providing HIV care in this study. The costs excludes the direct cost for the time health professionals spent in direct contact with patients at the health facilities providing one to one consultation. The *average cost per health facility visit* was US\$2.42 (INT\$6.71), US\$3.25 (INT\$9.03), and US\$3.57 (INT\$9.75) for Ndirande, Chilomoni and QECH HIV clinics, respectively.

Table 20: Annual Direct Health Provider costs of HIV Treatment Clinics (excluding clinical contact)

Costs	Ndirande HIV clinic			Chilomoni HIV Clinic			QECH HIV Clinic		
	US Dollars (2014)	INT Dollars (2014)	% of Total*	US Dollars (2014)	INT Dollars (2014)	% of Total*	US Dollars (2014)	INT Dollars (2014)	% of Total*
Personnel Cost*	12,524	34,789	22.4%	11,494	31,928	24.1%	58,632	162,865	29.9%
Consumables	29,543	82,004	52.9%	19,140	53,105	40.1%	60,621	159,689	29.3%
Rental Space	1,504	4,179	2.7%	1,504	4,179	3.2%	5,732	15,921	2.9%
Equipment	7,233	20,092	13.0%	7,621	21,169	16.0%	21,140	57,440	10.5%
Central Support and Overheads	5,069	14,081	9.1%	7,947	22,075	16.7%	53,559	148,775	27.3%
Total cost (excluding clinical contact)	55,874	155,146		47,706	132,456		199,683	544,690	
Average cost per clinic visitation (excluding clinical contact)	2.42	6.71		3.25	9.03		3.57	9.75	

*Personnel cost excludes the proportion of time clinical personnel spent in direct contact with patients

6.3.3 Pre-ART observation

6.3.3.1 Cost analysis for pre-ART observational period

Figure 35 to Figure 37 show the respective distributions for the total health provider costs, total direct non-medical costs and total societal costs for participants during the pre-ART observational period by the modality of HIV testing received and their CD4 count. The box plot shows the mean costs with 95% confidence intervals, and dots represent outliers.

Figure 35: Box plot showing the distribution of total health provider costs (2014 US Dollars) by HIV testing modality and CD4 count (n=297)

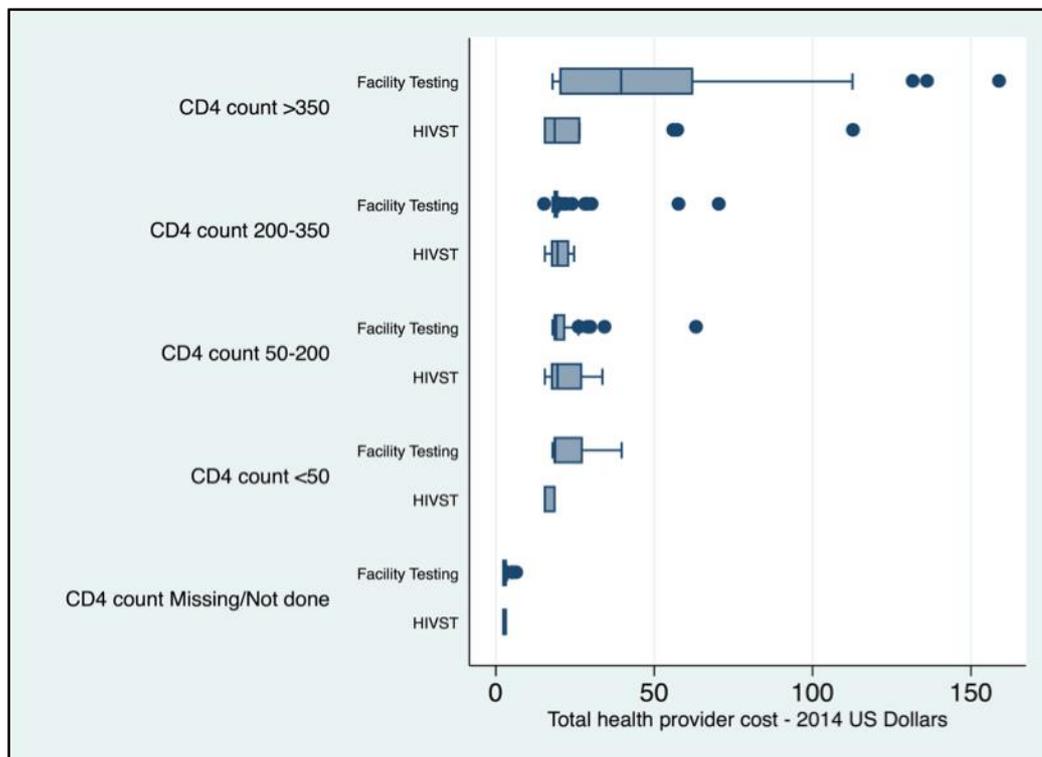


Figure 36: Box plot showing the distribution of total direct non-medical and indirect costs (2014 US dollars) by HIV testing modality and CD4 count (n=297)

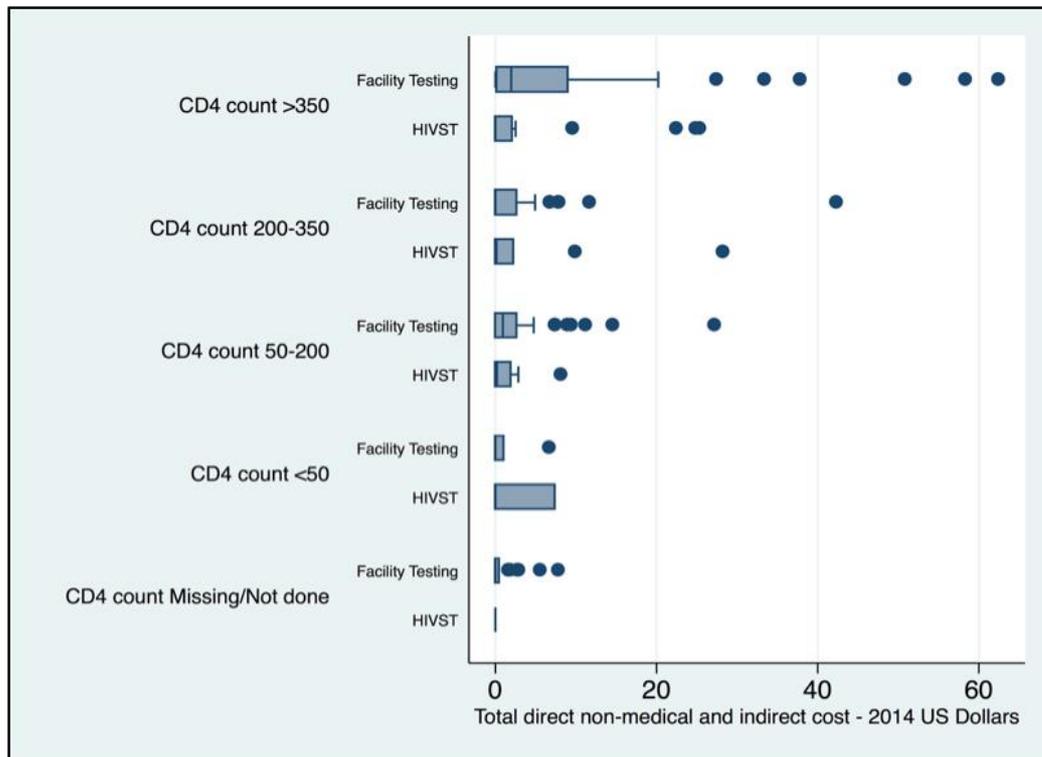


Figure 37: Box plot showing the distribution of total societal costs (2014 US dollars) by HIV testing modality and CD4 count (n=297)

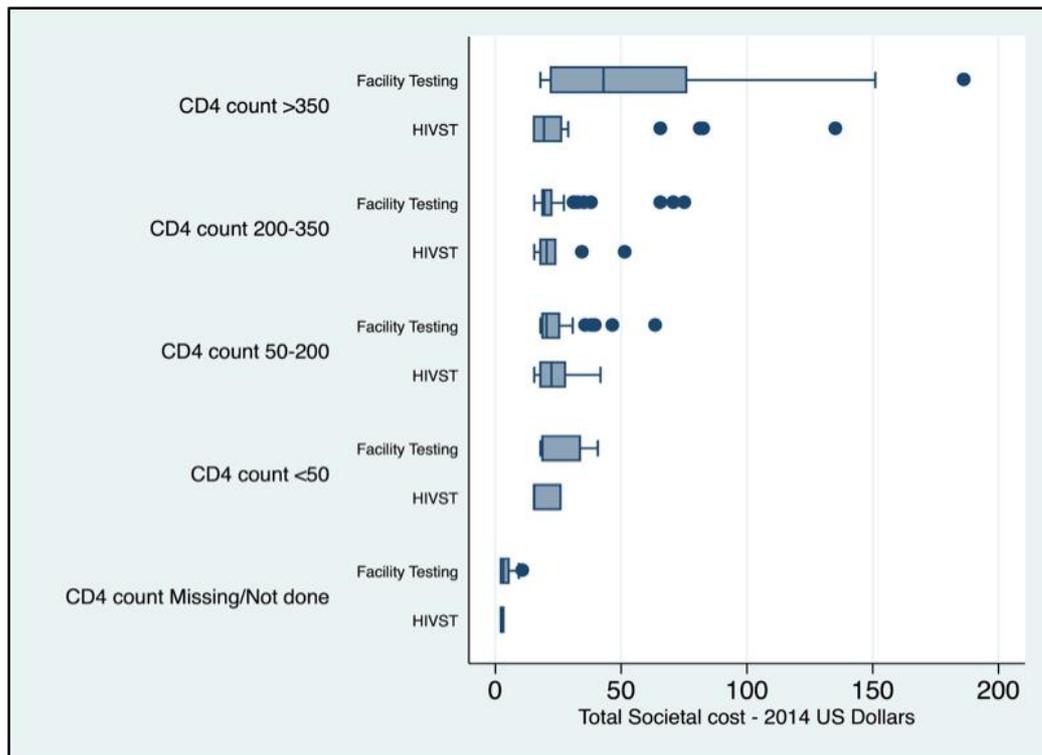


Table 21 shows the mean total health provider cost, mean total direct non-medical and indirect costs and mean total societal cost for all participants, and by the participants CD4 count.

For all the participants, the mean total health provider cost of the pre-ART period was US\$27.28 (INT\$71.83). The mean total health provider cost during the pre-ART period was highest for participants with a CD4 count greater than 350 cells/ μ l (US\$43.05; bootstrap 95%CI, US\$337.26-US\$48.83).

During the pre-ART period, the mean total direct non-medical and indirect costs incurred by participants was US\$3.69 (INT\$10.24). The mean total direct non-medical and indirect costs was highest for participants with a CD4 count greater than 350 cells/ μ l (US\$6.70; bootstrap 95%CI, US\$4.48-US\$8.91).

For all participants, the mean total societal cost was US\$30.97 (INT\$82.07). The mean total societal costs were highest for participants with a CD4 count greater than 350 cells/ μ l (US\$49.74; bootstrap 95%CI, US\$42.84-US\$56.64).

Table 21: Mean total costs for pre-ART observations

		n	Mean Total Costs	
			2014 US Dollars	2014 INT Dollars
			Mean (95% CI)*	Mean (95% CI)*
Total health provider cost	ALL	297	27.28 (24.69, 29.87)	71.83 (65.47, 78.20)
	CD4 count >350	107	43.05 (37.26, 48.83)	109.37 (95.29, 123.46)
	CD4 count 200-350	71	21.10 (19.21, 22.99)	58.29 (53.16, 63.42)
	CD4 count 50-200	79	21.44 (20.09, 22.78)	58.98 (55.27, 62.70)
	CD4 count <50	10	20.99 (16.35, 25.63)	57.56 (46.01, 69.11)
	Not done or missing	30	3.16 (2.76, 3.56)	8.60 (7.65, 9.54)
Total direct non-medical and indirect cost	ALL	297	3.69 (2.75, 4.62)	10.24 (7.68, 12.79)
	CD4 count >350	107	6.70 (4.48, 8.91)	18.60 (12.37, 24.83)
	CD4 count 200-350	71	2.48 (1.02, 3.93)	6.88 (2.82, 10.95)
	CD4 count 50-200	79	2.08 (1.17, 2.99)	5.77 (3.19, 8.35)
	CD4 count <50	10	1.51 (-0.42, 3.44)	4.20 (-1.07, 9.47)
	Not done or missing	30	0.76 (0.08, 1.46)	2.13 (0.26, 4.01)
Total societal cost	ALL	297	30.97 (27.94, 33.99)	82.07 (74.32, 89.82)
	CD4 count >350	107	49.74 (42.84, 56.64)	127.97 (110.86, 145.08)
	CD4 count 200-350	71	23.58 (20.92, 26.24)	65.17 (58.19, 72.25)
	CD4 count 50-200	79	23.51 (21.83, 25.20)	64.75 (60.23, 69.28)
	CD4 count <50	10	22.50 (17.17, 27.83)	61.76 (48.03, 75.49)
	Not done or missing	30	3.92 (3.12, 4.73)	10.73 (8.50, 12.95)

*Bootstrapped estimates with 1000 replications for 95%CI

Table 22 shows the mean total health provider cost, mean total direct non-medical and indirect costs and mean total societal cost by the modality of HIV testing participants accessed before attending the HIV clinic to be assessed for ART eligibility. The mean total health provider cost during the pre-ART period was lower for those participants who had accessed HIVST to learn their HIV status (US\$22.74; bootstrap

95%CI: US\$18.48-US\$27.00), than those who had accessed facility-based HTC (US\$28.33; bootstrap 95%CI: US\$25.31-US\$35.36). In addition, the mean total direct non-medical and indirect costs, and the mean total societal costs were lower for participants who had accessed HIVST to learn their HIV status than those who had accessed facility-based HTC.

Table 22: Mean total costs of pre-ART observations by modality of HIV testing received

		Mean Total cost	
		HIV self-testers (n=62) Mean (95% CI)*	Facility HIV testers (n=268) Mean (95% CI)*
Total Health Provider cost	2014 US Dollars	22.74 (18.48, 27.00)	28.33 (25.31, 35.36)
	2014 INT Dollars	60.65 (50.49, 70.81)	74.43 (66.82, 82.04)
Total direct non-medical and indirect cost	2014 US Dollars	2.81 (1.09, 4.53)	3.89 (2.79, 4.99)
	2014 INT Dollars	7.81 (3.17, 12.46)	10.80 (7.85, 13.75)
Total Societal cost	2014 US Dollars	25.56 (20.20, 30.91)	32.22 (28.61, 35.83)
	2014 INT Dollars	68.47 (54.35, 82.59)	85.23 (75.99, 94.48)

*Bootstrapped estimates with 1000 replications for 95%CI

Table 23 shows the multivariable analysis investigating the independent effect of modality of HIV testing, baseline CD4 count and number of CD4 counts measured during the pre-ART period on mean **total health provider costs**. In the multivariable analysis (Table 23), after adjusting for individual characteristics and baseline CD4 count, the mean total health provider cost during the pre-ART period was US\$1.91 (95%CI: US\$0.60-US\$3.22) lower for those who had accessed HIV care after HIVST

than for those who had accessed HIV care after facility-based HTC (model 2). In comparison to those whose CD4 count was greater than 350 cells/ μ l, those with lower CD4 counts had a lower mean total health provider cost during the pre-ART observation period (Table 23). The mean total health provider cost was higher for those who had two or more CD4 counts measured, than for those who only had one CD4 count measured.

Table 24 shows the multivariable analysis investigating the independent effects of modality of HIV testing, baseline CD4 count and number of CD4 counts measured during the pre-ART period on the mean **total societal costs**. In this multivariable analysis, the mean total societal cost during the pre-ART period was US\$2.39 (95%CI: US\$0.69-US\$4.09) lower for those who had accessed HIV care after HIVST than for those who had accessed HIV care after facility-based HTC (model 2). In comparison to those whose CD4 count was greater than 350 cells/ μ l, those with lower CD4 counts had a lower adjusted mean total societal cost during the pre-ART observation period (Table 24). In the multivariable analysis, the mean total societal cost during the pre-ART period was US\$10.24 (95%CI: US\$5.32-US\$15.16) less for those whose CD4 count was between 200 cells/ μ l and 350 cells/ μ l than for those whose CD4 count was greater than 350 cells/ μ l (model 2). In the multivariable analysis, the mean total societal cost was also higher for those who had two or more CD4 counts measured, than for those who only had one CD4 count measured.

Table 23: Multivariable analysis exploring relationship between CD4 count and modality of HIV testing received and the total pre-ART Health Provider costs*

		Total Health Provider cost (2014 US Dollars)		Total Health Provider cost (2014 INT Dollars)	
		Model 1 (n=330)	Model 2 (n=330)	Model 1 (n=330)	Model 2 (n=330)
		Coef (95% CI)	Coef (95% CI)	Coef (95% CI)	Coef (95% CI)
Modality of HIV testing	Facility-tested	Ref	Ref	Ref	Ref
	HIV self-tested	-0.91** (-1.81, -0.01)	-1.91** (-3.22, -0.60)	-2.26** (-4.48, -0.05)	-5.25** (-8.64, -1.85)
Baseline CD4 count	CD4 count >350 cells/μl	Ref	Ref	Ref	Ref
	CD4 count 200-350 cells/μl	-7.64** (-11.31, -3.98)	-7.77** (-11.37, -4.17)	-15.77** (-24.37, -7.18)	-16.03** (-24.34, -7.72)
	CD4 count 50-200 cells/μl	-7.34** (-10.75, -3.93)	-7.47** (-10.84, -4.10)	-15.18** (-22.96, -7.39)	-15.46** (-23.04, -7.88)
	CD4 count <50 cells/μl	-7.59** (-12.76, -2.43)	-7.95** (-12.73, -3.16)	-15.96** (-28.51, -3.40)	-16.70** (-28.06, -5.35)
	Not done or missing	-25.58** (-28.75, -22.41)	-25.69** (-28.86, -22.53)	-65.39** (-72.40, -58.38)	-65.62** (-72.57, -58.67)
Number of CD4 counts during pre-ART period	0 or 1	Ref	Ref	Ref	Ref
	2	33.33** (25.45, 41.20)	32.91** (24.86, 40.96)	83.51 (66.26, 100.77)	82.44** (64.78, 100.11)
	3	88.33** (74.77, 101.89)	87.57** (74.02, 101.11)	216.62 (183.13, 248.11)	213.71** (181.27, 246.15)
	4	67.06** (63.78, 70.34)	64.36** (60.41, 68.31)	174.95 (167.53, 182.38)	168.28** (159.04, 177.52)
Constant		28.80 (25.53, 32.08)	29.76 (26.08, 33.43)	73.80 (66.48, 81.11)	75.75** (67.48, 84.03)

Model 1: adjusted for exposure, HIV test result, Age and Sex

Model 2: additionally adjusted for marital status, educational attainment, income and wealth quintile

*Findings from Generalized Linear Model with Poisson distribution and Identity link function

**p<0.05

Table 24: Multivariable analysis exploring relationship between CD4 count and modality of HIV testing received and the total pre-ART Societal costs*

		Total Societal cost (2014 US Dollars)		Total Societal cost (2014 INT Dollars)	
		Model 1 (n=330)	Model 2 (n=330)	Model 1 (n=330)	Model 2 (n=330)
		Coef (95% CI)	Coef (95% CI)	Coef (95% CI)	Coef (95% CI)
Modality of HIV testing	Facility-tested	Ref	Ref	Ref	Ref
	HIV self-tested	-1.27** (-2.35, -0.19)	-2.39** (-4.09, -0.69)	-3.11** (-5.74, -0.48)	-6.66** (-11.19, -2.14)
Baseline CD4 count	CD4 count >350 cells/ μ l	Ref	Ref	Ref	Ref
	CD4 count 200-350 cells/ μ l	-9.78** (-14.90, -4.66)	-10.24** (-15.16, -5.32)	-21.67** (-34.53, -8.81)	-22.66** (-34.76, -10.55)
	CD4 count 50-200 cells/ μ l	-9.77** (-14.47, -5.06)	-9.97** (-14.67, -5.28)	-21.89** (-33.50, -10.28)	-22.21** (-33.59, -10.84)
	CD4 count <50 cells/ μ l	-10.60** (-17.29, -3.90)	-10.85** (-17.42, -4.27)	-24.33** (-41.30, -7.40)	-24.66** (-41.14, -8.19)
	Not done or missing	-29.40** (-33.84, -24.97)	-29.52** (-33.96, -25.08)	-75.96** (-86.77, -65.14)	-76.05** (-86.68, -65.41)
Number of CD4 counts during pre-ART period	0 or 1	Ref	Ref	Ref	Ref
	2	40.70** (28.67, 52.73)	40.74** (28.36, 53.17)	104.02** (74.34, 133.69)	104.24** (73.84, 134.84)
	3	96.97** (79.56, 114.37)	95.76** (78.44, 113.08)	239.70** (195.95, 283.44)	236.71** (193.12, 280.29)
	4	69.05** (64.49, 73.60)	65.27** (59.84, 70.69)	180.65** (169.45, 191.84)	171.22** (158.02, 184.42)
	Constant	33.29 (28.67, 37.91)	31.12 (27.98, 38.27)	86.29 (74.91, 97.67)	84.67 (72.19, 97.15)

Model 1: adjusted for exposure, HIV test result, Age and Sex

Model 2: additionally adjusted for marital status, educational attainment, income and wealth quintile

*Findings from Generalized Linear Model with Poisson distribution and Identity link function

** $p < 0.05$

6.3.3.2 Health-related quality of life analysis

Figure 38 shows the distribution of the EQ-5D utility scores, derived from the Zimbabwean tariff, during the pre-ART observational period by the modality of HIV testing received prior to attending the HIV clinic, and the CD4 count on assessment for anti-retroviral therapy initiation. Figure 39 and Figure 40 show the distribution of the EQ-5D utility score, derived from the UK tariff, and the VAS scores, by modality of HIV testing received and CD4 count result. The box plots in Figure 38 to Figure 40 shows the mean costs with 95% confidence intervals (CIs), and dots represent outliers.

Figure 38: Box plot showing distribution of EQ-5D utility scores (Zimbabwean tariff) by HIV testing modality and CD4 count

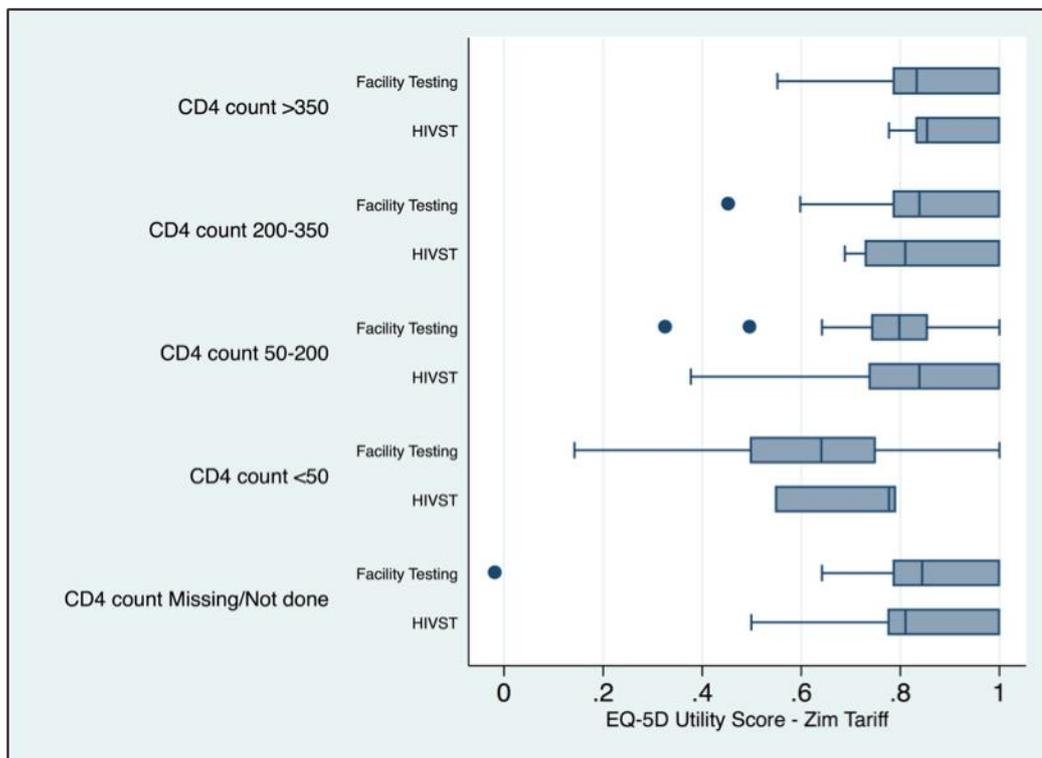


Figure 39: Box plot showing distribution of EQ-5D utility scores (UK tariff) by HIV testing modality and CD4 count

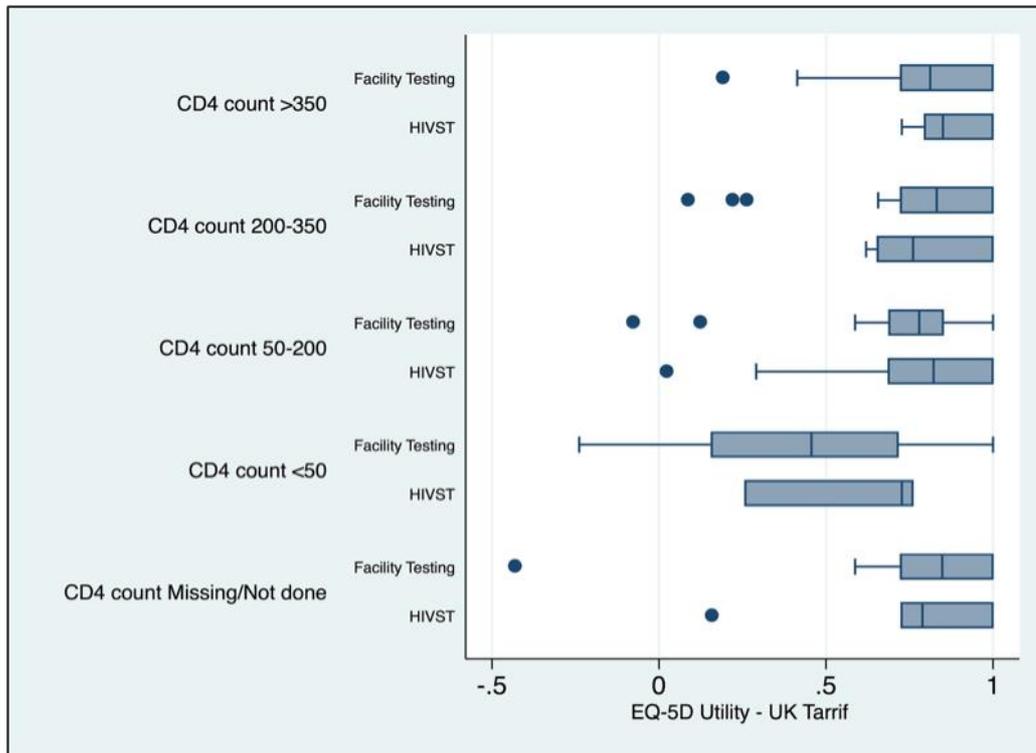


Figure 40: Box plot showing distribution of scores from the visual analogue scale by HIV testing modality and CD4 count

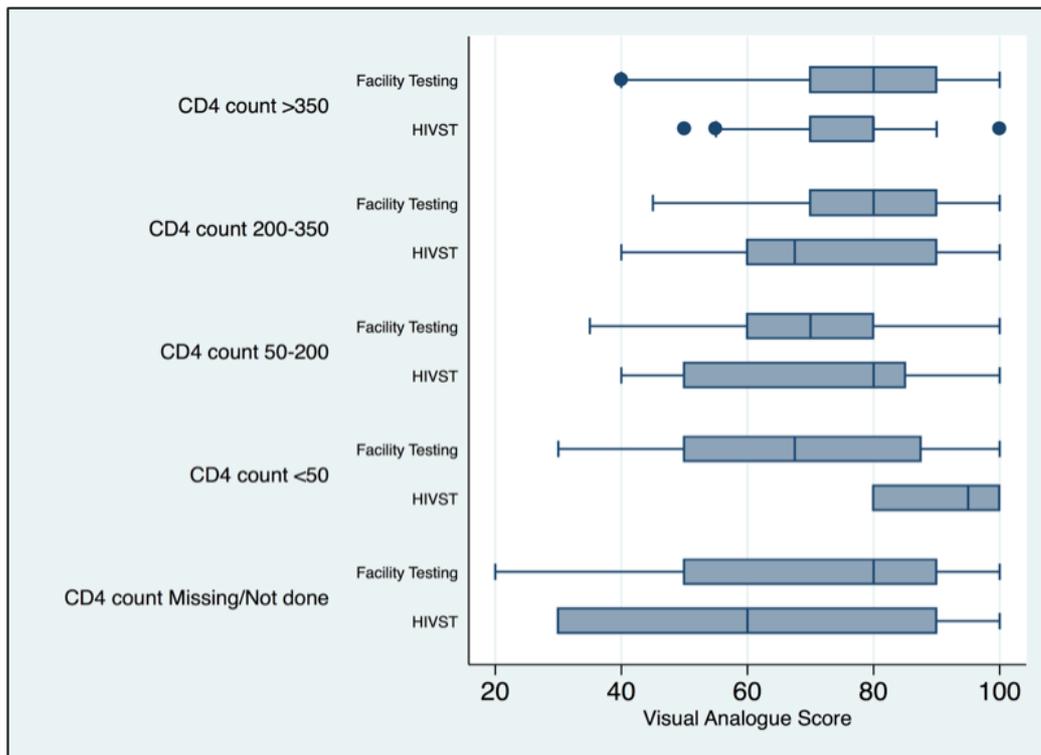


Table 25 shows the health-related quality of life scores for all participants, and by the participants' category of CD4 count measured in the assessment for ART initiation. The mean EQ-5D utility score was highest amongst those with a CD4 count greater than 350 cells/ μ l (0.872; bootstrap 95%CI, 0.852-0.892), and lowest for participants with a CD4 count below 50 cells/ μ l (0.640; bootstrap 95%CI, 0.536-0.744). The mean EQ-5D utility score was 0.860 (bootstrap 95%CI: 0.834-0.866) for those with a CD4 count between 200 cells/ μ l and 350 cells/ μ l, 0.817 (bootstrap 95%CI: 0.790-0.843) for those with a CD4 count between 50 cells/ μ l and 200 cells/ μ l, and 0.847 (bootstrap 95%CI: 0.784-0.910) for those with no recorded CD4 count.

Table 25: Health-related quality of life outcomes for pre-ART sample by CD4 counts

		Pre-ART Observation (n=330)
		Mean (95% CI)*
EQ-5D Utility Score	ALL	0.841 (0.825, 0.857)
	CD4 count \geq 350	0.872 (0.852, 0.892)
	CD4 count 200-350	0.860 (0.834, 0.886)
	CD4 count 50-200	0.817 (0.790, 0.843)
	CD4 count $<$ 50	0.640 (0.536, 0.744)
	Not done or missing	0.847 (0.784, 0.910)
EQ-5D Utility Score (UK Tariff)	ALL	0.798 (0.775, 0.821)
	CD4 count \geq 350	0.844 (0.818, 0.871)
	CD4 count 200-350	0.822 (0.784, 0.860)
	CD4 count 50-200	0.772 (0.732, 0.813)
	CD4 count $<$ 50	0.463 (0.288, 0.637)
	Not done or missing	0.806 (0.717, 0.894)
VAS Score	ALL	73.2 (71.3, 75.1)
	CD4 count \geq 350	76.3 (73.5, 79.1)
	CD4 count 200-350	75.5 (71.9, 79.2)
	CD4 count 50-200	68.9 (65.4, 72.4)
	CD4 count $<$ 50	72.0 (60.3, 83.7)
	Not done or missing	69.9 (62.6, 77.2)

*Bootstrapped estimates with 1000 replications for 95%CI

Table 26 shows the health-related quality of life scores by modality of HIV testing the participant underwent prior to attending the HIV clinic and the participant's CD4 count measured at assessment for ART initiation. The mean EQ-5D utility score was 0.856 (bootstrap 95%CI, 0.821-0.891) for all participants who accessed the HIV clinic after HIVST, compared to 0.837 (bootstrap 95%CI: 0.820-0.855) for those who had accessed the HIV clinic after facility-based HTC.

Table 26: Health-related quality of life outcomes for pre-ART sample by modality of HIV testing received and CD4 counts

		Pre-ART Observation	
		HIVST (n=61) Mean (95% CI)*	Facility HTC (n=269) Mean (95% CI)*
EQ-5D Utility Score	ALL	0.856 (0.821, 0.891)	0.837 (0.820, 0.855)
	CD4 count ≥350	0.909 (0.874, 0.944)	0.862 (0.839, 0.884)
	CD4 count 200-350	0.850 (0.777, 0.923)	0.862 (0.833, 0.891)
	CD4 count 50-200	0.826 (0.747, 0.904)	0.815 (0.788, 0.842)
	CD4 count <50	0.706 (0.374, 1.037)	0.624 (0.497, 0.750)
	Not done or missing	0.816 (0.654, 0.979)	0.853 (0.783, 0.922)
EQ-5D Utility Score (UK Tariff)	ALL	0.814 (0.761, 0.868)	0.794 (0.769, 0.819)
	CD4 count ≥350	0.901 (0.861, 0.940)	0.829 (0.797, 0.861)
	CD4 count 200-350	0.813 (0.722, 0.905)	0.824 (0.779, 0.868)
	CD4 count 50-200	0.761 (0.632, 0.890)	0.775 (0.735, 0.815)
	CD4 count <50	0.582 (0.205, 0.960)	0.433 (0.222, 0.644)
	Not done or missing	0.744 (0.469, 1.019)	0.818 (0.723, 0.912)
VAS Score	ALL	72.9 (68.0, 77.8)	73.3 (71.1, 75.4)
	CD4 count ≥350	74.8 (69.0, 80.6)	76.7 (73.5, 79.9)
	CD4 count 200-350	72.5 (61.4, 83.7)	76.1 (72.3, 79.9)
	CD4 count 50-200	71.3 (61.7, 80.8)	68.4 (64.7, 72.0)
	CD4 count <50	91.7 (56.9, 126.5)	67.1 (53.8, 80.3)
	Not done or missing	61.7 (35.3, 88.1)	71.5 (64.1, 78.9)

*Bootstrapped estimates with 1000 replications for 95%CI

In the multivariable analysis, the model diagnostics revealed the OLS estimator performed as well or better than the other estimators (Table 27 and Table 28). The CLAD estimator did not converge as the median observed EQ-5D utility score was censored. The EQ-5D utility scores predicted by the OLS estimator show close approximation to the observed EQ-5D utility scores in the sample.

Table 27: Estimated predicted values compared to actual utility scores

	Model	Obs	Mean	Min	Max	MSE	MAE
	Observed	330	0.841	-0.018	1.000		
	OLS	330	0.841	0.606	0.984	0.000	0.097
Model	TOBIT	330	0.847	0.592	0.961	0.006	0.098
	CLAD*	N/A	N/A	N/A	N/A	N/A	N/A
	Flogit	330	0.841	0.578	0.950	0.000	0.098

OLS: Ordinary Least Squares
Flogit: Fractional logit
CLAD: Censored least Absolute deviations

MSE: Mean Squared Error
MAE: Mean Absolute Error
*No convergence as median EQ-5D score censored at 1.0

Table 28: MSE and MAE for regression models by utility score range

		Observed EQ-5D utility score													
		<0		0 to <0.2		0.2 to <0.4		0.4 to <0.6		0.6 to <0.8		0.8 to <1		1	
Obs		1	1	2	2	11	11	127	127	83	83	105	105		
		MSE	MAE	MSE	MAE	MSE	MAE	MSE	MAE	MSE	MAE	MSE	MAE	MSE	MAE
OLS		0.829	0.829	0.465	0.465	0.461	0.461	0.196	0.196	0.071	0.081	0.011	0.036	0.137	0.137
TOBIT		0.842	0.842	0.458	0.458	0.467	0.467	0.199	0.199	0.077	0.087	0.016	0.040	0.129	0.129
Flogit		0.823	0.823	0.442	0.442	0.461	0.461	0.188	0.188	0.071	0.083	0.012	0.037	0.137	0.137

OLS: Ordinary Least Squares
MSE: Mean Squared Error

FLOGIT: Fractional logit
MAE: Mean Absolute Error

Table 29 shows the results of the multivariable analysis investigating the independent effects of modality of HIV testing and baseline CD4 count on the mean EQ-5D utility score predicted by the OLS estimator. In the multivariable analysis (Table 29), the fully adjusted model (model 2) found that there was no significant difference in the mean adjusted EQ-5D utility score between those who had accessed HIVST and those who had access facility-based HTC prior to attending the HIV clinic for assessment for ART initiation.

In the multivariable analysis (Table 29), the fully adjusted model (model 2) found that those with a CD4 count between 50 cells/ μ l and 200 cells/ μ l had a significantly lower mean adjusted EQ-5D utility score (0.053, 95%CI: 0.014-0.090) than those with a CD4 count greater than 350 cells/ μ l. Additionally, those with a CD4 count below 50 cells/ μ l also had a significantly lower mean adjusted EQ-5D utility score (0.234, 95%CI: 0.161-0.308) than those with a CD4 count greater than 350 cells/ μ l. In the fully adjusted model (model 2), there was no significant difference in mean EQ-5D utility scores between those with CD4 count greater than 350 cells/ μ l, and either those with a CD4 count between 200 cells/ μ l and 300 cells/ μ l, or those who had no CD4 count recorded.

Table 29: Multivariable analysis exploring relationship between CD4 count and modality of HIV testing received and the EQ-5D utility score before starting anti-retroviral therapy*

		EQ-5D Utility Score		Sensitivity analysis EQ-5D Utility Score (UK Tariff)	
		Model 1 (n=330)	Model 2 (n=330)	Model 1 (n=330)	Model 2 (n=330)
		Coef (95% CI)	Coef (95% CI)	Coef (95% CI)	Coef (95% CI)
Modality of HIV testing	Facility-tested	Ref	Ref	Ref	Ref
	HIV self-tested	0.018 (-0.019, 0.055)	0.022 (-0.026, 0.060)	0.021 (-0.034, 0.075)	0.027 (-0.029, 0.082)
Baseline CD4 count	CD4 count ≥350	Ref	Ref	Ref	Ref
	CD4 count 200-350	-0.008 (-0.047, 0.031)	-0.013 (-0.052, 0.027)	-0.017 (-0.074, 0.040)	-0.022 (-0.081, 0.035)
	CD4 count 50-200	-0.051** (-0.090, -0.013)	-0.053** (-0.092, -0.014)	-0.067** (-0.123, -0.010)	-0.069** (-0.126, -0.012)
	CD4 count <50	-0.234** (-0.307, -0.161)	-0.23**4 (-0.308, -0.161)	-0.385** (-0.492, -0.278)	-0.383** (-0.491, -0.276)
	Not done or missing	-0.024 (-0.074, 0.026)	-0.024 (-0.075, 0.028)	-0.037 (-0.111, 0.037)	-0.039 (-0.115, 0.037)
	Constant	0.896 (0.844, 0.948)	0.901 (0.819, 0.983)	0.880 (0.804, 0.956)	0.863 (0.743, 0.982)

Model 1: adjusted for exposure, HIV test result, Age and Sex

Model 2: additionally adjusted for marital status, educational attainment, income and wealth quintile

*Findings from OLS estimator

**p<0.05

6.3.4 ART observation period

6.3.4.1 Cost analysis

Table 30 (costs in 2014 US Dollars) and Table 31 (costs in 2014 INT Dollars) shows the mean monthly costs for participants by the baseline CD4 count for the period after initiating anti-retroviral therapy (ART), and the total costs for those participants who had been on ART for one year by the end of the study period. Figure 41 (costs in 2014 US Dollars) and Figure 42 (costs in 2014 INT Dollars) show the mean monthly costs of providing HIV treatment by the baseline CD4 count.

For all the participants, the mean health provider cost in the first month after initiating ART was US\$18.22 (INT\$30.64), with the costs falling in the second month to US\$13.82 (INT\$19.71). The mean monthly health provider costs in the subsequent months were comparable to that seen in the second month after initiating ART (Figure 41 **and** Figure 42). The mean monthly health provider costs for those with higher CD4 counts before initiating ART were comparable to those with lower CD4 counts, and remained comparable in the subsequent months (Figure 41 **and** Figure 42).

The mean total health provider cost for the first year of ART provision was US\$166.20 (INT\$226.16) in those who had one year of follow-up (Table 30 **and** Table 31). The costs were comparable across those with different baseline CD4 counts.

For all the participants, the mean direct non-medical and indirect costs in the first month after initiating ART was US\$2.85 (INT\$7.91), with the costs falling in the subsequent months (Figure 41 **and** Figure 42). The mean total direct non-medical and indirect cost for the first year of ART was US\$8.98 (INT\$36.90) in those who had one year of ART follow-up. Participants who had a CD4 count between 200 cells/ μ l and 350 cells/ μ l incurred the highest mean direct non-medical and indirect costs in the first year of ART (US\$12.51: bootstrap 95%CI, US\$5.74-US\$19.28). Participants who had a CD4 count greater than 350 cells/ μ l incurred the lowest mean direct non-medical and indirect costs in the first year of ART (US\$1.35; bootstrap 95%CI, US\$0.27-US\$2.43).

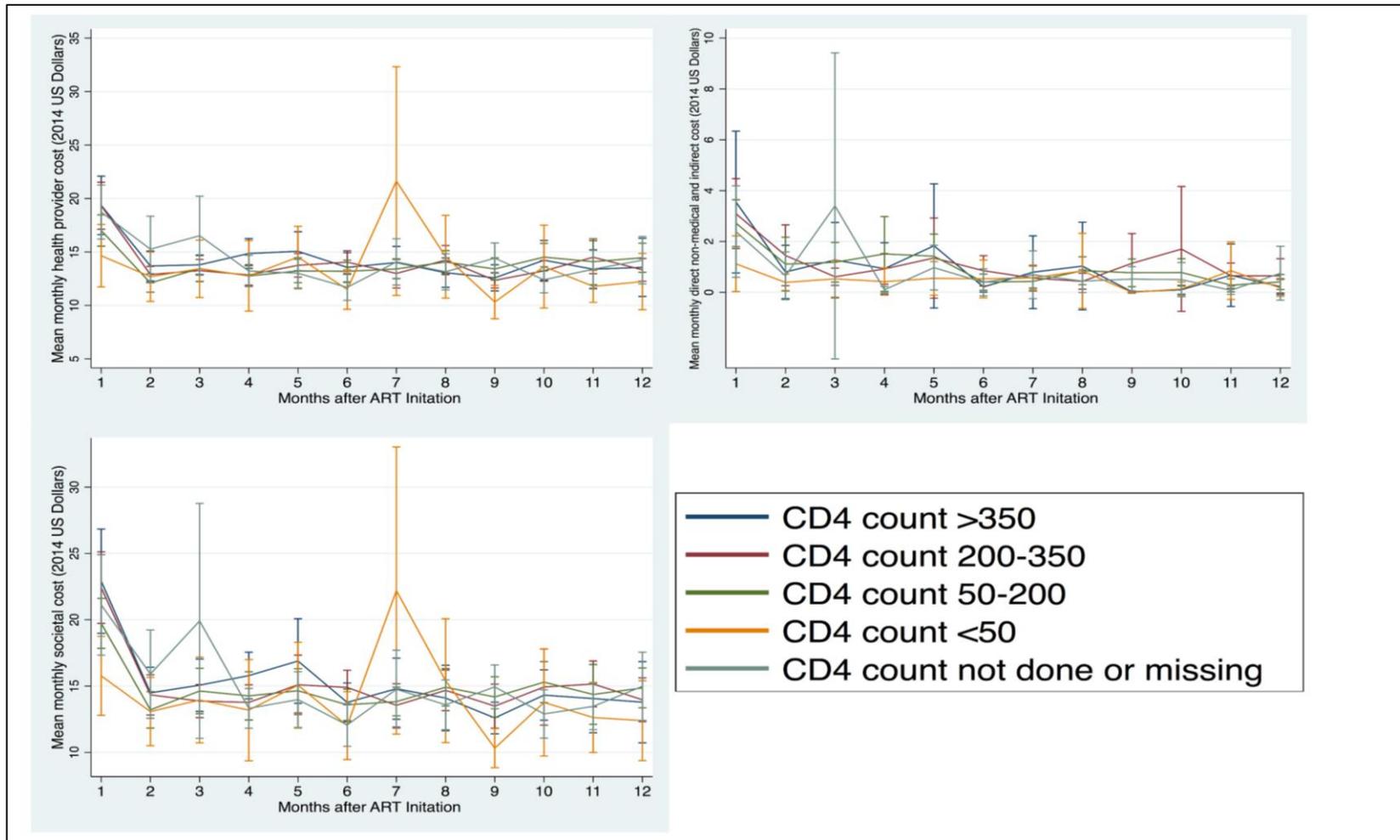
For all the participants, the mean societal cost in the first month after initiating ART was US\$21.07 (INT\$38.55), with the costs falling in the subsequent months (Figure 41 **and** Figure 42). The mean monthly societal costs for those with higher CD4 counts before initiating ART were comparable to those with lower CD4 counts, and remained comparable in the subsequent months (Figure 41 **and** Figure 42). The mean total societal cost for the first year of ART provision in those who had one year of follow-up was US\$178.35 (INT\$259.90). The costs were comparable across those with different baseline CD4 counts (Table 30 **and** Table 31).

Table 30: Mean total monthly and first year costs (in 2014 US Dollars) after initiation of anti-retroviral therapy by baseline CD4 count

		Mean monthly costs after ART initiation (2014 US Dollars)				Total 1 st year (2014 US Dollars) (n=100)
		1 st month (n=225) Mean (95% CI)*	3 rd month (n=187) Mean (95% CI)*	6 th month (n=153) Mean (95% CI)*	12 th month (n=100) Mean (95% CI)*	Mean (95% CI)
Total Health Provider cost	ALL	18.22 (17.12, 19.32)	13.82 (13.06, 14.57)	13.24 (12.67, 13.80)	13.85 (13.10, 14.61)	166.20 (161.98, 170.43)
	CD4 count ≥350	19.36 (16.63, 22.09)	13.80 (12.90, 14.71)	13.56 (12.18, 14.94)	13.56 (10.84, 16.28)	170.20 (160.66, 179.73)
	CD4 count 200-350	19.33 (17.13, 21.53)	13.26 (12.23, 14.30)	14.05 (12.98, 15.11)	13.33 (12.26, 14.39)	165.12, 159.49, 170.76)
	CD4 count 50-200	17.01 (15.55, 18.47)	13.45 (12.25, 14.65)	13.18 (12.15, 14.24)	14.46 (13.10, 15.81)	164.89 (158.87, 170.91)
	CD4 count <50	14.65 (11.73, 17.57)	13.43 (10.74, 16.11)	11.50 (9.60, 13.35)	12.23 (9.60, 14.86)	158.12 (130.18, 186.06)
	CD4 not done or missing	18.73 (16.20, 21.26)	16.52 (12.82, 20.22)	11.69 (10.48, 12.89)	14.23 (12.01, 16.45)	176.62 (158.91, 194.33)
Total direct non-medical and indirect cost	ALL	2.85 (2.16, 3.54)	1.25 (0.42, 2.09)	0.53 (0.29, 0.76)	0.49 (0.22, 0.75)	8.98 (5.86, 12.11)
	CD4 count ≥350	3.55 (0.76, 6.34)	1.27 (-0.22, 2.75)	0.21 (0.01, 0.41)	0.22 (-0.09, 0.53)	1.35 (0.27, 2.43)
	CD4 count 200-350	3.09 (1.72, 4.47)	0.61 (0.27, 0.95)	0.85 (0.25, 1.44)	0.65 (-0.03, 1.32)	12.51 (5.74, 19.28)
	CD4 count 50-200	2.72 (1.80, 3.64)	1.18 (0.40, 1.96)	0.40 (0.08, 0.72)	0.41 (0.11, 0.70)	7.58 (5.00, 10.17)
	CD4 count <50	1.12 (0.03, 2.22)	0.53 (-0.19, 1.24)	0.53 (-0.22, 1.27)	0.17 (-0.16, 0.50)	5.10 (2.99, 7.22)
	CD4 not done or missing	2.39 (0.59, 4.19)	3.40 (-2.62, 9.42)	0.39 (-0.14, 0.92)	0.75 (-0.31, 1.81)	12.53 (-7.14, 32.21)
Total Societal cost	ALL	21.07 (19.72, 22.42)	15.07 (13.67, 13.80)	13.76 (13.08, 14.45)	14.34 (13.44, 15.24)	178.35 (171.88, 184.82)
	CD4 count ≥350	22.91 (18.98, 26.84)	15.07 (13.09, 17.04)	13.77 (12.31, 15.23)	13.79 (10.73, 16.84)	172.18 (163.16, 181.21)
	CD4 count 200-350	22.42 (19.73, 25.12)	13.87 (12.63, 15.11)	14.90 (13.60, 16.19)	13.97 (12.32, 15.62)	182.17 (170.50, 193.84)
	CD4 count 50-200	19.73 (17.85, 21.61)	14.63 (12.92, 16.34)	13.59 (12.41, 14.77)	14.86 (13.36, 16.37)	175.25 (168.41, 182.08)
	CD4 count <50	15.77 (12.80, 18.75)	13.95 (10.73, 17.18)	12.02 (9.46, 14.58)	12.40 (9.38, 15.41)	164.47 (137.84, 191.09)
	CD4 not done or missing	21.12 (17.33, 24.91)	19.91 (11.06, 28.77)	12.07 (10.46, 13.68)	14.98 (12.41, 17.55)	193.03 (154.09, 231.97)

*Bootstrapped estimates with 1000 replications for 95%CI

Figure 41: Mean monthly costs* (in 2014 US Dollars) after initiation of anti-retroviral therapy by the baseline CD4 count



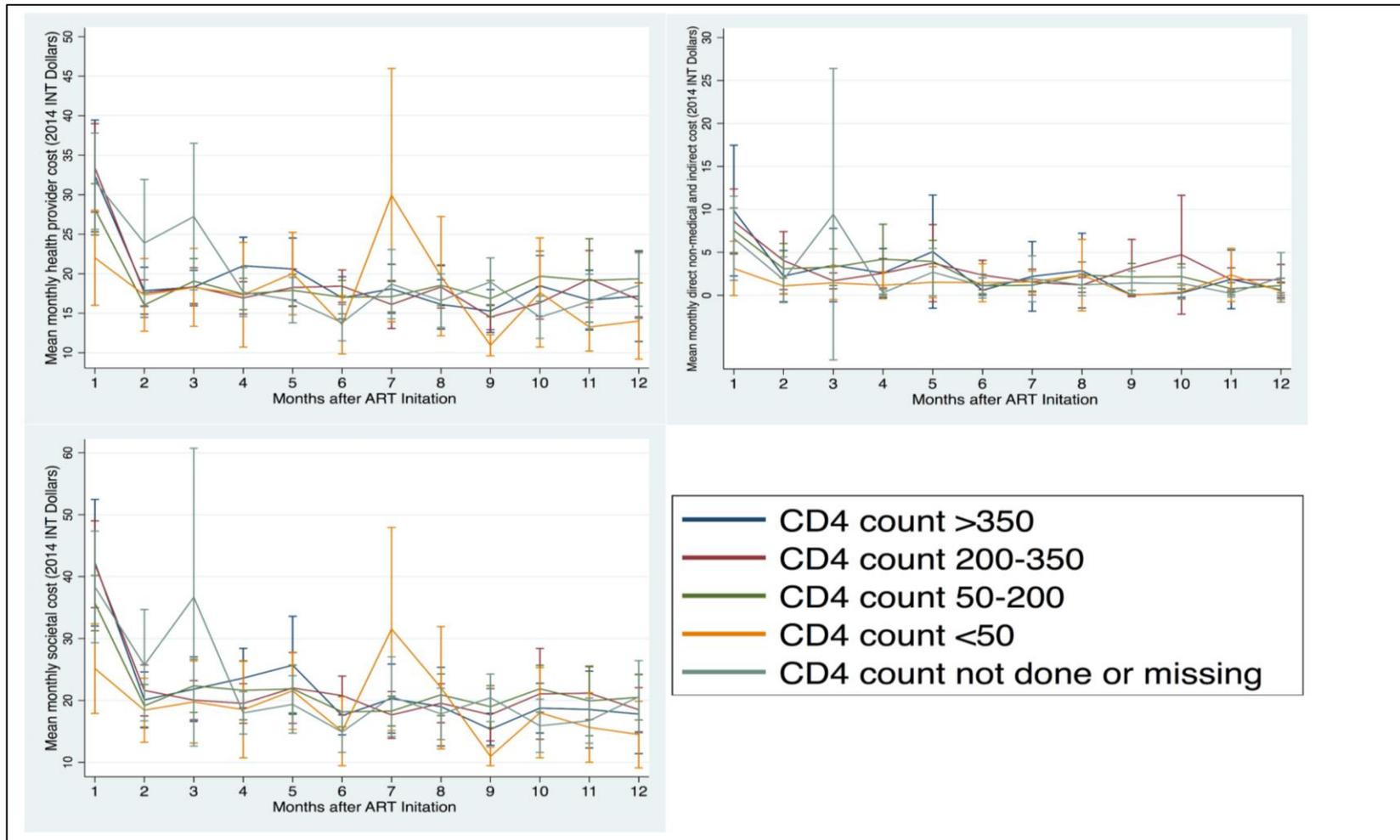
*Graphs show all three cost categories: health provider; direct non-medical and indirect; and societal costs

Table 31: Mean total monthly and first year costs (in 2014 INT Dollars) after initiation of anti-retroviral therapy by baseline CD4 count

		Mean monthly costs after ART initiation (2014 INT Dollars)				Total 1 st year (2014 INT Dollars) (n=100)
		1 st month (n=225) Mean (95% CI)*	3 rd month (n=187) Mean (95% CI)*	6 th month (n=153) Mean (95% CI)*	12 th month (n=100) Mean (95% CI)*	Mean (95% CI)
Total Health Provider cost	ALL	30.64 (28.22, 33.07)	19.71 (17.89, 21.52)	16.88 (15.72, 18.03)	17.89 (16.15, 19.63)	226.16 (217.16, 235.16)
	CD4 count ≥350	33.39 (27.80, 38.99)	18.31 (16.19, 20.43)	16.95 (14.28, 19.62)	17.11 (11.42, 22.92)	227.60 (208.47, 246.73)
	CD4 count 200-350	32.37 (27.80, 38.99)	18.35 (15.95, 20.75)	18.43 (16.39, 20.47)	16.70 (14.53, 18.86)	222.46 (209.97, 234.95)
	CD4 count 50-200	28.15 (24.91, 31.39)	19.07 (16.23, 21.91)	17.04 (14.93, 19.15)	19.36 (15.89, 22.83)	225.28 (210.93, 239.63)
	CD4 count <50	22.02 (16.01, 28.02)	18.28 (13.35, 23.21)	13.55 (9.85, 17.24)	14.01 (9.20, 18.82)	206.96 (170.44, 243.47)
	CD4 not done or missing	31.70 (25.62, 37.79)	27.23 (17.95, 36.52)	13.81 (11.51, 16.11)	18.50 (14.34, 22.65)	251.17 (211.64, 290.71)
Total direct non-medical and indirect cost	ALL	7.91 (5.86, 9.96)	3.49 (1.11, 5.86)	1.46 (0.76, 2.16)	1.36 (0.63, 2.08)	36.90 (24.34, 49.47)
	CD4 count ≥350	9.85 (2.25, 17.46)	3.51 (-0.75, 7.78)	0.58 (0.00, 1.16)	0.62 (-0.28, 1.52)	6.16 (1.14, 11.18)
	CD4 count 200-350	8.59 (4.80, 12.37)	1.69 (0.76, 2.61)	2.35 (0.64, 4.07)	1.79 (0.00, 3.59)	51.87 (23.16, 80.58)
	CD4 count 50-200	7.56 (4.96, 10.16)	3.28 (1.15, 5.41)	1.11 (0.19, 2.03)	1.13 (0.29, 1.98)	31.56 (21.64, 41.48)
	CD4 count <50	3.12 (-0.03, 6.28)	1.46 (-0.50, 3.43)	1.46 (-0.75, 3.67)	0.47 (-0.47, 1.41)	18.87 (11.08, 26.66)
	CD4 not done or missing	6.63 (1.74, 11.53)	9.43 (-7.53, 26.40)	1.08 (-0.32, 2.47)	2.08 (-0.80, 4.97)	49.46 (-22.29, 122.20)
Total Societal cost	ALL	38.55 (35.11, 42.00)	23.19 (19.74, 26.64)	18.34 (16.83, 19.84)	19.24 (17.10, 21.39)	259.90 (243.41, 276.38)
	CD4 count ≥350	42.23 (32.01, 52.45)	21.82 (16.61, 27.04)	17.53 (14.43, 20.63)	17.79 (11.39, 24.20)	233.12 (214.57, 251.68)
	CD4 count 200-350	41.98 (34.97, 49.00)	20.04 (16.87, 23.20)	20.78 (17.66, 23.91)	18.49 (14.91, 22.06)	269.80 (239.28, 300.32)
	CD4 count 50-200	35.71 (31.24, 40.18)	22.35 (18.05, 26.66)	18.15 (15.74, 20.56)	20.49 (16.84, 24.15)	254.06 (236.73, 271.40)
	CD4 count <50	25.14 (17.90, 32.38)	19.75 (13.10, 26.39)	15.01 (9.46, 20.56)	14.48 (9.11, 19.85)	224.58 (188.88, 260.29)
	CD4 not done or missing	38.33 (29.32, 47.35)	36.67 (12.61, 60.73)	14.89 (11.60, 18.18)	20.58 (14.74, 26.42)	296.76 (201.82, 391.69)

*Bootstrapped estimates with 1000 replications for 95%CI

Figure 42: Mean monthly costs* (in 2014 INT Dollars) after initiation of anti-retroviral therapy by the baseline CD4 count



*Graphs show all three cost categories: health provider; direct non-medical and indirect; and societal costs

Table 32 (costs in 2014 US Dollars) and Table 33 (costs in 2014 INT Dollars) show the mean total monthly and first year costs amongst those who initiated ART by the modality of HIV testing that participants received prior to initiating treatment. Figure 43 (costs in 2014 US Dollars) and Figure 44 (costs in 2014 INT Dollars) show the mean monthly costs by the modality of HIV testing received.

The mean health provider cost in the first month after initiating ART for those who had previously accessed HIVST was significantly lower (US\$15.43: bootstrap 95%CI, US\$13.62-US\$17.24), than for those who had previously accessed facility-based HTC (US\$18.81: bootstrap 95%CI, US\$17.61-US\$20.00). For the subsequent months on ART, the mean monthly health provider costs were comparable (Figure 43 **and** Figure 44).

The mean total health provider costs for the first year of accessing ART, in those who completed one year of follow-up, were comparable between those who had previously accessed HIVST (US\$160.78: bootstrap 95%CI, US\$148.17-US\$173.39) and those who previously accessed facility-based HTC (US\$167.24: bootstrap 95%CI, US\$163.01-US\$171.46).

The mean monthly and mean total first year direct non-medical and indirect costs during the ART period were comparable for those who had previously accessed

HIVST and those who had previously accessed facility-based HTC. The mean monthly and mean total first year societal costs during the ART period were also comparable between those who had previously accessed HIVST and those who had previously accessed facility-based HTC. The mean total societal costs, for those who had one year of follow-up, was US\$173.60 (bootstrap 95%CI: US\$54.31-US\$192.88) amongst those who had previously accessed HIVST, and US\$179.26 (bootstrap 95%CI: US\$172.43-US\$186.08) amongst those who had previously accessed facility-based HTC.

Table 32: Mean total monthly and first year costs (in 2014 US Dollars) after initiation of anti-retroviral therapy by modality of HIV testing

		Mean monthly costs after ART initiation (2014 US Dollars)				Total 1 st year (2014 US Dollars) (n=100) Mean (95% CI)
		1 st month (n=225) Mean (95% CI)	3 rd month (n=187) Mean (95% CI)	6 th month (n=153) Mean (95% CI)	12 th month (n=100) Mean (95% CI)	
Total Health Provider cost	Facility testers	18.81 (17.61, 20.00)	13.99 (13.16, 14.82)	13.40 (12.76, 14.03)	13.82 (13.07, 14.55)	167.24 (163.01, 171.46)
	HIVST	15.43 (13.62, 17.24)	13.03 (10.98, 15.09)	12.55 (11.44, 13.65)	14.09 (11.10, 17.07)	160.78 (148.17, 173.39)
Total direct non-medical and indirect cost	Facility testers	2.89 (2.10, 3.67)	1.20 (0.24, 2.15)	0.46 (0.26, 0.67)	0.57 (0.26, 0.88)	8.86 (5.48, 12.25)
	HIVST	2.65 (1.02, 4.28)	1.52 (-0.04, 3.08)	0.78 (-0.16, 1.73)	0.07 (-0.08, 0.23)	9.62 (-0.55, 19.78)
Total Societal cost	Facility testers	21.69 (20.15, 23.24)	15.19 (13.75, 16.62)	13.86 (13.11, 14.61)	14.38 (13.48, 15.27)	179.26 (172.43, 186.08)
	HIVST	18.08 (15.62, 20.54)	14.55 (11.39, 17.72)	13.33 (11.67, 14.99)	14.16 (11.18, 17.14)	173.60 (154.31, 192.88)

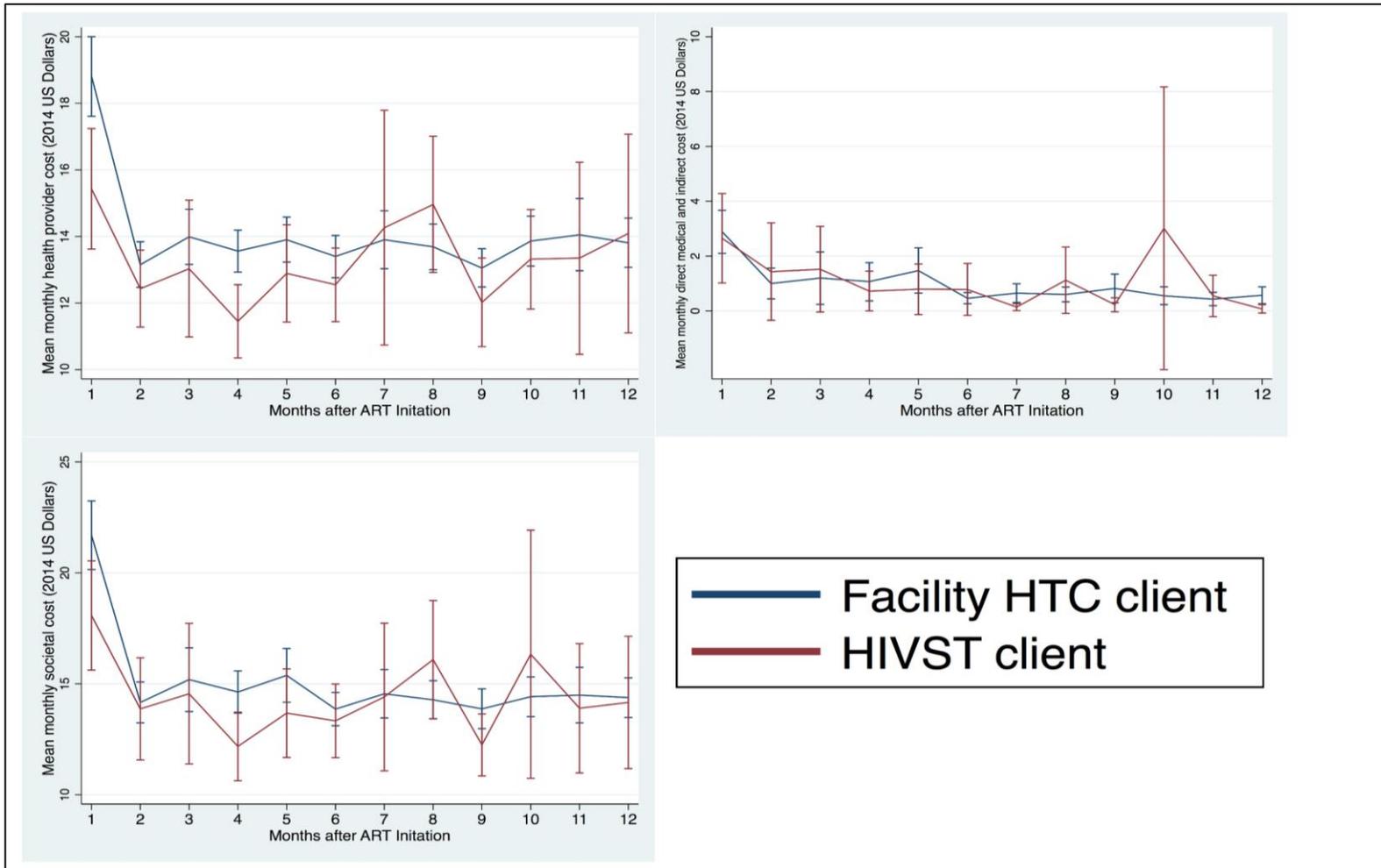
*Bootstrapped estimates with 1000 replications for 95%CI

Table 33: Mean total monthly and first year costs (in 2014 INT Dollars) after initiation of anti-retroviral therapy by modality of HIV testing

		Mean monthly costs after ART initiation (2014 INT Dollars)				Total 1 st year (2014 INT Dollars) (n=100) Mean (95% CI)
		1 st month (n=225) Mean (95% CI)	3 rd month (n=187) Mean (95% CI)	6 th month (n=153) Mean (95% CI)	12 th month (n=100) Mean (95% CI)	
Total Health Provider cost	Facility testers	32.09 (29.18, 35.00)	20.03 (18.14, 21.92)	17.14 (15.78, 18.51)	17.70 (16.15, 19.26)	228.18 (218.39, 237.97)
	HIVST	23.75 (20.03, 27.48)	18.27 (13.23, 23.31)	15.74 (13.56, 17.91)	18.86 (10.93, 26.79)	215.53 (190.16, 240.89)
Total direct non-medical and indirect cost	Facility testers	8.02 (5.68, 10.37)	3.32 (0.61, 6.03)	1.29 (0.71, 1.87)	1.57 (0.68, 2.47)	36.54 (23.16, 49.93)
	HIVST	7.37 (2.97, 11.77)	4.23 (0.06, 8.39)	2.18 (-0.45, 4.81)	0.20 (-0.19, 0.59)	38.81 (-0.07, 77.69)
Total Societal cost	Facility testers	40.11 (36.08, 44.15)	23.35 (19.40, 27.29)	18.43 (16.80, 20.07)	19.28 (17.27, 21.29)	261.57 (243.67, 279.47)
	HIVST	31.12 (24.79, 37.46)	22.50 (14.11, 30.89)	17.92 (14.04, 21.79)	19.06 (11.19, 26.94)	251.14 (204.33, 297.94)

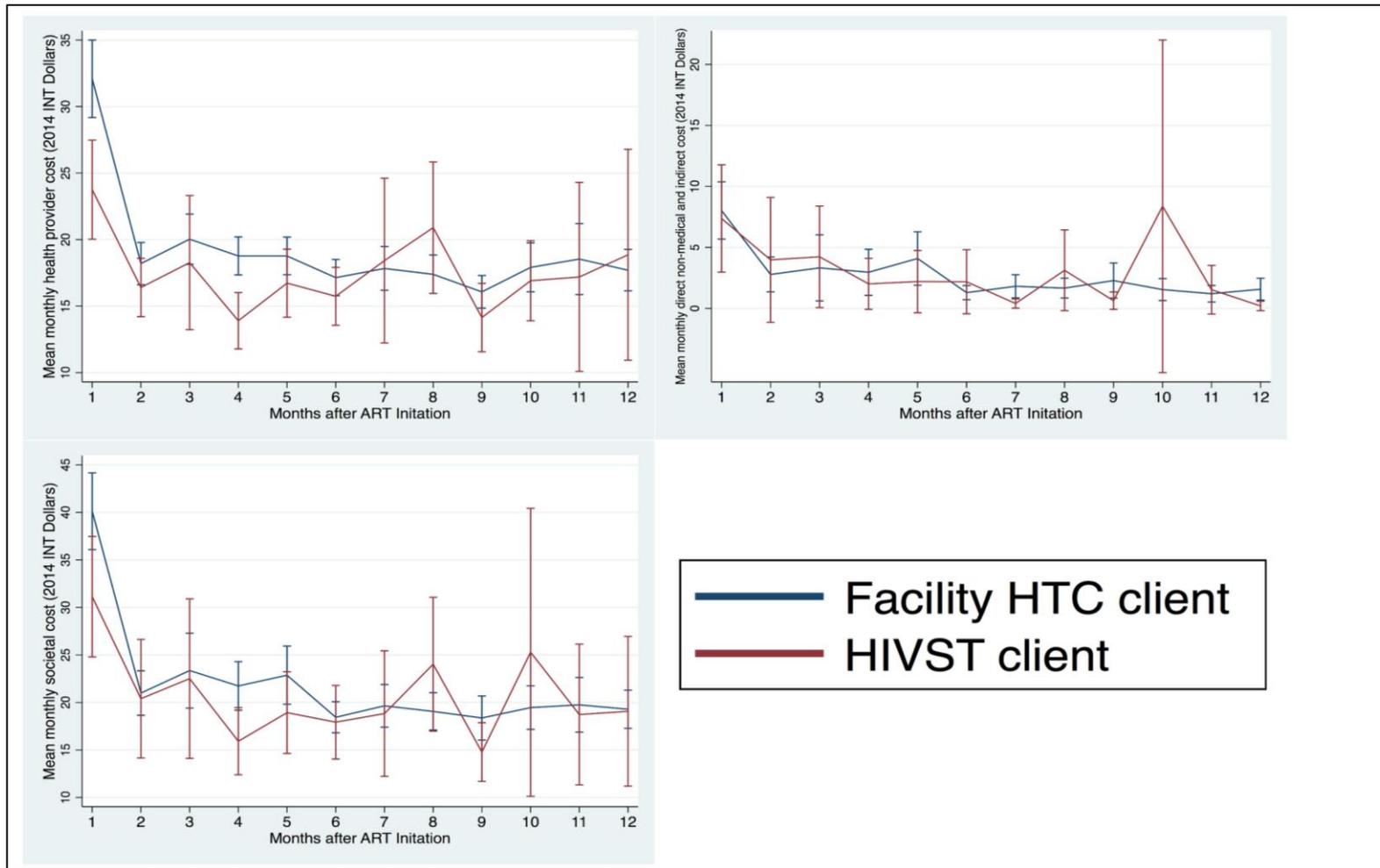
*Bootstrapped estimates with 1000 replications for 95%CI

Figure 43: Mean monthly costs* (in 2014 US Dollars) after initiation of anti-retroviral therapy by modality of HIV testing received



*Graphs show all three cost categories: health provider; direct non-medical and indirect; and societal costs

Figure 44: Mean monthly costs* (in 2014 INT Dollars) after initiation of anti-retroviral therapy by modality of HIV testing received



*Graphs show all three cost categories: health provider; direct non-medical and indirect; and societal costs

Table 34 shows the results of the multivariable analysis investigating the independent effects of modality of HIV testing, baseline CD4 count and the month on anti-retroviral treatment on the mean monthly health provider and societal cost of providing HIV treatment during the ART observation period.

In this multivariable analysis, the mean monthly health provider costs for those who had previously accessed HIVST were US\$0.89 (95%CI: US\$0.26-US\$1.52) lower than for those who had previously accessed facility-based HTC. There was no significant difference between the two groups with respect to adjusted mean monthly societal costs.

The baseline CD4 count did not have a significant impact on the adjusted mean monthly health provider or societal costs of providing anti-retroviral therapy. In the multivariable analysis, the adjusted mean monthly health provider costs was US\$5.19 (95%CI: US\$4.00-US\$6.38) lower in the second month of ART provision than in the first month of ART provision, and remained comparable in the subsequent months. The adjusted mean monthly societal cost was US\$6.88 (95%CI: US\$5.30-US\$8.47) lower in the second month of ART provision than in the first month of ART provision, and remained comparable in the subsequent months.

Table 34: Multivariable analysis exploring relationship between CD4 count and modality of HIV testing received and the monthly cost of providing HIV treatment*

		Monthly Health Provider costs**		Total Societal costs**	
		2014 US Dollars	2014 INT Dollars	2014 US Dollars	2014 INT Dollars
		Coef (95% CI)	Coef (95% CI)	Coef (95% CI)	Coef (95% CI)
Modality of HIV testing	Facility-tested	Ref	Ref	Ref	Ref
	HIV self-tested	-0.89 (-1.52, -0.26)	-1.83 (-3.16, -0.50)	-0.84 (-1.70, 0.03)	-1.68 (-3.77, 0.41)
Baseline CD4 count	CD4 count >350 cells/μl	Ref	Ref	Ref	Ref
	CD4 count 200-350 cells/μl	-0.50 (-1.23, 0.56)	-0.64 (-2.33, 1.05)	-0.25 (-1.28, 0.77)	0.06 (-2.54, 2.66)
	CD4 count 50-200 cells/μl	-0.85 (-1.53, -0.17)	-1.07 (-2.63, 0.49)	-0.94 (-1.84, 0.07)	-1.31 (-3.86, 1.25)
	CD4 count <50 cells/μl	-0.59 (-2.06, 0.87)	-1.42 (-4.22, 1.39)	-1.38 (-3.09, 0.32)	-3.61 (-7.23, 0.00)
	Not done or missing	-0.45 (-1.38, 0.49)	-0.07 (-2.30, 2.16)	-0.47 (-1.89, 0.96)	-0.13 (-3.81, 3.55)
Month of anti-retroviral treatment	1 st Month	Ref	Ref	Ref	Ref
	2 nd Month	-5.19 (-6.38, 4.00)	-12.73 (-15.60, -9.86)	-6.88 (-8.47, -5.30)	-17.43 (-21.50, -13.37)
	3 rd Month	-4.37 (-5.65, -3.09)	-10.85 (-13.95, -7.75)	-5.90 (-7.79, -4.00)	-15.09 (-20.01, -10.16)
	4 th Month	-5.04 (-6.21, -3.86)	-12.72 (-15.52, -9.92)	-6.82 (-8.39, -5.24)	-17.67 (-21.68, -13.65)
	5 th Month	-4.46 (-5.68, -3.25)	-12.12 (-14.95, -9.28)	-5.81 (-7.51, -4.11)	-15.85 (-20.11, -11.60)
	6 th Month	-4.91 (-6.10, -3.73)	-13.57 (-16.36, -10.78)	-7.08 (-8.59, -5.57)	-19.58 (-23.35, -15.82)
	7 th Month	-4.18 (-5.57, -2.78)	-12.51 (-15.56, -9.45)	-6.30 (-8.00, -4.60)	-18.37 (-22.39, -14.37)
	8 th Month	-4.22 (-5.46, -2.98)	-12.42 (-15.56, -9.45)	-6.18 (-7.76, -4.60)	-17.88 (-21.82, -13.94)
	9 th Month	-5.24 (-6.14, -4.07)	-14.65 (-17.44, -11.87)	-7.19 (-8.76, -5.62)	-20.07 (-24.03, -16.11)
	10 th Month	-4.38 (-5.63, -3.12)	-12.72 (-15.73, -9.72)	-6.12 (-7.90, -4.33)	-17.56 (-22.12, -13.00)
	11 th Month	-4.19 (-5.64, -2.74)	-12.15 (-15.69, -8.61)	-6.40 (-8.12, -4.68)	-18.28 (-22.61, -13.85)
	12 th Month	-4.29 (-5.58, -3.00)	-12.61 (-15.68, -9.54)	-6.46 (-8.08, -4.74)	-18.64 (-22.67, -14.61)
Constant		19.16 (17.45, 20.86)	31.90 (27.93, 35.88)	20.93 (18.75, 23.12)	36.84 (31.37, 42.31)

*Findings from Generalized Linear Model with Gaussian distribution and Identity link function (i.e. OLS estimator)

** Findings from Model 2: adjusted Age and Sex for marital status, educational attainment, income and wealth quintile

6.3.4.2 Health-related quality of life analysis

Table 35 shows the mean EQ-5D utility scores and VAS scores for participants who started ART, by the baseline CD4 count. Figure 45 shows the mean EQ-5D utility scores and VAS scores over time by the baseline CD4 count. The participants who started ART had a mean EQ-5D utility score of 0.845 (bootstrap 95%CI: 0.829-0.862) before they started ART, with the mean EQ-5D utility score rising to 0.882 (bootstrap 95%CI: 0.867-0.896) one month after initiating treatment. Across all participants, the mean EQ-5D utility score rose in the subsequent months to 0.920 (bootstrap 95%CI: 0.829-0.862) by the end of the 3rd month on ART, to 0.940 (bootstrap 95%CI: 0.925-0.955) by the end of the 6th month on ART, and 0.974 (bootstrap 95%CI: 0.961-0.987) by the end of the 12th month on ART. Figure 45 shows that the increases in mean EQ-5D utility scores over time on ART occurred across all baseline CD4 categories. After 12 months on ART, the mean EQ-5D utility score was broadly similar in those with a higher baseline CD4 count and those with a lower baseline CD4 count.

The participants who started ART had a mean VAS score of 72.0 (bootstrap 95%CI: 69.8-74.2) before they started treatment, with the mean VAS score rising to 74.0 (bootstrap 95%CI: 71.9-76.1) one month after initiating treatment. For all participants, the mean VAS score was higher in the subsequent months. The mean VAS score was 78.0 (bootstrap 95%CI: 75.6-80.3) by the end of the 3rd month on ART, 80.1 (bootstrap 95%CI: 77.5-82.6) by the end of the 6th month on ART, and 81.5 (bootstrap 95%CI: 78.2-84.7) by the end of the 12th month on ART.

Table 35: Health-related quality of life outcomes amongst those started onto ART by month from initiation of treatment

		Pre-ART (n=225) Mean (95% CI)*	Month after starting ART			
			1 st month (n=225) Mean (95% CI)*	3 rd month (n=187) Mean (95% CI)*	6 th month (n=153) Mean (95% CI)*	12 th month (n=100) Mean (95% CI)*
EQ-5D Utility Score	ALL	0.845 (0.829, 0.862)	0.882 (0.867, 0.896)	0.920 (0.903, 0.937)	0.940 (0.925, 0.955)	0.974 (0.961, 0.987)
	CD4 count ≥350	0.884 (0.849, 0.919)	0.917 (0.883, 0.950)	0.960 (0.922, 0.999)	0.964 (0.928, 1.000)	0.991 (0.972, 1.010)
	CD4 count 200-350	0.863 (0.835, 0.890)	0.891 (0.864, 0.917)	0.916 (0.892, 0.940)	0.945 (0.923, 0.968)	0.965 (0.939, 0.992)
	CD4 count 50-200	0.821 (0.792, 0.850)	0.874 (0.851, 0.898)	0.922 (0.891, 0.953)	0.930 (0.900, 0.960)	0.969 (0.948, 0.990)
	CD4 count <50	0.694 (0.602, 0.786)	0.790 (0.700, 0.881)	0.864 (0.798, 0.930)	0.886 (0.819, 0.952)	0.985 (0.897, 1.074)
	CD4 not done or missing	0.874 (0.832, 0.917)	0.871 (0.829, 0.912)	0.895 (0.842, 0.948)	0.957 (0.922, 0.990)	1.000 (1.000, 1.000)
EQ-5D Utility Score (UK Tariff)	ALL	0.805 (0.779, 0.831)	0.851 (0.830, 0.872)	0.898 (0.873, 0.923)	0.925 (0.905, 0.945)	0.971 (0.956, 0.985)
	CD4 count ≥350	0.864 (0.821, 0.907)	0.900 (0.859, 0.940)	0.945 (0.888, 1.003)	0.960 (0.918, 1.002)	0.991 (0.972, 1.009)
	CD4 count 200-350	0.825 (0.783, 0.866)	0.862 (0.823, 0.900)	0.895 (0.862, 0.928)	0.932 (0.904, 0.961)	0.961 (0.931, 0.991)
	CD4 count 50-200	0.777 (0.730, 0.824)	0.845 (0.812, 0.878)	0.901 (0.854, 0.948)	0.912 (0.870, 0.953)	0.964 (0.939, 0.990)
	CD4 count <50	0.545 (0.365, 0.725)	0.696 (0.529, 0.863)	0.820 (0.715, 0.924)	0.841 (0.738, 0.945)	0.984 (0.901, 1.091)
	CD4 not done or missing	0.850 (0.799, 0.901)	0.837 (0.780, 0.895)	0.866 (0.794, 0.939)	0.945 (0.892, 0.997)	1.000 (1.000, 1.000)
VAS Score	ALL	72.0 (69.8, 74.2)	74.0 (71.9, 76.1)	78.0 (75.6, 80.3)	80.1 (77.5, 82.6)	81.5 (78.2, 84.7)
	CD4 count ≥350	76.0 (70.5, 81.5)	80.7 (76.2, 85.4)	83.3 (77.2, 89.4)	83.3 (77.2, 89.4)	87.7 (76.4, 99.1)
	CD4 count 200-350	75.0 (71.2, 78.8)	75.9 (72.3, 79.2)	76.0 (71.7, 80.2)	78.5 (73.6, 83.4)	82.8 (76.9, 88.6)
	CD4 count 50-200	67.5 (63.7, 71.3)	71.2 (67.3, 74.8)	77.9 (74.0, 81.9)	81.6 (77.8, 85.4)	81.5 (76.9, 86.0)
	CD4 count <50	77.0 (62.4, 91.6)	74.7 (60.8, 88.0)	84.4 (77.6, 91.2)	82.2 (75.2, 89.2)	80.7 (66.4, 95.0)
	CD4 not done or missing	70.2 (63.5, 77.0)	69.2 (62.5, 75.8)	72.4 (65.3, 79.6)	73.8 (65.0, 82.5)	73.7 (60.6, 86.8)

*Bootstrapped estimates with 1000 replications for 95%CI

Figure 45: Changes in health-related quality of life outcomes over time since initiating anti-retroviral therapy by baseline CD4 count

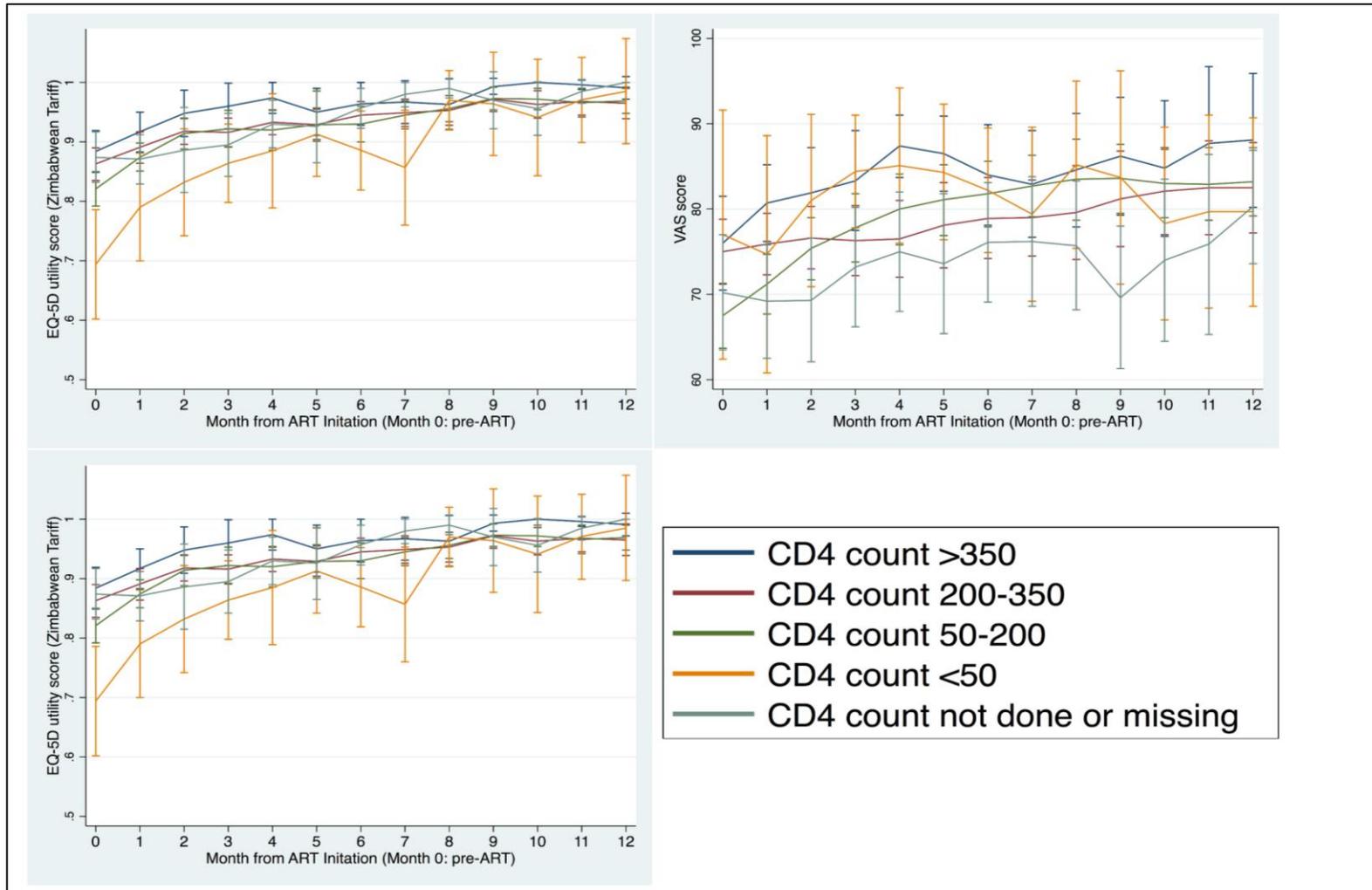


Table 36 shows the mean EQ-5D utility scores and VAS scores of participants who started ART by the modality of HIV testing they accessed prior to entering HIV care, whilst Figure 46 shows changes in these health-related quality of life scores over time on ART.

The mean EQ-5D utility scores before starting ART was broadly similar in those who had previously accessed HIVST and those who had previously accessed facility-based HTC. In the months after starting ART, those who had previously accessed HIVST had comparable EQ-5D utility scores to those who had previously accessed facility-based HTC (Figure 46).

Table 36: Health-related quality of life outcomes before and after initiation of anti-retroviral therapy by modality of HIV testing

		Pre-ART (n=225) Mean (95% CI)	Month after starting ART			
			1 st month (n=225) Mean (95% CI)	3 rd month (n=187) Mean (95% CI)	6 th month (n=153) Mean (95% CI)	12 th month (n=100) Mean (95% CI)
			EQ-5D Utility Score	Facility testers	0.846 (0.828, 0.864)	0.881 (0.865, 0.898)
	HIVST	0.844 (0.798, 0.889)	0.883 (0.849, 0.917)	0.901 (0.849, 0.917)	0.938 (0.905, 0.971)	0.938 (0.905, 0.971)
EQ-5D Utility Score (UK Tariff)	Facility testers	0.806 (0.780, 0.833)	0.851 (0.827, 0.874)	0.906 (0.884, 0.928)	0.927 (0.903, 0.951)	0.966 (0.950, 0.983)
	HIVST	0.797 (0.728, 0.866)	0.851 (0.800, 0.902)	0.862 (0.778, 0.945)	0.918 (0.872, 0.964)	0.993 (0.982, 1.004)
VAS Score	Facility testers	71.5 (69.0, 73.9)	73.7 (71.4, 76.1)	77.8 (75.3, 80.3)	80.1 (77.4, 82.7)	81.7 (78.4, 85.0)
	HIVST	74.4 (68.2, 80.7)	75.3 (69.6, 81.0)	80.1 (77.4, 82.7)	82.3 (75.9, 88.6)	84.6 (78.4, 85.0)

*Bootstrapped estimates with 1000 replications for 95%CI 84.6 (76.7, 92.6)

Figure 46: Changes in health-related quality of life outcomes after initiating anti-retroviral therapy by modality of HIV testing

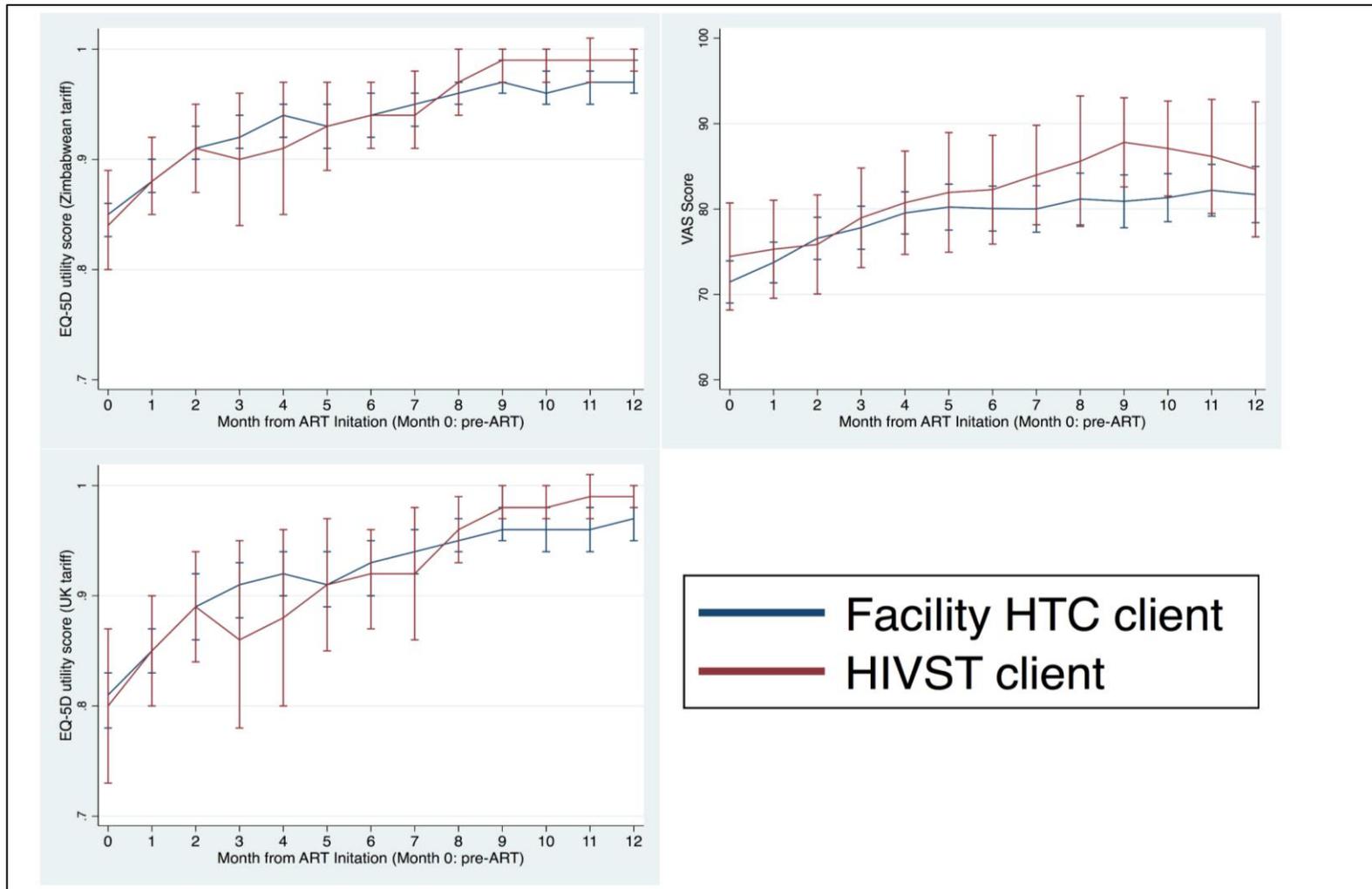


Table 37 shows the results of the multivariable analysis investigating the independent effects of modality of HIV testing, baseline CD4 count, on the mean EQ-5D utility score measured in the months after initiating anti-retroviral therapy. The multivariable analysis in model 3 additionally adjusted for the baseline EQ-5D utility score. In both models 2 and 3, the adjusted mean EQ-5D utility score was not significantly different for those who had previously accessed HIVST from those who had previously accessed facility-based HTC.

In the multivariable analysis, the baseline CD4 count did not have a significant effect on the adjusted mean EQ-5D utility score after adjusting for the baseline EQ-5D utility score. The multivariable analysis shows that there was a significant improvement in the adjusted EQ-5D utility score with time on ART. In model 3, after adjusting for baseline EQ-5D utility score, with each additional month on ART, the mean adjusted EQ-5D utility score increased by 0.008 (95%CI: 0.007-0.009).

Table 37: Multivariable analysis exploring relationship between CD4 count and modality of HIV testing received on the EQ-5D utility score after starting ART*

		EQ-5D utility score		Sensitivity Analysis EQ-5D utility score (UK Tariff)**	
		Model 2	Model 3	Model 2	Model 3
		Coef (95% CI)	Coef (95% CI)	Coef (95% CI)	Coef (95% CI)
Modality of HIV testing	Facility-tested	Ref	Ref	Ref	Ref
	HIV self-tested	0.008** (-0.015, 0.032)	0.006 (-0.016, 0.028)	0.008 (-0.022, 0.039)	0.005 (-0.024, 0.033)
Baseline CD4 count	CD4 count >350 cells/ μ l	Ref	Ref	Ref	Ref
	CD4 count 200-350 cells/ μ l	-0.029** (-0.057, -0.001)	-0.023 (-0.049, 0.003)	-0.035 (-0.071, 0.002)	-0.024 (-0.058, 0.010)
	CD4 count 50-200 cells/ μ l	-0.041** (-0.068, -0.013)	-0.026 (-0.052, 0.0001)	-0.048** (-0.084, -0.012)	-0.030 (-0.064, 0.004)
	CD4 count <50 cells/ μ l	-0.069** (-0.117, -0.022)	-0.026 (-0.072, 0.020)	-0.095** (-0.157, -0.033)	-0.035 (-0.095, 0.025)
	Not done or missing	-0.031 (-0.064, 0.003)	-0.032 (-0.063, -0.0003)	-0.039 (-0.083, 0.005)	-0.039 (-0.080, 0.002)
Month on ART		0.008** (0.007, 0.009)	0.008** (0.007, 0.009)	0.011** (0.009, 0.012)	0.011** (0.009, 0.012)
Baseline EQ-5D		N/A	0.236** (0.169, 0.302)	N/A	0.201** (0.143, 0.260)
	Constant	0.973 (0.924, 1.022)	0.762 (0.686, 0.838)	0.973 (0.909, 1.037)	0.800 (0.722, 0.879)

Model 2: Adjusted for Age, Sex marital status, educational attainment, income and wealth quintile

Model 3: Additionally adjusted for EQ-5D score before starting anti-retroviral therapy

ART: Anti-retroviral therapy

*Findings from GEE model (Gaussian distribution and Identity link function)

** $p < 0.05$

6.3.5 Findings from sensitivity analysis

In the sensitivity analysis, when the UK tariff was used to derive EQ-5D utility scores, the EQ-5D utility scores were generally lower; however, this did not impact on the overall findings from the multivariable analysis. The findings from the sensitivity analysis using the UK tariff for the pre-ART observational period are shown in Figure 39; Table 25; Table 26; Table 29. The findings from the sensitivity analysis using the UK tariff for the ART observational period are shown in Figure 45; Figure 46; Table 35; Table 36; Table 37.

6.4 Discussion

In this component of the PhD I found that the costs of assessing HIV positive individuals for ART eligibility was higher for those detected through facility-based HTC than HIV self-testing, and was higher for those with a CD4 count above 350 cells/ μ l than for those with a CD4 count below 350 cells/ μ l. I found the cost of providing ART was highest in the first month after initiating ART, but was comparable in the subsequent months, with the modality of HIV testing and CD4 count not independently impacting on these costs. In addition, I found that the health-related quality of life was lower for those with more advanced HIV disease (measured by their CD4 count) and improved once they started ART, with the majority reporting perfect health after being on treatment for one year.

In the pre-ART observation period, where individuals are assessed for eligibility to start ART, the costs (health provider and societal) were higher for those detected through facility-based HTC and those who had higher CD4 counts. Individuals who accessed HIV testing at the health facility are often doing so because they were attending the facility to access other medical care (e.g. TB screening) and referred for HIV testing by medical personnel as part of provider-initiated HIV testing and counselling (PITC). Consequently those who tested positive through facility-based HTC may be affected by another medical illness (e.g. TB), because of their weakened immune system, and need medical care in addition to their assessment for ART eligibility. This is likely to explain why the health provider and societal costs were

higher for this group, who may have needed more clinic visits and additional medications or investigations.

At the time of this study, individuals were initiated onto ART if their CD4 count was below 350 cells/ μ l or they had clinically advanced HIV disease (WHO stage 3 or 4). Individuals with clinically advanced HIV disease (WHO stage 3 or 4) can potentially have a CD4 count above 350 cells/ μ l, especially in Malawi where Tuberculosis (TB) is common, and developing active pulmonary TB disease would mean individuals would be clinically staged as WHO stage 3. This may explain why those who had CD4 counts above 350 cells/ μ l incurred higher health provider and societal costs in the assessment for eligibility to initiate ART.

In the multivariable analysis, I adjusted for the number of CD4 counts measured to take into account that some individuals were not eligible to start ART but retained in pre-ART care with further assessment undertaken months later. In the multivariable analysis of health provider costs during the pre-ART observation period (Table 23; model 2), those who had two CD4 counts measured incurred an additional cost of US\$32.91 in comparison to those who had one CD4 count measured. This additional cost is not too dissimilar to the mean adjusted cost for those who had one CD4 count measured (2014 US\$29.76). This suggests that the cost of re-assessing for ART eligibility remains comparable to the cost of the initial assessment. Individuals not found eligible for start ART are retained in pre-ART care. There are no

recommendations about medical care that should be provided to this population (WHO, 2014), and whilst this may reduce costs of retaining patients in HIV treatment it also significantly impact on retention with large numbers of those not found eligible not returning for further assessment (Plazy et al., 2015).

In the study I estimated the annual health provider cost of managing a patient on ART to be approximately 2014 US\$166.20 (2014 INT\$ 226.16). Table 38 shows previous estimates for the annual health provider cost of providing ART for HIV positive individuals from other countries in sub-Saharan Africa. The annual HIV treatment estimates from this study are broadly similar to previous estimates for Malawi (2011 US\$136) (Tagar et al., 2014), or estimates from studies undertaken more recently and in countries with comparable health systems and economies (Larson et al., 2013, Scott et al., 2014, Bratt et al., 2011, Tagar et al., 2014, Johns et al., 2014, Bikilla et al., 2009).

Evidence suggests that as HIV treatments programmes grow and mature the average per patient costs of providing care will fall (Menzies et al., 2012), whilst the last decade has seen a significant fall in the cost of anti-retroviral drug prices (Tagar et al., 2014). This will explain many of the differences seen in the Table 38. The higher cost of providing ART in South Africa is driven by the fact that much of HIV care is provided by medical doctors and the higher cost of wages in the country.

Table 38: Average annual HIV treatment costs for patients on ART

Country of study	Year of data collection	Year of cost	Estimated cost per patient per year on ART (US Dollars)	Reference
Malawi	2010-2011	2011	\$136	(Tagar et al., 2014)
Kenya	2007	2009	\$230 to \$288	(Larson et al., 2013)
Zambia	2004-2008	2010	\$556	(Marseille et al., 2012)
Zambia	2007-2008	2011	\$198	(Scott et al., 2014)
Zambia	2008	2008	\$278	(Bratt et al., 2011)
Zambia	2010-2011	2011	\$278	(Tagar et al., 2014)
Ethiopia ¹	2003-2005	2004/5	\$235	(Bikilla et al., 2009)
Ethiopia	2006-2007	2009	\$781	(Menzies et al., 2011)
Ethiopia ²	2008-2010	2011	\$197-\$216	(Johns et al., 2014)
Ethiopia	2010-2011	2011	\$186	(Tagar et al., 2014)
Uganda	2006-2007	2009	\$967	(Menzies et al., 2011)
Rwanda	2010-2011	2011	\$232	(Tagar et al., 2014)
Lesotho ³	2008-2009	2009	\$261 to \$345	(Jouquet et al., 2011)
Multiple countries ⁴	2007-2010	2010	\$365	(Menzies et al., 2012)
South Africa	2002-2003	2004	\$2502	(Harling and Wood, 2007)
South Africa ⁵	2004-2005	2004	\$483	(Harling et al., 2007)
South Africa ⁵	2004-2005	2004	\$1,177	(Martinson et al., 2009)
South Africa	2005	2006	\$928	(Rosen et al., 2008)
South Africa ^{2,5}	2008-2009	2009	\$708 to \$1176	(Long et al., 2011)
South Africa	2010-2011	2011	\$682	(Tagar et al., 2014)
Nigeria	2006-2007	2009	\$969	(Menzies et al., 2011)
Burkina Faso ⁶	2010	2012	\$1,098	(Cianci et al., 2014)

1: ART provided in Hospital outpatient setting

2: Range of costs depending on degree of task shifting

3: Range of costs for different ART drug Regimens

4: Botswana, Ethiopia, Mozambique, Nigeria, Uganda and Vietnam

5: Estimated from monthly cost

6: Clinic for Female sex workers

In the study I found the costs (health provider and societal) of managing HIV positive individuals on ART was not effected by either their HIV disease stage (by CD4 count) on initiating treatment, or the modality of HIV testing received prior to entering HIV care services. This finding is not unexpected. Malawi has followed a public health approach to scaling-up their HIV treatment services. This has required them to utilise

medical personnel other than doctors to provide the majority of care, with less reliance on diagnostic tests for clinical assessment prior to initiating ART or once on treatment. Consequently the majority of individuals being clinically assessed prior to initiating treatment, and starting treatment are provided comparable levels of medical care.

The higher cost in the first month of providing treatment is expected because patients are asked to return more frequently to ensure no early side effects of treatment and good adherence (Malawi MoH, 2011a). Previous studies have found the health provider cost of providing HIV care amongst those initiated onto treatment with more advanced HIV disease was higher (Leisegang et al., 2009, Harling and Wood, 2007). In these studies the cost of hospitalisations was included. In my study it was not possible to estimate this at the individual level because of the lack of recording in the medical records and because patients could not accurately provide information on their hospitalisation episodes. This was one of the driving factors for undertaking the hospital costing study described in Chapter 7 of the PhD.

The study demonstrates the high costs incurred by patients when accessing HIV care. Individuals incurred a cost of approximately US\$9 during their assessment for ART eligibility, and US\$40 during the first year after starting ART. Anti-retroviral therapy is provided free but those accessing care may still incur costs including the costs of transportation to health facilities, or indirect costs as a result of losing income from

taking time off work to attend health facilities (Mshana et al., 2006, Rosen et al., 2007). Additionally, these costs can also have an impact on long-term adherence to therapy resulting in many individuals stopping treatment (Hardon et al., 2007, Mills et al., 2006). In Chapter 5 of the PhD I showed how providing HIV testing in homes saved users considerable time and money. Previous studies have shown that in sub-Saharan Africa, ART can be effectively provided in people's homes through community distribution models (Jaffar et al., 2009, MacPherson et al., 2014). HIV infected individuals on ART require frequent and life-long attendance at health facilities to access care, and it may be necessary to consider home provision of treatment in the region.

In this study, I found CD4 count to be significantly associated with the EQ-5D utility score, with participants who had lower CD4 counts to have lower EQ-5D utility scores. In addition, in those who started ART the EQ-5D utility scores gradually improved over the first year of receiving treatment with the majority of individuals reporting '*perfect health*', equivalent to an EQ-5D utility score of 1. The findings are comparable to previous studies that have shown that those with advanced HIV disease (or lower CD4 counts) have poorer health-related quality of life (HRQoL), with quality of life improving after starting ART (Beard et al., 2009). In Chapter 5 of the PhD I discussed the issue that HIV self-testers reported better HRQoL and how this may be related to the service being utilised HIV infected people earlier in their disease progression (Figure 31 and Figure 32). In the study undertaken in this Chapter we found that HRQoL in HIV-positive individuals improves once they start

ART. The findings from this chapter and Chapter 5 highlight some of the potential gains in HRQoL through early uptake of HIV testing and timely initiation of ART in HIV-positive individuals unaware of their status.

Qualitative studies amongst HIV positive individuals living in Africa have found individuals experience improvements in their HRQoL within six months of starting ART (Mutabazi-Mwesigire et al., 2014). Quantitative assessments of HRQoL in HIV positive individuals starting ART have also found significant improvement with initiation of ART, with much of the improvement occurring in the first few months after initiating treatment (Pitt et al., 2009, Jelsma et al., 2005, Stangl et al., 2007). In this study, participants who initiated ART also experienced significant improvements in their EQ-5D utility scores, with very few participants reporting any problems in any of the five dimensions of HRQoL within the EQ-5D descriptive system. In addition, I found that even amongst those with low CD4 counts, the majority reported perfect health (EQ-5D utility score of 1.0) after initiating ART. The findings support the beneficial impact of ART on quality as well as quantity of life lived amongst HIV infected individuals. This would support the importance of measuring quality of life improvements, and undertaking cost-utility analysis, when investigating interventions aimed at improving health outcomes amongst HIV infected individuals.

Health-related quality of life is an important outcome for patients, and studies investigating the impact of earlier initiation of ART or other interventions in HIV

positive individuals will need to consider this in their outcomes. The EQ-5D measure has previously been shown to be responsive to changes in HRQoL amongst HIV positive patients accessing ART in high-income settings (Wu et al., 2013). However, very few studies use the EQ-5D to measure HRQoL amongst HIV infected individuals in sub-Saharan Africa (Beard et al., 2009, Robberstad and Olsen, 2010). The EQ-5D allows us measure HRQoL and therefore undertake a cost-utility analysis (CUA). The findings from a CUA can be more informative for policy makers than a cost-effective analysis as they will often need to consider funding decisions across a range of healthcare intervention (Drummond et al., 2005b). Researchers in sub-Saharan Africa have often used disability-adjusted life years (DALYs) to undertake CUA, but as discussed in Chapter 4 of the PhD, DALY's have limitations. In this study, I found that the EQ-5D detected differences between those with advanced HIV disease and those with less advanced disease, as well as detecting improvements in HRQoL in participants who initiated ART. These findings support previous work that suggest the EQ-5D measure has value in HIV research (Tran et al., 2015, Tran et al., 2012), and consequently will support the development of economic evaluations by allowing outcomes to be quantified in quality-adjusted life years.

In this study I would that the EQ-5D utility scores derived using the Zimbabwean tariff were higher than those derived from the UK tariff. There is no current Malawian tariff to derive EQ-5D utility scores from the responses to the descriptive component of the EQ-5D measure. In the PhD I have assumed that Malawians are more likely to value health like Zimbabweans than people from the UK (discussed in

Chapter 4 of PhD). However, this may not be true, and may suggest the potential value of developing a Malawian tariff to derive EQ-5D utility scores. However, the conclusions regarding the impact of HIV disease stage and impact of ART, on the EQ-5D utility scores were comparable in the sensitivity analysis (using the UK tariff) as the primary analysis (using the Zimbabwean tariff). The findings from Chapter 7 of the PhD were I investigate the HRQoL amongst hospitalised patients, a sicker population, and Chapter 8 of the PHD, the final cost-utility analysis, will provide more information on the potential benefits of developing a Malawian tariff.

I found that the modality of HIV testing received prior to accessing HIV treatment services had no independent impact on the EQ-5D utility score. In Chapter 5 of the thesis, I found EQ-5D utility scores were lower amongst HIVST who tested HIV positive. This difference is likely to be related to the stage of their HIV disease at the time of accessing HIV testing. HIV self-testing is provided in the community whilst facility-based HTC to those attending the health facility. Those attending the health facility will include those who are there seeking other medical care, including for diseases (e.g. TB) that arise as a consequence of their advanced HIV disease.

The findings that relate to the impact of the modality of HIV testing received and costs or providing pre-ART and ART care, and EQ-5D utility scores should be taken with caution. In this study the cohort of individuals entering HIV care were recruited after they had attended the HIV clinic. The findings could therefore be potentially

biased by differential rates of linkage into HIV treatment services after HIV testing. Those who underwent HIVST are likely to be healthier than those who underwent facility-based HTC. Additionally facility HTC clients in the majority attended the health facility to learn their HIV status. It is likely facility HTC clients were keener to enter HIV care and therefore the comparisons made between these groups could be potentially biased.

6.5 Summary of Chapter 6

In this Chapter I recruited a cohort of HIV positive individuals in Blantyre who had accessed wither HIVST or facility-based HTC to learn their HIV status. I followed them up until they had completed one year of anti-retroviral therapy (ART). I collected data on the healthcare resources used during this period and undertook primary costing studies to estimate the health provider costs of assessing them for eligibility to start ART, and for providing the first year of ART. I also asked participants on the costs they incurred and about the health-related quality of life (HRQoL).

The findings suggest that there are initial differences in the health provider costs (during the pre-ART period) but once individuals are on ART the costs are not affected by their HIV disease stage. Additionally I show HRQoL is poorer amongst those with advanced HIV disease, but all those who start ART report near perfect health by the end of the first year of receiving treatment. I also show the modality of HIV testing received prior to entering HIV care did not have an impact on the majority of the economic outcomes.

The economic data collected from this chapter will be used to inform the decision-analytic modeling of the cost-effectiveness of HIV self-testing (Chapter 8). This study provides estimates for the health provider and societal cost of assessing individuals for eligibility to start ART and for providing ART. In addition, this chapter provides

EQ-5D utility scores for health states to describe the progression of HIV disease before starting ART and after starting treatment.

As the study did not allow us to quantify the economic impact of HIV disease on hospitalisation, a common occurrence, I will investigate this issue in Chapter 7 of the PhD. In Chapter 7, I will describe the study I undertook amongst adults admitted to the medical wards at Queen Elizabeth Central Hospital, Blantyre, Malawi.

**CHAPTER 7: Economic and Health-
Related Quality of Life Outcomes
for Hospitalised Patients Co-
infected with HIV in Blantyre,
Malawi**

7 Overview of Chapter 7

In this chapter I describe an investigation of one of the secondary objectives of my PhD.

To estimate the costs, to individuals and to healthcare providers, and health-related quality of life of adults who are admitted to the medical wards in Queen Elizabeth Central Hospital, Blantyre, Malawi, for the management of medical illnesses.

To investigate the relative impact of HIV infection on costs and health-related quality of life of adults who are admitted to the medical wards in Queen Elizabeth Central Hospital, Blantyre, Malawi, for the management of medical illnesses.

As previously mentioned this Chapter is written as a stand-alone study. In this Chapter, I follow-up a cohort of adults admitted to the medical wards at Queen Elizabeth Central hospital, a teaching hospital in Blantyre, Blantyre. I will investigate the health provider, direct non-medical and indirect costs, and societal costs associated with managing a range of medical conditions. I will investigate the impact of these medical conditions on individual's health-related quality of life. One of the main objectives is to obtain primary economic and health-related quality of life data for the final cost-effectiveness modelling study to be presented in Chapter 8.

7.1 Introduction

Hospitals are an essential component of health services, however in sub-Saharan Africa there is a lack of understanding of the costs of providing care to inform policy or research (Adam and Evans, 2006, Adam et al., 2003, Grimes et al., 2014, Mills, 1990, Beck et al., 2010). Policy makers and healthcare providers need to understand these costs to make budgetary and planning decisions. Importantly, the costs of providing hospital care accounts for a large proportion of the total health expenditure (Chopra et al., 2009). Providing care in primary health facilities is significantly less costly and more equitable than providing care in hospital settings (Adam and Evans, 2006, Lombard et al., 1991, Mills et al., 2012).

In the region HIV infection, and the co-morbidities those infected develop, is the commonest reason for hospitalisation, with up to three quarters of adults admitted for medical reasons HIV positive (SanJoaquin et al., 2013). Moreover, hospital care is over twice as costly for individuals infected with HIV as for those who do not have HIV (Tshamba et al., 2014, Guinness et al., 2002), with those admitted having poor outcomes (SanJoaquin et al., 2013). In comparison to those who are not HIV infected, HIV positive individuals often need to stay in hospital longer, and they may require more investigations and medications (Hansen et al., 2000).

In resource-rich countries the costs of managing HIV-infected individuals have changed over the last decade or two. After the introduction of anti-retroviral therapy

(ART) the costs of managing individuals with HIV rose, driven by the high costs of anti-retroviral drugs (Rizzardini et al., 2011, Mandalia et al., 2010). However as medical care for HIV infected individuals became more effective, and individuals are treated earlier in the course of their disease, the need for hospital care and costs fell (Rizzardini et al., 2011, Mandalia et al., 2010). This set of changes is likely to occur in sub-Saharan Africa over the next 10-20 years with earlier initiation of ART reducing the risks of opportunistic and TB disease (Cohen et al., 2011, Group et al., 2015b, Group et al., 2015a). Much of the potential cost savings achievable through earlier initiation of ART is felt to be through reduced hospitalisation amongst the HIV infected population (Munderi et al., 2012, Granich et al., 2012, Meyer-Rath et al., 2013), however, there is currently a lack of primary economic evidence to support this argument (Beck et al., 2010, Adam and Evans, 2006).

In this component of the PhD I investigate the economic impact of hospitalisation amongst adults in Blantyre, Malawi, I recruited a cohort of adults admitted to the medical wards at Queen Elizabeth Hospital in Blantyre, Malawi. I collected medical diagnostic and resource use data, and undertook primary (resource-based) costing studies to estimate the costs of managing a range of HIV-related and other illness in the hospital. I also investigated the costs incurred by patients and their families as a result of the hospitalisations, and evaluated their health-related quality of life outcomes.

7.2 Methods

7.2.1 Ethics

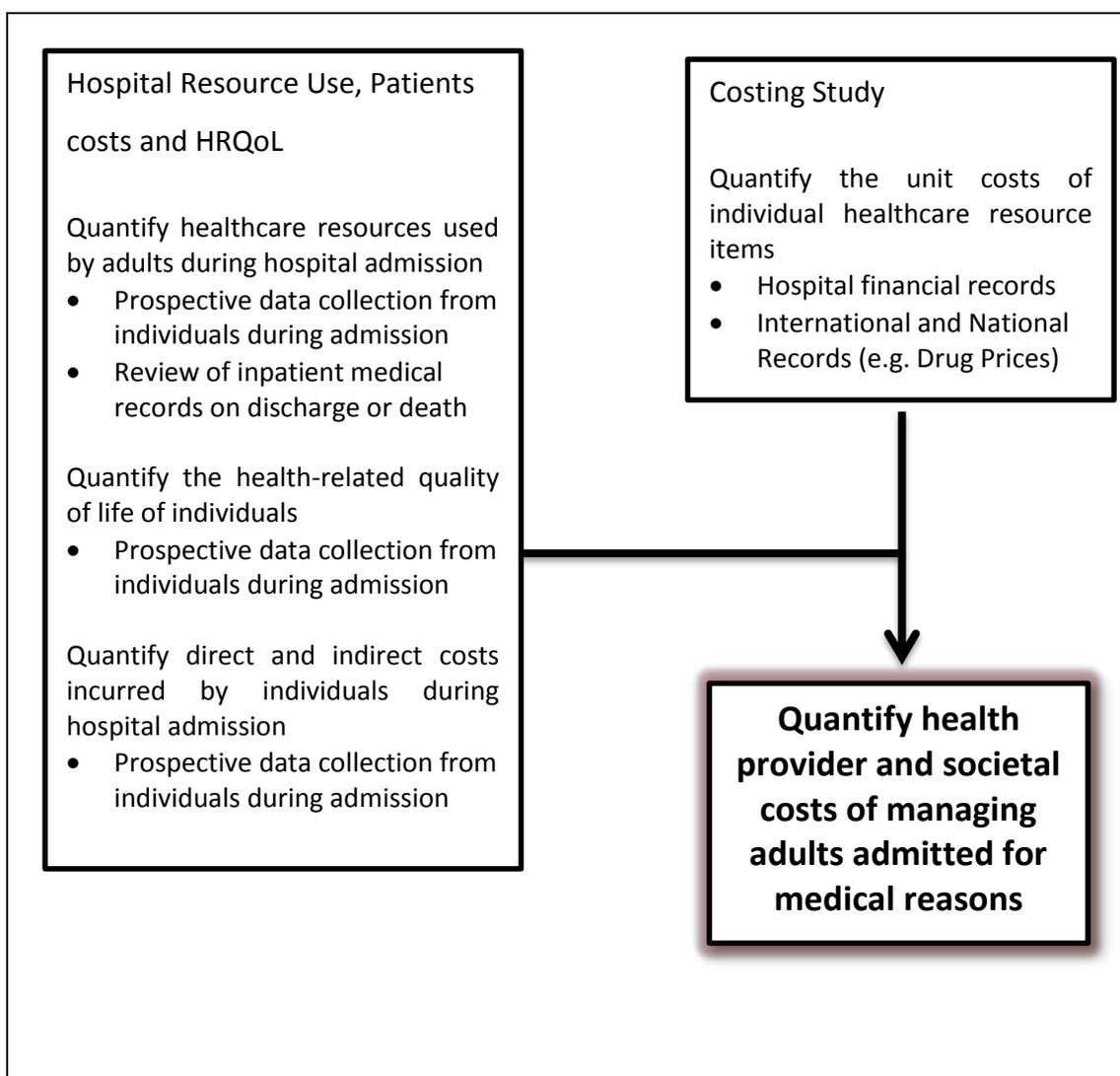
I obtained ethical approval from the College of Medicine Ethics Review Committee, University of Malawi; and the University of Warwick Biomedical Research Ethics Committee (**Appendix I**). All participants were provided with an information leaflet explaining the study and thereafter informed consent was sought (**Appendix XIV and XV**).

7.2.2 Study overview

The study was undertaken between June 2014 and December 2014. I recruited individuals admitted to the medical wards in Queen Elizabeth Central Hospital (QECH), Blantyre.

Participants were asked about their direct non-medical costs, indirect non-medical costs and health-related quality of life outcomes during their hospital admission. The medical notes were reviewed after discharge to determine the medical reasons for admission and the medical resources used during admission. Primary costing studies were undertaken to estimate the direct health provider costs. Figure 47 provides an overview of the study design.

Figure 47: Overview of study design



7.2.3 Study setting and study population

QECH is the largest hospital in Malawi, with approximately 1,500 beds and 25,000 adult inpatients per year (SanJoaquin et al., 2013). The HIV prevalence amongst medical inpatients has previously been reported to be as high as 70% (SanJoaquin et al., 2013). The hospital has a large emergency department where all new patients are triaged and assessed by a medical doctor. The decision is then made on whether

the patient needs hospital admission, and to which department they should be admitted. The doctor also makes a preliminary medical diagnosis. Patients with medical diagnoses are transferred to one of three medical wards: 3A (TB ward); 3B (male medical); and 4A (female medical). Patients admitted to either the male or female medical ward, and who are then diagnosed and started on TB treatment are subsequently transferred to ward 3A (TB ward).

In this study I recruited a cohort of adults (aged ≥ 18 years) admitted to these three medical wards. A study nurse reviewed the medical admission book on each of the three wards. Every fifth participant admitted to each of the three wards was recruited into the study during the study period June 2014 and December 2014. In addition, all adults who were admitted and had been given a preliminary medical diagnosis of less common late stage HIV-related diseases (Pneumocystis Carinii Pneumonia; Candidiasis; Cryptococcal Meningitis; or Kaposi's Sarcoma) were recruited. **Appendix XVI** shows the template of the book designed for each ward to record admission information and identify participants eligible for recruitment.

All participants were seen by the field worker on the first working day after their admission for recruitment and initial data collection. Participants were subsequently also seen by the field worker every three to seven days that followed and on the day of discharge. After discharge a doctor working on the ward reviewed the medical notes of each participant, and extracted medical associated resource use data. Table

39 provides an overview of the data collection, and timing of consent and administering questionnaires.

Table 39: Overview of data collection and timing of administering questionnaires

		1 st working Day of Admission	Every 3-7 after Admission (where applicable)	On Discharge or Death	After discharge
Individual Interviews – Completed by Field worker with participants					
Participant information leaflet:	<i>HTC-500</i>	✓			
Consent:	<i>HTC-500X</i>	✓			
Socio-demographic:	<i>HTC-501</i>	✓			
HRQoL – EQ-5D:	<i>HTC-QOL</i>	✓	✓	✓	
Participant time and out-of pocket costs:					
	<i>HTC-502</i>	✓			
	<i>HTC-503</i>		✓	✓	
Medical data extraction – Completed by Medical doctor reviewing medical notes					
Primary and Secondary Diagnosis	<i>HTC-DOC</i>				✓
HIV +/- ART Status	<i>HTC-DOC</i>				✓
Investigations performed	<i>HTC-DOC</i>				✓
Procedures performed	<i>HTC-DOC</i>				✓
Medications given	<i>HTC-DOC</i>				✓

7.2.4 Medical data extraction

A medical doctor reviewed the medical notes for each study participant after the end of the hospital stay and extracted data on their primary medical diagnosis, HIV status and the medical care provided. The doctor recorded the duration of hospital admission, and the patient's outcome (discharged home; transferred to another hospital; absconded; or died during hospitalisation). The doctor also recorded their HIV status, CD4 count and anti-retroviral drug use. For the CD4 count the doctor recorded the CD4 count and the date the CD4 count was measured. For anti-retroviral drug use, the doctor recorded whether the patient had been initiated prior

to hospital admission or initiated during the hospital admission, as well as the drug regime patient was prescribed.

The primary medical diagnosis was recorded using two approaches. The first was a single-level coding of the diagnosis using one of 22 options (**Appendix XVII**), including one option for 'other' and one for 'not known'. The options were based on the internal surveillance system for hospital admission at QECH (SanJoaquin et al., 2013). The second was a multi-level coding system based on *International Classification of Diseases, 9th Revision, Clinical Modification* (IDC-9-CM) (Elixhauser et al., 2014) (**Appendix XVIII**).

An extensive list of the investigations and procedures, undertaken at QECH was derived after discussions with doctors working at the hospital. The doctor recorded which investigations and procedures were performed for each patient and how many times they were performed. A list of all drugs available at the pharmacy at QECH was obtained. The doctor recorded the drug name, dosage, route of administration and total number of doses given. Data extraction tools were pilot tested by the medical doctors, and adapted after discussions with them. **Appendix XVII** shows the final data extraction tool used by the doctors and **Appendix XVII** shows the medical diagnosis classification codebook.

7.2.5 Cost analysis

7.2.5.1 Direct health provider costs

THE UNAIDS costing guidelines were used to undertake the primary costing studies to estimate the costs for all medical resource outputs used (UNAIDS, 2011). Broadly, a list of medical resource outputs (e.g. days of admission; full blood count) was identified from the medical data extracted by the doctors. Secondly, interviews were conducted with medical and administrative personnel to identify and quantify the individual resources required to produce the medical resource outputs. Thirdly, the financial data from hospital administration systems, in combination with National and International resource data (Frye, 2012, UNAIDS, 2011, WHO-CHOICE), were used to value individual resource inputs. Fourthly, the data was used to estimate the cost of each medical resource output. Finally, the estimated resource output costs were used to estimate the total health provider cost for each study participant.

I used a combination of top-down and bottom-up methods to estimate the relevant costs. Figure 48 provides an overview of how the bottom-up approach was used to estimate the cost of medical resource outputs. Figure 49 shows how the top-down method was used to allocate costs of support services to the medical resource outputs.

Figure 48: Bottom-up approach to costing resources used

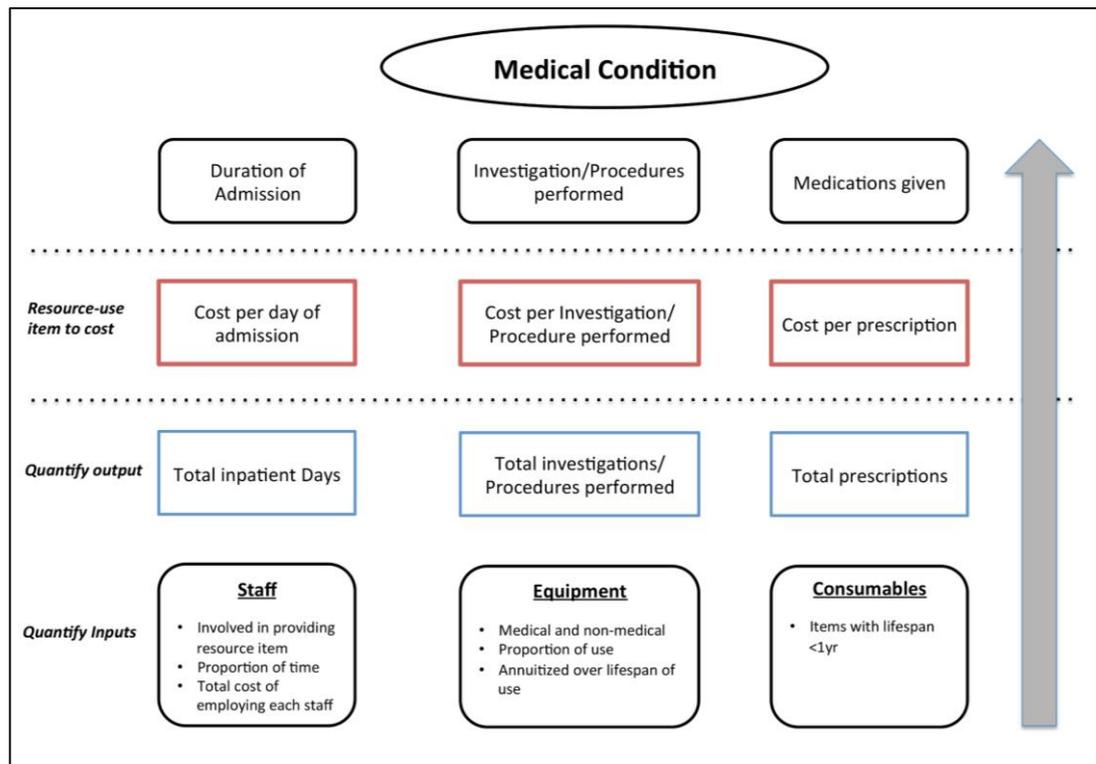
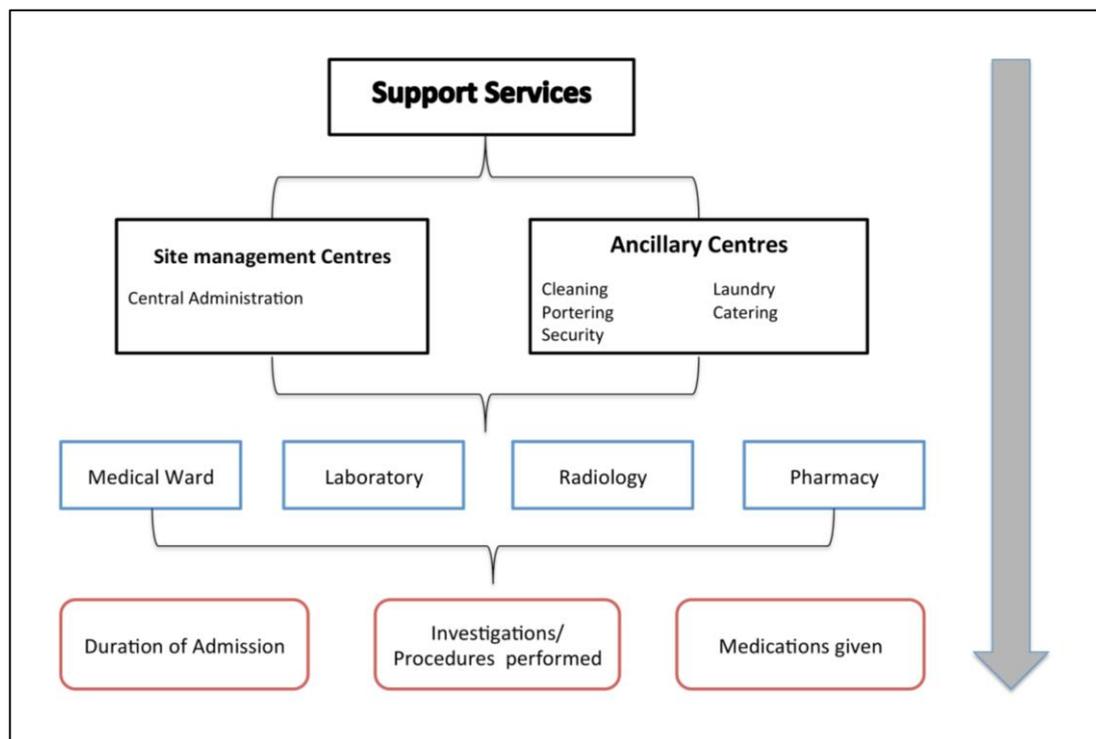


Figure 49: Top-down approach to allocating support



I undertook interviews with central support services to estimate the total central support service costs for running the hospital. This cost was then allocated to each department (Medical wards, Laboratory, Radiology and Pharmacy). I used the number of staff working in each of these departments divided by the total number of staff at the hospital to estimate the proportion of the total central support costs consumed by each relevant department. Some central support costs (e.g. catering, costs of locum staff) were only allocated to the medical wards, as the other departments do not benefit from them. For this we used the number of clinical staff working on the medical wards and divided by the total number of clinical staff working in the hospital to determine what proportion of the specific form of central support cost should be allocated to each medical ward.

For the medical wards, I estimated the cost per day of hospital care. Interviews were undertaken with the nurse in charge on the wards to determine the staff who worked on the ward and the time they spent on the ward. Information was obtained on the consumables used, and the quantity of each consumable used annually. A list of all the equipment on the wards was also documented. A unit cost was obtained for all consumables and equipment's. The total average annual cost of running the ward was estimated. This comprised the cost of staff, consumables and equipment. The cost of central support services was added to these total costs. During the study period I also recorded the daily number of patients on each ward, and this was used to estimate the total number of patient days of admission per year

(Appendix XIX). The total average annual cost for each ward was divided by annual patient days to estimate the average cost per patient day of admission.

I repeated the same procedure for the pharmacy department. I estimated the total average annual cost of running the pharmacy. This comprised the costs of staff, consumables and equipment, in addition to an allocated proportion of the central support services. The pharmacy keeps a record of the total drugs supplied per annum, broken down by drug formulation and doses given. The total average annual cost of running the pharmacy was divided by the total number of drug doses supplied to estimate the average cost per dose of drug dispensed by the pharmacy. This cost was added to the cost of the drug to estimate the total cost of providing the drug to the patient. For the cost of the drugs I used the international market price (Health, 2013). The cost of shipping and insurance was excluded from the international market price for the drugs.

Figure 50 **and** Figure 51 compares the costs of drugs obtained from the Malawian MoH price catalogue, which includes the cost of shipping and insurance, to the price of drugs provided by the International drug price indicator guide, which excludes these costs (Health, 2013). For the majority of the drug prices, the prices were comparable.

Figure 50: Comparison of drug prices between Malawi MoH and international market price (prices < US\$0.05)

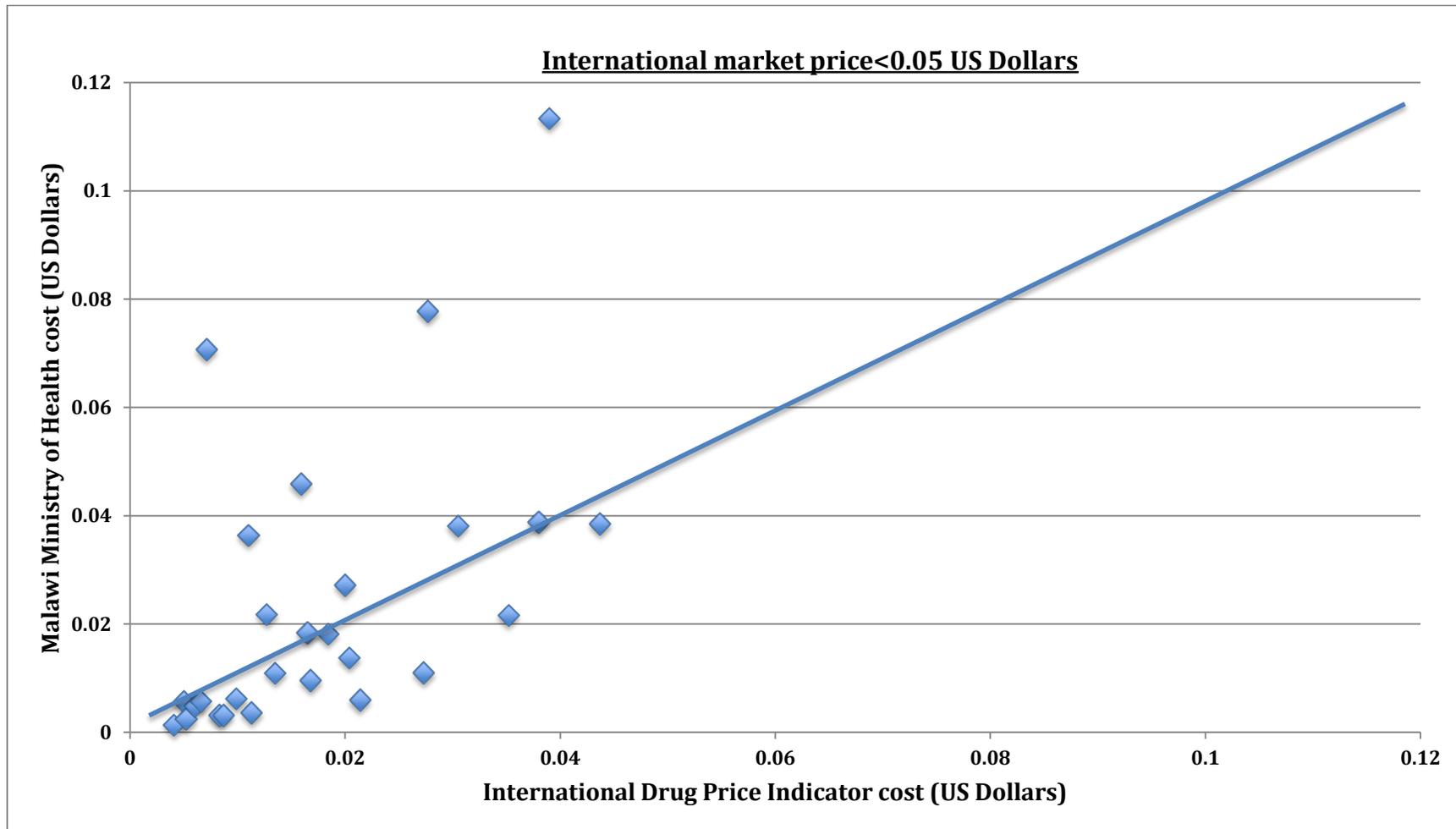
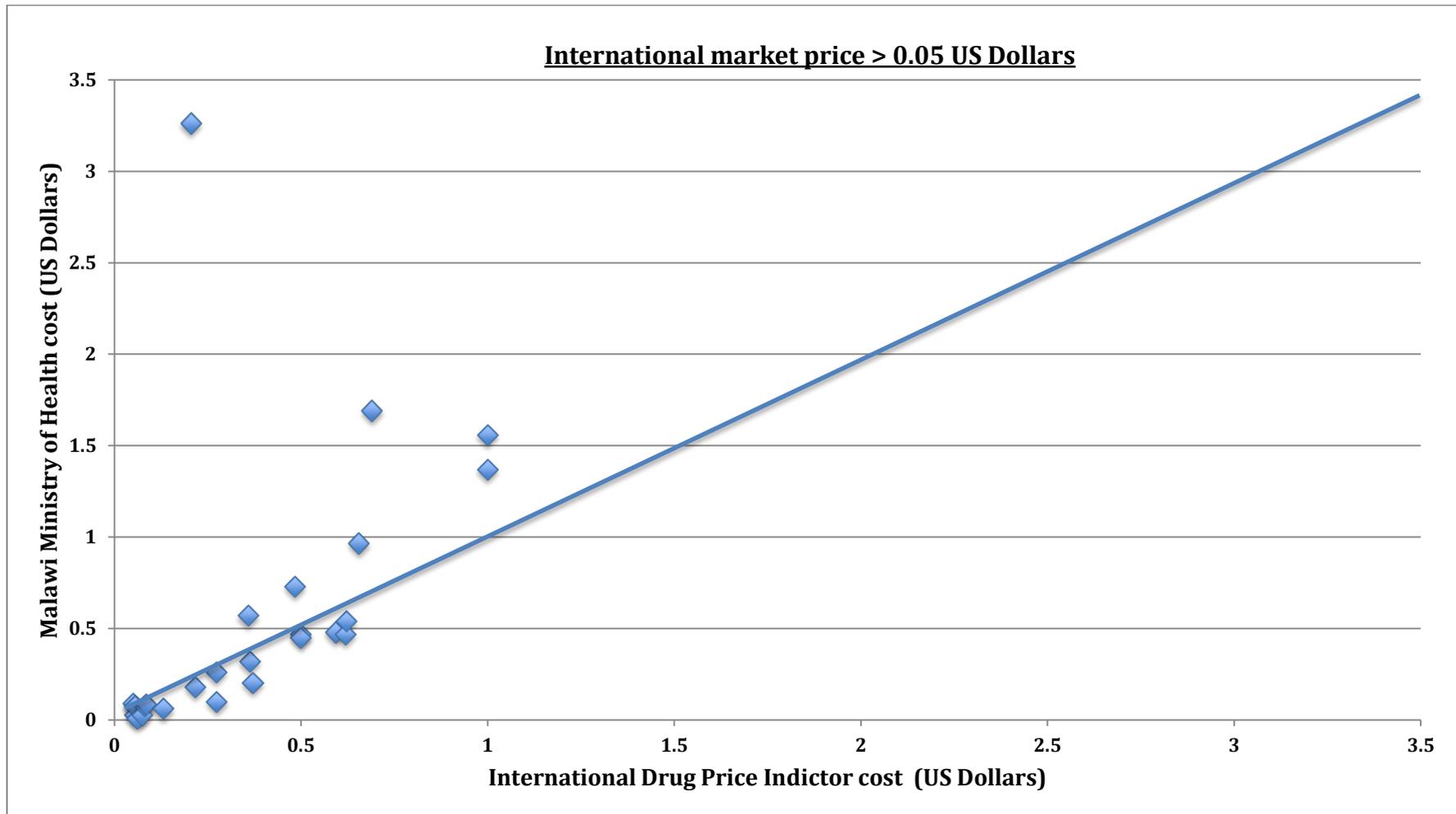


Figure 51: Comparison of drug prices between Malawi MoH and international market price (prices > US\$ 0.05)



Investigations and procedures are performed through the Laboratory and Radiology department at QECH or on the medical wards. For investigations and procedures, I estimated the direct cost of performing the investigation and the indirect cost of the investigation or procedure. The direct cost of the investigation or procedure comprised the attributable cost of personnel, consumables and equipment. I undertook interviews with the medical, laboratory and radiology staff to quantify each of these items. For equipment and personnel, I recorded the approximate time spent in performing the investigation. A unit cost of each item was obtained and the total direct cost of the investigation or procedure was estimated. The indirect cost of the investigation comprised the cost per test of the department and the cost of the central support services. For this I estimated total cost, including the cost of central support services, and divided this by the total outputs of the department. For investigations and procedures performed in the Laboratory and Radiology department, I used the total number of tests performed as the denominator. For the Laboratory and Radiology department, I undertook interviews to estimate the numbers and grades of staff working in the department, and the consumables and equipment used. For all these items I quantified the proportion of the time spent on performing investigations or procedures, and the proportion of time spent on general duties or activities. For the indirect costs I summed total costs based on resources used for activities other than performing a specific investigation or procedure.

I investigated the validity of the costs estimated for a range of investigations and procedures for QECH. For this I compared the costs I estimated from the primary costing study to the cash price provided by two different private healthcare providers in Malawi (findings described in the results section of this Chapter: Figure 53 and Figure 54).

I used the estimated direct cost of performing investigations and procedures performed on the ward. Some investigations are performed outside QECH. For these we used the cost charged to QECH as the total cost of the investigation.

For all the costings, I obtained staff salaries from the QECH Human Resources departments and included employer contributions and fringe benefits. The costs of consumables and equipment were obtained from the Malawi Ministry of Health price catalogue. For costs that were not available in the catalogue, I used the international or reference prices (WHO-CHOICE). I first contacted local suppliers to obtain costs, and if these were not available, I contacted international suppliers and manufacturers. Equipment costs were annuitized over their useful life with an annual discount rate of 3%. For large laboratory and imaging equipment, I assumed the useful lifetime to be 5 years. This assumption was based on discussions with laboratory and radiology staff on time before equipment should be replaced. For all other equipment, including general office equipment, I assumed the useful lifetime to be 3 years.

For all the above interviews to determine resources use by each department I used the same data extraction tool developed in Chapter 5 of the PhD that component of the study (**Appendix XII**).

7.2.5.2 Direct non-medical and indirect costs

A questionnaire was developed to capture the direct non-medical and indirect costs incurred by each study participant and their main family member or carer who remained with them at hospital during the admission. The direct non-medical costs included the cost of transportation, food, drinks, toiletries, clothing and other items bought during their hospital admission. For indirect costs, I recorded whether participants had taken time off work, and if so, the amount of time, and multiplied this by their self-reported income (Pritchard and Sculpher, 2000). Two questionnaires (HTC-502 and HTC-503) were developed to estimate these costs and are shown in **Appendix XXI and XXII**.

Table 39 shows when these two questionnaires were administered. A field worker interviewed the participant during their hospital admission to complete these questionnaires. The first (HTC-502) was administered to participants on the first working day after hospital admission (**Appendix XXI**). All these direct non-medical and indirect costs were related the costs incurred on the day of their hospital admission. The second (HTC-503) was administered to participants every three to seven days after the first questionnaire. This second questionnaire asked

participants about direct non-medical and indirect costs for the preceding day they were in hospital (**Appendix XXII**).

The questionnaires were forward translated into Chichewa, the local language of the study population, and back translated by two independent bilingual Malawians. The questionnaires were then pilot tested, and discussions were held with senior Malawian staff working at the Malawi-Liverpool Wellcome Trust Clinical Research Programme before the final version was agreed upon.

7.2.5.3 Cost conversions

As described in preceding chapters, all costs were converted into 2014 US Dollars and International Dollars (Drummond et al., 2005b) using data reported by the World Bank (Evans et al., 2005). The cost, currency, price year and source country of cost were recorded for all items. The costs were adjusted to the year of reporting using the Gross Domestic Product (GDP) deflator index, provided by the World Bank. The costs were then converted to 2014 US Dollars using the market exchange rate, and to 2014 International dollars using purchasing power parity conversion factor (Krijnse Locker and Faerber, 1984, Shemilt et al., 2010).

7.2.6 Health-related quality of life

All study participants recruited into the study were asked about their general health and their health-related quality of life (HRQoL) as soon as possible after admission, and every three to seven days thereafter until final hospital discharge. The questionnaire (HTC-QOL) that was administered to participants by the field worker is shown in **Appendix XXIII**. Table 39 shows when the field worker administered this questionnaire.

The self-assessed health (SAH) measure was used to ask individuals to rate their general health on a five-point Likert scale, with responses coded as: very good; good; fair; poor; or very poor. The SAH measure has been found to be a strong predictor of future health outcomes in high-income settings (Idler and Benyamini, 1997), and has been used in resource-constrained settings (Gilbert and Soskolne, 2003, WHO, 2002).

The Chichewa version of the EuroQoL EQ-5D-3L (Dolan, 1997) was used to estimate HRQoL of participants recruited into this study. Participants completed both the descriptive EQ-5D-3L system and a visual analogue scale at each time point they were asked about their HRQoL (EuroQoL, 1990). Chapter 4 of the PhD provides a more detailed description of the EQ-5D tool, the process used to translate it into Chichewa and how EQ-5D utility scores are derived. Briefly, participants are asked to respond to the descriptive component of the EQ-5D-3L tool, with the EQ-5D utility score derived by using a tariff set. The tariff sets have been derived from national

surveys of the general population, with a subset of the 243 health states being valued, most commonly using the time trade-off method (EuroQoL, 1990). The remainder of the EQ-5D health states are subsequently valued through the estimation of a multivariable model. As there is no Malawian EQ-5D tariff, I used the Zimbabwean EQ-5D tariff set (Jelsma et al., 2003) to derive an EQ-5D utility score for each study participant. The visual analogue scale (VAS) is similar to a thermometer, and ranges from 100 (best imaginable health state) to 0 (worst imaginable health state). Participants record how good or bad their health is on that day by drawing a line on the scale.

7.2.7 Statistical analysis

All analysis was undertaken in Stata version 13.0 (Stata Corporation, Texas, USA). Socio-demographic data was collected on all participants recruited into the study. This included sex, age marital status, educational attainment, employment status, and self-reported income. For socio-economic position, we collected data on household assets, nine in total, and information on home environment, for example distance to toilet. We undertook principal component analysis to classify an individual's socio-economic position based on their wealth quintiles (Filmer and Pritchett, 2001). **Appendix XX** shows the questionnaire (HTC-501) used to collect individual-level socio-demographic and socio-economic data.

The *total direct health provider cost* was estimated for each study participant. The total direct health provider cost per participant was comprised of the cost of the stay on the hospital ward, the cost of all investigations and procedures and the cost of all drugs given. The cost of stay on the hospital ward was estimated by multiplying the average cost per day of admission by the total number of days on the ward. This was estimated for each ward the participant was admitted to. The total cost of investigations and procedures per participant was estimated by multiplying the cost by the number of times they were performed. This was done for all investigations or procedures performed and summing the costs. For drug costs per participant the cost of each drug, including the cost of dispensing the drug through the pharmacy department, was multiplied by the number of doses given. The total cost of drugs per participant was estimated by summing the costs of each individual drug given.

The *total direct non-medical and indirect cost* per participant was estimated for the duration of the hospital admission. This included the total direct non-medical cost and indirect costs incurred by the participant and their main family member/carer who stayed with them during their hospital admission. For participants who died during their hospital admission, this was estimated for the period from admission till death. I estimated the total direct non-medical and indirect cost for the day of admission, using responses from HTC-502. I estimated the average daily direct non-medical and indirect cost of each subsequent day of their hospital stay using responses from HTC-503. For participants who only had the questionnaire administered more than once, the average from each time questionnaire was

administered was estimated. The total direct non-medical and indirect cost was estimated by adding the costs on the day of admission, to the average daily cost multiplied by the total duration of the hospital admission minus one day.

The *total societal cost* per participant cost was estimated by adding the *total direct health provider cost*, and the *total direct non-medical and indirect cost*.

I estimated the total health provider costs; the total direct non-medical and indirect costs; the total societal cost and the EQ-5D utility score by the primary diagnosis of participants. For the primary medical diagnosis, I used the data extracted by the doctor on primary reason for the medical admission. The data was recorded from the multi-level coding system based on the *International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM)* (Elixhauser et al., 2014). For each participant, the medical diagnosis was classified up to four-levels. The classification system provides a more specific diagnosis at the higher level, but with the sample sizes used, would result in few participants for many of the diagnosis. I therefore re-coded the primary medical diagnosis to ensure at least five participants had the same primary medical diagnosis. I worked iteratively from the higher level to the lower levels to ensure that there were at least 5 participants for each of the final diagnostic categories.

For the EQ-5D utility score and VAS score, I estimated the scores on admission, the average score during the hospital admission, the last recorded score prior to discharge, and the change in score from admission to the final recorded score. For those who died on admission, or after admission, I recorded their utility and VAS scores as zero. For the change in EQ-5D utility and VAS scores, I subtracted their last recorded score from the first recorded score.

I undertook multivariable analysis to investigate the independent effect of HIV status on the total health provider cost and total societal cost. For HIV status, I classified individuals as HIV negative; HIV positive and taking anti-retroviral therapy prior to hospital admission; HIV positive and started anti-retroviral therapy during hospital admission; HIV positive and not on anti-retroviral therapy; and HIV status not known. As all participants incurred a cost, and the cost data was skewed, I used generalized linear models (GLM) for multivariable analyses of cost data (Barber and Thompson, 2004). I used the same approach as described in chapter 5 and ran model diagnostics to determine the optimal choices for the distributional family and link function (Manning and Mullahy, 2001). The Park test, link test, Akaike Information Criterion and visual inspection of plots of the deviance residuals were examined to determine the optimal choice for the link function and the distributional family.

I also undertook multivariable analysis to investigate the independent effect of HIV status on the EQ-5D utility score on hospital admission. EQ-5D utility scores were

non-normally distributed, skewed and truncated at 1.0. I used the same approach as described in Chapter 5 and evaluated four commonly used estimators to analyse these data: ordinary least squares (OLS) regression; Tobit regression, Fractional logit (Flogit) regression, and censored least absolute deviations (CLAD) regression (Powell, 1984, Austin et al., 2000, Papke and Wooldridge, 1996). The mean squared error (MSE) and mean absolute error (MAE) statistics were compared between the observed EQ-5D utility score and the estimated scores for the whole sample, and for sub-groups of the sample based on observed EQ-5D utility scores, to determine the choice of preferred estimator.

For all multivariable analyses I ran three alternative models, the first adjusted for HIV status, and age and sex. The second model was additionally adjusted for marital status, educational attainment, income and socio-economic position (Stangl et al., 2007). The third model was additionally adjusted for the primary medical diagnosis.

7.2.8 Sensitivity analysis

I also undertook sensitivity analyses to investigate the impact of using an alternative tariff set to determine EQ-5D utility scores. I used the UK York A1 tariff (Dolan et al., 1996a), which has been found to translate health states with 'severe' problems in one or more of the five dimensions to a lower EQ-5D utility scores than the Zimbabwean tariff (Jelsma et al., 2003).

7.3 Results

7.3.1. Participant characteristics

1,036 individuals were admitted to the adult medical wards and eligible for recruitment during the study period (Figure 52). In total, 822 (79.3%) participants were recruited into the study, and medical data extraction was possible for 661 (80.4%) of these. Table 40 shows the characteristics of those who were and were not recruited into the study.

Figure 52: Recruitment of participant

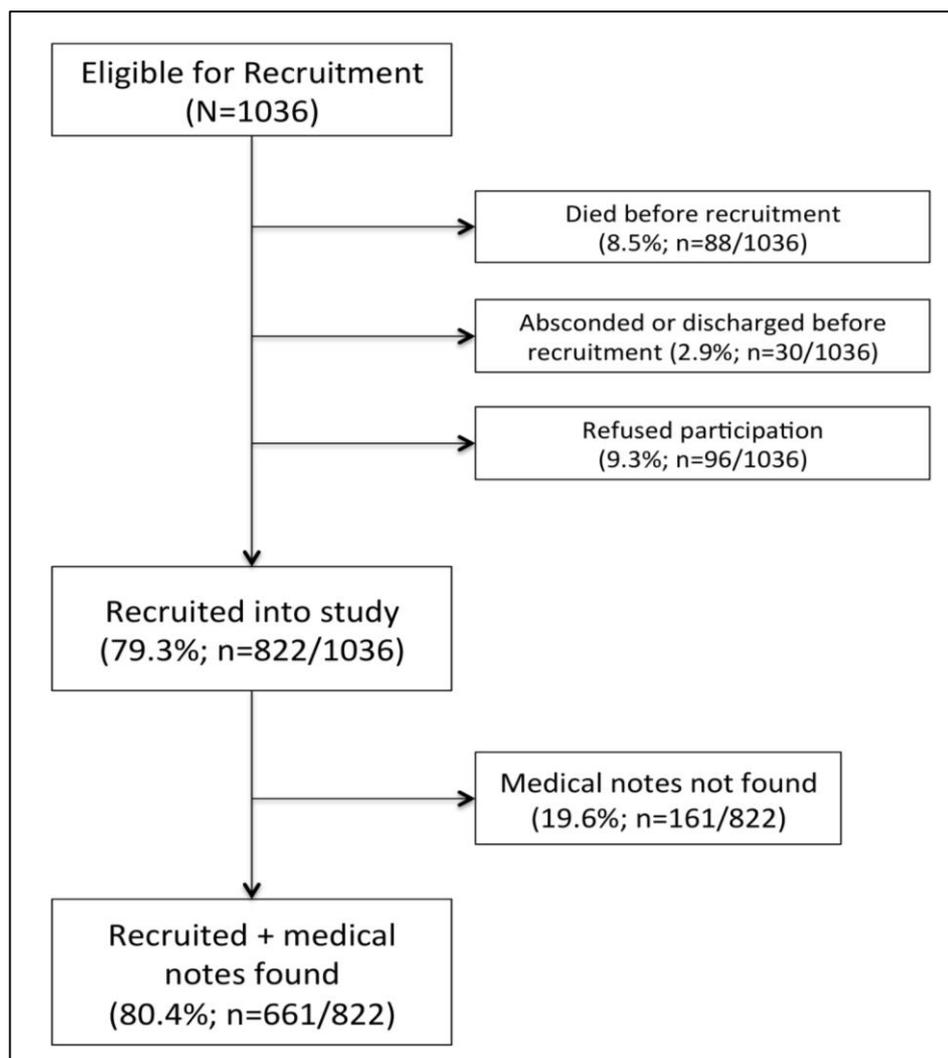


Table 40: Characteristics of participants eligible for recruitment

		Died before recruitment	Absconded/ Discharged before recruitment	Not consented	Recruited, medical notes not found	Recruited + medical notes found
		n (%)	n (%)	n (%)	n (%)	n (%)
All		88	30	96	161	661
Sex						
	Male	52 (59.1%)	19 (63.3%)	52 (54.2%)	69 (42.9%)	348 (52.7%)
	Female	36 (40.9%)	11 (36.7%)	44 (45.8%)	89 (57.1%)	313 (47.3%)
Age (years)						
	18-24	8 (9.1%)	4 (13.3%)	12 (12.5%)	19 (11.8%)	76 (11.5%)
	25-34	21 (23.9%)	7 (23.3%)	25 (26.0%)	63 (39.1%)	185 (28.0%)
	35-44	31 (35.2%)	4 (13.3%)	27 (28.1%)	39 (24.2%)	189 (28.6%)
	45+	28 (31.8%)	13 (43.3%)	32 (33.3%)	38 (23.6%)	205 (31.0%)
	Missing	0 (0%)	2 (6.7%)	0 (0%)	2 (1.2%)	6 (0.9%)

Table 41 shows the characteristics of participants who were recruited into the study and from whom individual-level data was collected on direct non-medical and indirect costs and HRQoL, and those for whom I was also able to trace the medical notes for data extraction.

Table 42 shows the characteristics, HIV status and outcomes of participants within the final analysable sample by the primary medical diagnosis. 52.7% were male, 31.4% were over the age of 45 years, 69.2% were HIV positive and 21.1% died in hospital. The mean duration of hospital admission was 12.1 days (SE: 0.5).

All participants who had a primary diagnosis of Tuberculosis of meninges and central nervous system, Candidiasis, Cryptococcal meningitis Pneumocystis Carinii Pneumonia and Kaposi's Sarcoma were HIV positive. Participants with a primary medical diagnosis of Tuberculosis of bones and joint had the highest mortality rate (60.0%). Participants with a primary medical diagnosis of Tuberculosis in general had high rates of mortality (range 27.8% to 60.0%). Participants who were being re-treated for their Tuberculosis disease had the longest duration of hospital admission (41.2 days; SE: 11.8). All participants with a primary medical diagnosis of diabetes mellitus, with or without complications, mental health disorders and diseases of the musculoskeletal system were discharged home.

Table 41: Characteristics of recruited participants

		Data Collection from individuals	Data extraction from medical notes
		n (%)	n (%)
All		822	661
Sex	Male	417 (50.7%)	348 (52.6%)
	Female	405 (49.3%)	313 (47.4%)
Age (years)	18-24	95 (11.6%)	76 (11.5%)
	25-34	248 (30.2%)	185 (28.0%)
	35-44	228 (27.7%)	189 (28.6%)
	45+	243 (29.6%)	205 (31.0%)
	Missing	8 (1.0%)	6 (0.9%)
Marital Status	Single (never-married)	90 (10.9%)	73 (11.0%)
	Married/cohabiting	454 (55.2%)	362 (54.8%)
	Separated/divorced	133 (16.2%)	101 (15.3%)
	Widower/widow	107 (13.0%)	92 (13.9%)
	Missing	38 (4.6%)	33 (5.0%)
Educational attainment	Up to standard 8	463 (56.3%)	368 (55.7%)
	Up to form 6	297 (36.1%)	241 (36.5%)
	University or training college	24 (2.9%)	19 (2.9%)
	Missing	38 (4.6%)	33 (5.0%)
Income	Not working	395 (48.1%)	303 (45.8%)
	Up to 4,000 Kwacha/week	107 (13.0%)	87 (13.2%)
	4,000 to 8,000 kwacha/week	101 (12.3%)	80 (12.1%)
	8,000 to 12,000 kwacha/week	47 (5.7%)	39 (5.9%)
	Over 12,000 kwacha/week	160 (19.5%)	143 (21.6%)
	Missing	12 (1.5%)	9 (1.4%)
Employment status	Formal employment	148 (18.0%)	131 (19.8%)
	Informal employment/Unemployed	276 (33.6%)	224 (33.9%)
	School/University	37 (4.5%)	31 (4.7%)
	Retired	12 (1.5%)	4 (0.6%)
	Housework	279 (33.9%)	211 (31.9%)
	Sick leave	59 (7.2%)	52 (7.9%)
	Missing	11 (1.3%)	8 (1.2%)
Socio-economic position	Highest quintile	154 (18.7%)	129 (19.5%)
	2nd highest quintile	157 (19.1%)	123 (18.6%)
	Middle quintile	155 (18.9%)	129 (19.5%)
	2nd lowest quintile	154 (18.7%)	119 (18.0%)
	Lowest quintile	157 (19.1%)	121 (18.3)
	Missing	45 (5.5%)	40 (6.05%)
HIV Status	HIV negative	216 (26.3%)	178 (26.9%)
	HIV positive	566 (68.9%)	458 (69.3%)
	Unknown/not disclosed	40 (4.9%)	25 (3.8%)
Outcome of participant	Discharged home	664 (80.8%)	522 (79.0%)
	Died	158 (19.2%)	139 (21.0%)

Table 42: Characteristics of participants by the primary medical diagnosis

Primary Medical Diagnosis	n	Sex		Age (years)			HIV Status	Days of admission	Outcome
		% Male	% 18-24	% 25-34	% 35-44	% 45+	% HIV Positive	Mean (SE)	% Died
ALL	661	52.7	11.6	28.1	28.9	31.4	69.2	12.1 (0.5)	21.1
Pulmonary Tuberculosis	55	70.4	7.4	38.9	35.2	18.5	87.0	23.9 (2.9)	27.8
Tuberculosis of meninges and central nervous system	17	58.8	12.5	12.5	43.8	31.3	100	38.2 (7.2)	47.1
Tuberculosis of intestines, peritoneum	9	66.7	11.1	11.1	44.4	33.3	77.8	19.3 (7.2)	33.3
Tuberculosis of bones and joint	5	80.0	0	0	20.0	80.0	40.0	16.0 (5.3)	60.0
Tuberculosis of other organs	15	66.7	0	20.0	46.7	33.3	80.0	26.0 (9.3)	46.7
Miliary Tuberculosis	17	64.7	0	52.9	23.5	23.5	82.4	10.7 (1.0)	58.8
Tuberculosis - Retreatment	6	66.7	16.7	33.3	33.3	16.7	83.3	41.2 (11.8)	33.3
Septicaemia (except in labour)	60	41.7	24.1	29.3	22.4	24.1	65.0	8.4 (1.0)	18.3
Candidiasis	6	33.3	0	60.0	20.0	20.0	100	5.7 (1.7)	16.7
Cryptococcal meningitis	38	73.7	10.5	34.2	47.4	7.9	100	15.8 (1.7)	26.3
Viral infection	9	55.6	22.2	44.4	11.1	22.2	100	13.9 (3.7)	55.6
Pneumocystis Carinii Pneumonia	9	44.4	12.5	37.5	37.5	12.5	100	13.4 (1.9)	22.2
Malaria	13	23.1	30.8	15.4	30.8	23.1	76.9	5.2 (1.6)	7.7
Kaposi's Sarcoma	20	80.0	5.0	50.0	35.0	10.0	100	9.1 (1.2)	25.0
Neoplasms - excluding Kaposi's	8	50.0	25.0	12.5	12.5	50.0	37.5	16.0 (1.7)	12.5
Diabetes mellitus without complications	5	0	20.0	20.0	0	60.0	0	3.8 (1.2)	0
Diabetes mellitus with complications	9	55.6	0	0	33.3	66.7	11.1	8.2 (1.2)	0
Anaemia	35	40.0	11.4	34.3	22.9	31.4	74.3	9.4 (1.3)	17.1
Mental Health disorders	9	66.7	22.2	22.2	33.3	22.2	22.2	6.6 (1.9)	0
Meningitis (except that caused by TB or Cryptococcal)	37	29.7	13.5	29.7	27.0	29.7	70.3	9.2 (0.8)	13.5
Epilepsy; Convulsions	11	45.5	45.5	18.2	9.1	27.3	36.4	5.9 (0.9)	9.1
Other Neurological Problems	16	75.0	6.3	25.0	43.8	25.0	50.0	10.3 (2.6)	6.3
Cerebrovascular disease	25	48.0	0	12.5	20.8	66.7	40.0	8.6 (1.1)	8.0
Hypertension	7	71.4	0	14.3	14.3	71.4	28.6	11.1 (4.4)	28.6
Congestive heart failure; non-hypertensive	15	40.0	0	0	20.0	80.0	13.3	9.4 (2.1)	33.3
Other Cardiovascular Problems	13	30.8	15.4	7.7	7.7	69.2	46.2	13.1 (4.5)	15.4
Pneumonia (except that caused by TB)	93	55.3	7.5	30.9	37.2	24.5	79.8	7.5 (0.9)	13.8
Other Respiratory Problems	11	27.3	9.1	27.3	9.1	54.6	45.5	9.9 (2.4)	9.1
Acute - Intestinal Infection	10	100	0	20.0	40.0	40.0	60.0	12.6 (3.5)	10.0
Chronic - Intestinal Infection	14	35.7	14.3	35.7	21.4	28.6	78.6	6.7 (1.4)	28.6
Upper gastrointestinal disorders	11	18.2	36.4	18.2	9.1	36.4	72.7	5.7 (0.6)	18.2
Liver disease	14	57.1	7.1	35.7	28.6	28.6	64.3	10.0 (1.9)	42.9
Diseases of the genitourinary system	19	42.1	5.3	15.8	31.6	47.4	79.0	7.9 (1.2)	15.8
Diseases of the musculoskeletal system	6	83.3	0	33.3	0	66.7	33.3	15.0 (4.2)	0
Other Problems (<5 cases)	14	38.5	30.8	38.5	7.7	23.1	7.7	7.5 (0.9)	7.7

7.3.2 Direct health provider unit costs for healthcare resources

Table 43 to Table 45 shows the unit health provider cost for the investigations and procedures performed on participants. For investigations undertaken in either the Radiology department (Table 43) or the Laboratory department (Table 44), the total cost includes the indirect cost estimated for the department. For the Radiology department, the indirect cost per investigation performed was estimated to be US\$1.68 (INT\$4.64). For the Laboratory department, the indirect cost per investigation performed was estimated to be US\$0.67 (INT\$1.86).

Table 46 shows the costs of the Pharmacy department at QECH. The average cost per dosage of drug dispensed through the department was estimated to be US\$0.0058 (INT\$0.0162). Table 47 shows the health provider costs of the three wards to which participants were admitted. The average health provider cost per day of admission was US\$14.48, US\$15.35 and US\$16.17 for wards 3A, 3B, and 4A, respectively.

Figure 53 and Figure 54 compares the price of a selection of investigations and procedures estimated for QECH from the primary costing study to the prices provided by two different private health care providers in Malawi. The prices estimated for QECH were lower than the prices charged by the two private healthcare providers.

Table 43: Mean Health Provider costs - Radiological and Imaging Investigations

Investigation	Mean Direct Cost		Mean Total Cost	
	2014 US Dollars	2014 INT Dollars	2014 US Dollars	2014 INT Dollars
Chest X-Ray	9.05	22.92	10.73	27.56
Abdominal X-Ray	9.05	22.92	10.73	27.56
Cervical Spine X-Ray	6.17	17.14	7.85	21.78
Thoracic Spine X-Ray	6.17	17.14	7.85	21.78
Lumbar Spine X-Ray	6.17	17.14	7.85	21.78
Other plain X-Ray	9.05	22.92	10.73	27.56
Abdominal/ Renal Ultrasound	15.13	42.03	16.81	46.67
Pelvic Ultrasound	15.13	42.03	16.81	46.67
Neck Ultrasound	15.13	42.03	16.81	46.67
Doppler Ultrasound	17.57	48.80	19.25	53.45
Chest Ultrasound	15.13	42.03	16.81	46.67
*MRI Head	49.21	63.91	50.89	68.55
*MRI Spine	49.21	63.91	50.89	68.55
*CT Head	20.41	56.69	22.08	61.33
*CT Thorax	20.41	56.69	22.08	61.33
*CT Abdomen	20.41	56.69	22.08	61.33

*Service out-sourced to external provider
MRI: Magnetic resonance imaging
CT: Computed Tomography

Table 44: Mean Health Provider costs - Laboratory Investigations

Investigation +/- Procedure	Mean Direct Cost		Mean Total Cost	
	2014 US Dollars	2014 INT Dollars	2014 US Dollars	2014 INT Dollars
Malaria Film	1.89	5.25	2.56	7.11
Peripheral blood film	4.26	11.57	4.93	13.43
Group and X match	12.55	35.00	13.22	36.86
Full Blood Count (FBC)	4.68	12.41	5.35	14.28
Erythrocyte sedimentation rate (ESR)	0.80	2.22	1.47	4.08
*Prothrombin Time	12.24	34.00	12.24	34.00
Urea + Electrolytes (U+Es)	10.65	29.70	11.33	31.56
Creatinine	3.27	9.18	3.94	11.04
Liver Function Tests (LFTs)	8.09	22.57	8.76	24.44
Lipid Profile	9.77	27.23	10.44	29.09
Cardiac enzymes	7.52	20.97	8.19	22.83
Random / Fasting glucose	3.02	8.50	3.69	10.36
CD4 count	14.81	41.13	15.48	42.99
HIV Viral Load	26.96	29.18	27.63	31.04
Hepatitis B surface antigen (Hep B sAg)	2.65	7.36	3.32	9.22
Hepatitis C antibody (Hep C Ab)	5.21	7.65	5.88	9.51
VDRL	2.68	7.45	3.35	9.31
Malaria rapid diagnostic test	2.16	6.00	2.16	6.00
Blood Culture	33.10	80.31	33.77	82.18
Urine microscopy	1.73	4.83	2.40	6.70
Stool microscopy	1.43	3.98	2.10	5.85
CSF/LP	40.96	112.41	41.63	114.27
Sputum smear (Microscopy and AFB)	5.19	13.15	5.86	15.01
Sputum for GeneXpert (rapid TB test)	24.84	58.82	25.51	60.69
*Sputum culture for Tuberculosis	16.75	46.53	17.42	48.39
Lymph node aspirate for Micro (AFB, cell count)	7.09	18.34	7.76	20.21
*Lymph node aspirate for Cytology	29.87	82.98	29.87	82.98
Lymph node biopsy for Micro (AFB)	6.09	15.70	6.77	17.57
Lymph node biopsy for Histology	48.86	134.76	49.53	136.63
Cytology	27.66	76.84	27.66	76.84
Pregnancy Test	3.26	9.08	3.93	10.94
**Diagnostic Pleural Tap	4.55	12.63	17.60	47.73
**Diagnostic Ascitic Tap	4.55	12.63	17.60	47.73
**Therapeutic and Diagnostic Ascitic Tap	10.55	29.30	23.60	64.40
**Diagnostic Knee Aspirate	3.00	8.35	16.06	43.45
**Therapeutic and Diagnostic Pleural Tap	10.55	29.30	23.60	64.40

*Service out-sourced to external provider

**Includes cost of procedure

Urea + Electrolytes (U+Es): Urea, Sodium and Potassium

Liver Function Tests (LFTs): Total protein, Albumin, Bilirubin, Aspartate aminotransferase (AST), Alanine aminotransferase (ALT) Gamma-glutamyl transpeptidase (GGT) and Lactate dehydrogenase (LDH)

Lipid Profile: Total Cholesterol (TC), Triglyceride (TG), Low-density lipoprotein (LDL), high-density lipoprotein (HDL)

Cardiac enzymes: Creatine Kinase (CK & CKMD), Lactate dehydrogenase (LD)

VDRL: Venereal Disease Research Laboratory test for Syphilis

CSF/LP: Lumbar puncture to obtain cerebrospinal fluid

AFB: Acid-fast bacilli test for Tuberculosis

Table 45: Mean Health Provider costs - Ward-based Investigations and Procedures

Investigation or Procedure	Mean Total Cost	
	2014 US Dollars	2014 INT Dollars
Urine Dipstick	4.08	11.33
HIV Test	3.87	10.74
Electrocardiography (ECG)	2.61	7.24
Echocardiogram	15.05	41.82
Therapeutic Pleural Tap	12.88	35.78
Therapeutic Ascitic Tap	4.55	12.63
Lymph node aspirate	2.21	6.14
Insertion of Naso-Gastric tube	3.87	10.74
Insertion urinary catheter	11.65	32.37
Incision and drainage	3.40	9.44
Chest Drain	32.71	88.63
Therapeutic Lumbar Puncture	8.55	22.13
*Gastroscopy/Endoscopy/Laryngoscopy	470.70	1307.51
*Colonoscopy	470.70	1307.51
*Bronchoscopy	470.70	1307.51
*Endoscopy +/- Banding	470.70	1307.51
Laparoscopic Surgery	Not costed	
Laparotomy	Not costed	

*Not costed, cost obtained from private health provider

Table 46: Mean Health Provider costs - Pharmacy department

Cost category	Pharmacy costs		
	2014 US Dollars	2014 INT Dollars	% Total*
Personnel Cost	120,359.32	334,331.44	66.1%
Consumables	8179.75	21244.10	4.2%
Rental Space	2256.53	6268.15	1.2%
Equipment	6571.98	18255.49	3.6%
Central Support and Overheads	45250.66	125696.29	24.9%
Annual health provider cost	182,618.25	505,795.48	
Mean cost per table, vial, ampoule dispensed	0.0058	0.0162	

*Percentages based on costs estimated in International Dollars

Table 47: Mean Health Provider costs - Ward Stay

Cost category	Ward 3A (TB ward)			Ward 3B (Male Medical)			Ward 4A (Female Medical)		
	2014 US Dollars	2014 INT Dollars	% Total*	2014 US Dollars	2014 INT Dollars	% Total*	2014 US Dollars	2014 INT Dollars	% Total*
Personnel Cost	50,375	139,929	16.6%	66,757	185,437	15.5%	74,922	208,117	18.8%
Consumables	72,027	199,258	23.7%	154,950	429,102	35.8%	122,792	338,569	30.5%
Rental space	4,513	12,536	1.5%	4,513	12,536	1.0%	4,513	12,536	1.1%
Equipment	106,894	296,895	35.3%	119,201	331,082	27.6%	111,102	308,585	27.8%
Central Support and Overheads	69,334	192,596	22.9%	86,668	240,745	20.1%	86,668	240,745	21.7%
Annual health provider cost	303,142	841,215		432,090	1,198,903		399,997	1,108,551	
Mean cost per day of admission	14.48	40.17		15.35	42.58		16.17	44.80	

*Percentages based on costs estimated in International Dollars

Figure 53: Comparison of Investigation/Procedure prices between QECH and Private healthcare provider 1

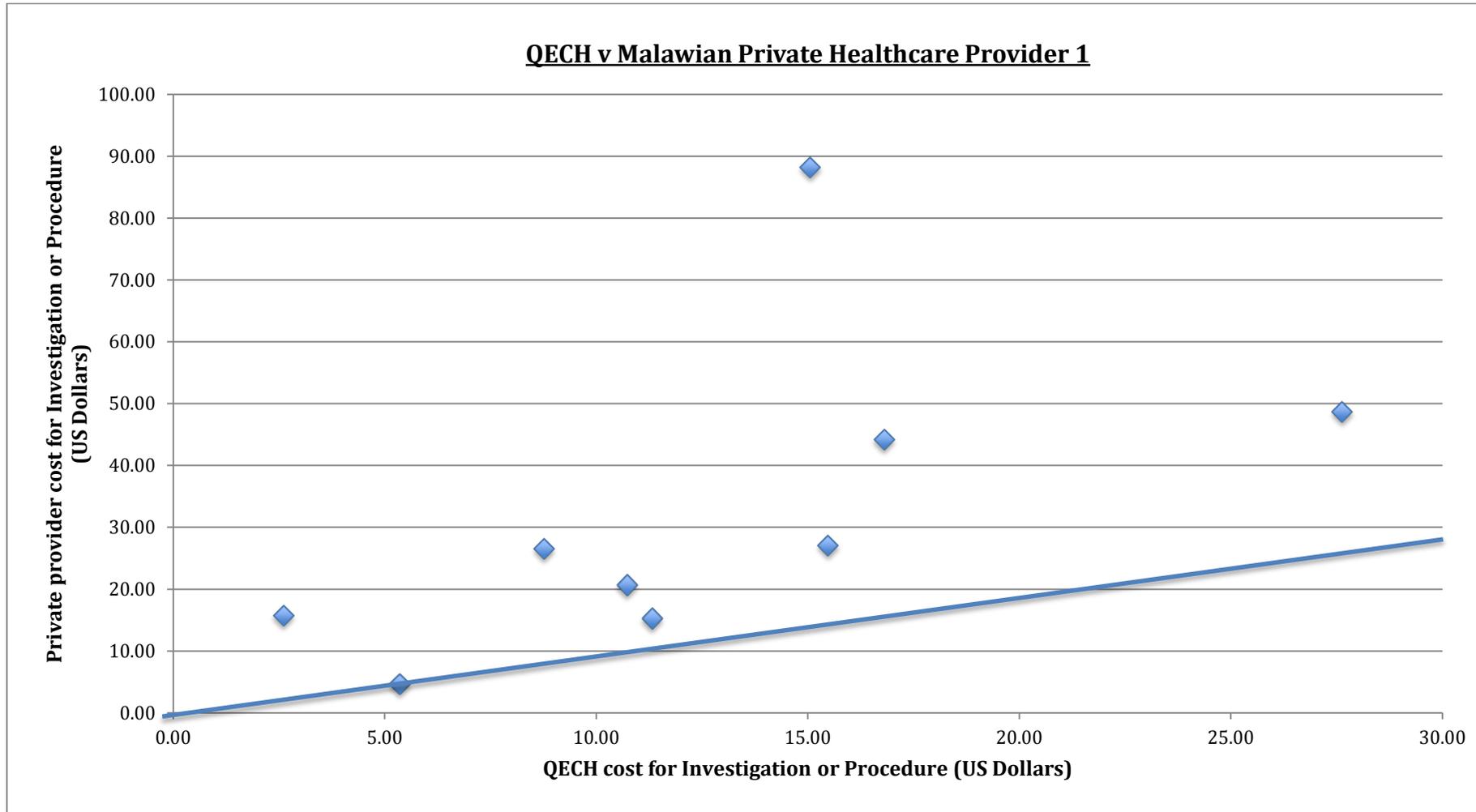
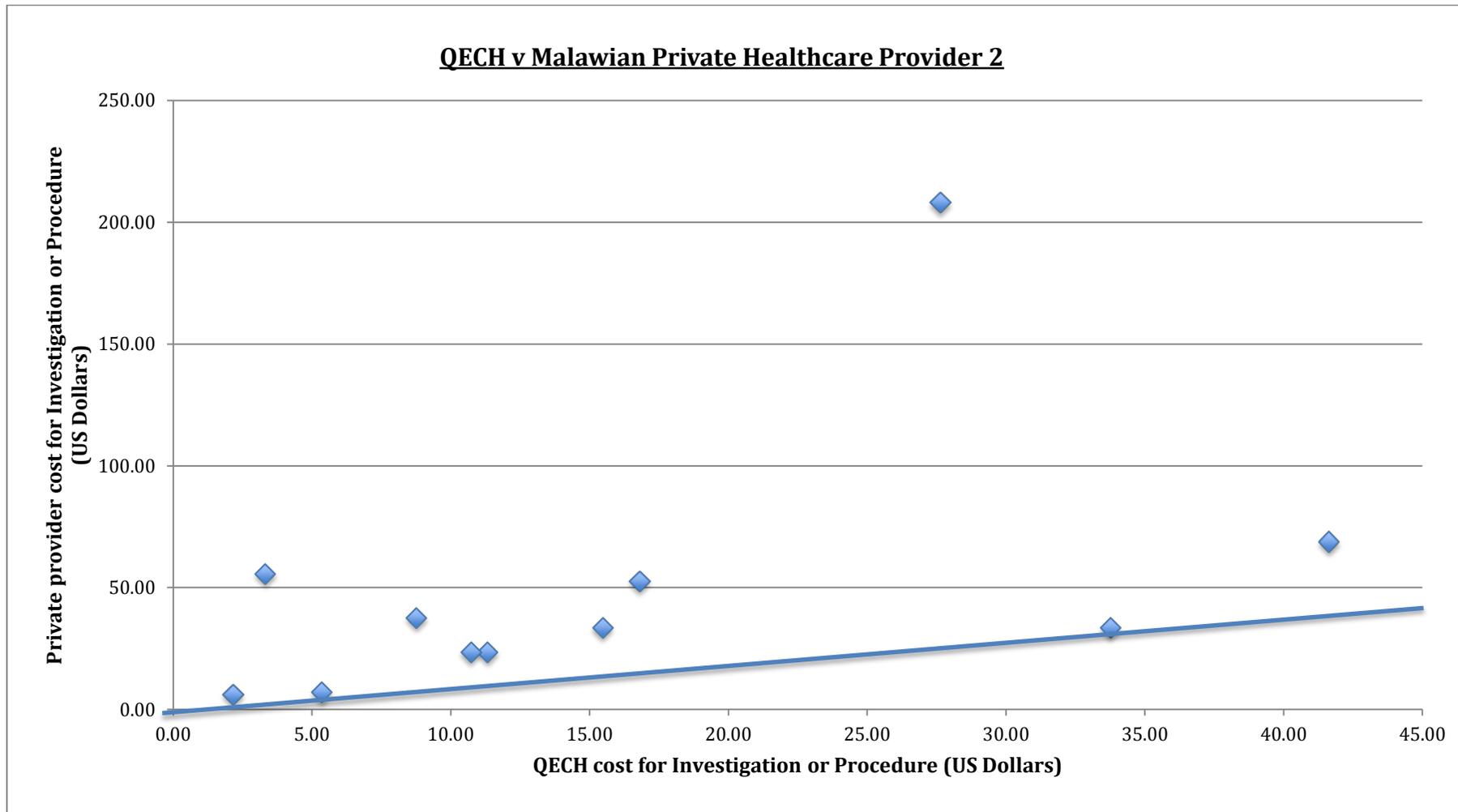


Figure 54: Comparison of Investigation/Procedure prices between QECH and Private Healthcare Provider 2



7.3.3 Cost analysis

Table 48 shows the total health provider costs for managing participants by the primary medical diagnosis. Across all the participants, the mean total health provider cost of the hospital admission was US\$314.93 (INT\$791.47). The average daily health provider cost was US\$32.14 (INT\$80.74). The 'hotel' cost of ward stay accounted for the majority of the costs (60.7%). Drugs accounted for approximately 3.6% of the total cost of admission for the sample, whilst investigations and procedures accounted for 35.9%.

The highest mean total health provider cost was for the management of patients with Cryptococcal Meningitis (US\$837.92; INT\$1568.22), with drugs accounting for 20.9% of this total health provider cost.

For participants diagnosed with Tuberculosis (TB), the mean total health provider cost ranged from US\$289.80 (INT\$754.21) for Miliary TB to US\$741.14 (INT\$1943.75) for those needing retreatment for TB. The mean total health provider cost of managing Pulmonary TB was US\$473.11 (INT\$1241.09). The mean total health provider cost of managing Pneumocystis Carinii Pneumonia was US\$325.92 (INT\$850.35). The mean total health provider cost of managing Kaposi's sarcoma was US\$231.48 (INT\$231.48).

Table 48: Total Health Provider costs by primary medical diagnosis

Primary Medical Diagnosis	N (%)	Total Health Provider Cost		Average Daily Cost		Mean of Total Health Provider Cost		
		2014 US Dollars Mean (SE)	2014 INT Dollars Mean (SE)	2014 US Dollars Mean (SE)	2014 INT Dollars Mean (SE)	% Drugs	% Investigations & Procedures	% Ward stay
ALL	661	314.92 (12.2)	791.47 (27.6)	32.14 (0.9)	80.74 (1.8)	3.6	35.9	60.7
Pulmonary Tuberculosis	55	473.11 (50.8)	1241.09 (135.2)	23.76 (1.0)	61.37 (2.5)	3.3	26.5	70.6
Tuberculosis of meninges and central nervous system	17	743.97 (113.1)	1958.77 (297.0)	31.06 (4.9)	82.57 (13.3)	2.7	32.5	65.2
Tuberculosis of intestines, peritoneum	9	396.14 (104.5)	1025.71 (272.6)	26.95 (4.0)	69.93 (10.4)	4.3	37.1	58.7
Tuberculosis of bones and joint	5	316.08 (102.4)	854.53 (276.5)	19.58 (0.8)	53.14 (1.6)	1.5	19.1	79.7
Tuberculosis of other organs	15	494.97 (140.0)	1306.25 (384.1)	26.26 (2.7)	67.21 (6.4)	3.8	33.9	62.6
Miliary Tuberculosis	17	289.80 (25.5)	754.21 (66.9)	28.18 (1.9)	73.29 (4.8)	3.1	35.8	61.5
Tuberculosis - Retreatment	6	741.14 (203.4)	1943.75 (535.0)	20.24 (2.1)	52.69 (5.4)	3.6	15.4	81.7
Septicaemia (except in labour)	60	222.95 (17.4)	583.39 (45.7)	33.86 (2.3)	88.30 (5.9)	2.4	40.7	57.2
Candidiasis	6	153.08 (43.1)	395.98 (113.9)	31.12 (6.0)	77.70 (11.9)	2.8	35.5	62.2
Cryptococcal meningitis	38	837.92 (97.8)	1568.22 (133.1)	63.71 (9.1)	113.84 (10.4)	20.9	32.6	46.9
Viral infection	9	273.32 (67.8)	734.24 (185.5)	24.41 (5.1)	64.29 (13.1)	2.0	19.1	79.5
Pneumocystis Carinii Pneumonia	9	325.92 (28.3)	850.35 (75.5)	26.82 (3.0)	69.63 (7.6)	2.9	30.0	67.3
Malaria	13	179.01 (36.0)	439.87 (94.3)	44.78 (6.7)	106.46 (14.4)	7.2	44.2	48.8
Kaposi's Sarcoma	20	231.48 (25.9)	611.05 (69.7)	29.02 (2.7)	75.65 (6.7)	2.5	35.6	62.4
Neoplasms - excluding Kaposi's	8	342.16 (42.7)	903.60 (118.8)	22.18 (0.9)	58.20 (2.6)	2.4	22.8	74.9
Diabetes mellitus without complications	5	161.32 (40.8)	410.83 (107.5)	46.81 (8.9)	118.32 (21.4)	5.4	51.5	43.1
Diabetes mellitus with complications	9	219.30 (31.2)	580.71 (82.6)	30.82 (4.6)	80.87 (11.3)	3.0	37.5	59.5
Anaemia	35	252.44 (25.8)	679.83 (70.9)	33.52 (4.2)	89.88 (11.5)	1.7	39.8	58.7
Mental Health disorders	9	186.64 (38.4)	496.95 (103.3)	33.14 (4.2)	87.91 (10.8)	2.0	44.5	53.5
Meningitis (except that caused by TB or Cryptococcal)	37	250.94 (17.8)	647.35 (46.0)	30.78 (1.8)	79.27 (4.6)	3.2	37.2	59.8
Epilepsy; Convulsions	11	186.94 (17.4)	481.81 (44.8)	36.50 (3.9)	93.65 (9.4)	2.6	46.5	51.1
Other Neurological Problems	16	261.58 (48.6)	682.28 (127.9)	32.85 (3.3)	86.00 (8.5)	1.5	42.1	56.6
Cerebrovascular disease	25	197.21 (23.7)	523.61 (60.0)	26.09 (1.8)	69.61 (4.7)	2.0	35.0	63.2
Hypertension	7	235.14 (79.1)	636.56 (212.0)	25.65 (3.5)	68.69 (8.5)	1.6	32.3	66.2
Congestive heart failure; non-hypertensive	15	240.16 (47.8)	648.29 (132.8)	27.89 (2.7)	74.81 (7.3)	1.4	33.6	65.0
Other Cardiovascular Problems	13	328.86 (95.2)	852.02 (240.1)	29.42 (2.2)	77.73 (5.9)	2.8	36.7	60.7
Pneumonia (except that caused by TB)	93	198.61 (14.4)	516.87 (39.5)	30.75 (0.9)	78.88 (2.3)	2.2	40.2	57.9
Other Respiratory Problems	11	243.27 (56.0)	642.00 (148.2)	25.95 (2.2)	68.06 (5.3)	2.6	29.6	68.0
Acute - Intestinal Infection	10	251.15 (53.1)	668.58 (147.5)	23.13 (1.8)	60.62 (4.6)	3.3	23.8	73.4
Chronic - Intestinal Infection	14	249.49 (61.0)	659.38 (166.3)	50.22 (18.8)	133.21 (52.0)	2.7	43.5	54.2
Upper gastrointestinal disorders	11	193.63 (46.3)	510.05 (130.0)	33.03 (5.0)	86.57 (14.2)	2.1	39.3	58.9
Liver disease	14	346.30 (103.8)	942.03 (287.4)	31.89 (3.2)	85.93 (8.8)	1.4	42.9	55.9
Diseases of the genitourinary system	19	209.58 (23.9)	556.56 (65.2)	29.13 (1.6)	76.97 (4.0)	2.0	38.7	59.6
Diseases of the musculoskeletal system	6	333.96 (79.5)	879.85 (203.9)	23.72 (1.5)	62.77 (4.0)	1.9	28.4	69.8
Other Problems (<5 cases)	14	209.42 (31.7)	561.10 (85.6)	24.56 (1.4)	65.66 (3.3)	1.7	29.2	69.2

Table 49 shows the mean total direct non-medical and indirect costs by primary medical diagnosis. For all the participants, the mean total direct non-medical and indirect costs incurred during their hospital admission was US\$86.93 (INT\$241.48).

Tuberculosis of the meninges and central nervous system was associated with the highest mean direct non-medical and indirect costs (US\$485.95, INT\$1349.86). Diabetes mellitus without complications was associated with the lowest mean direct non-medical and indirect costs (US\$21.63, INT\$60.07).

Table 49: Total direct non-medical and indirect costs

Primary Medical Diagnosis	2014 US Dollars		2014 INT Dollars
	n	Mean (SE)	Mean (SE)
ALL	660	86.93 (10.0)	241.48 (27.8)
Pulmonary Tuberculosis	55	133.27 (29.3)	370.21 (81.3)
Tuberculosis of meninges and central nervous system	17	485.95 (194.3)	1349.86 (539.7)
Tuberculosis of intestines, peritoneum	9	421.08 (336.8)	1169.68 (935.7)
Tuberculosis of bones and joint	5	72.35 (32.6)	200.96 (90.4)
Tuberculosis of other organs	15	299.43 (189.7)	831.74 (526.9)
Miliary Tuberculosis	17	48.55 (12.6)	134.86 (34.9)
Tuberculosis – Retreatment	6	174.18 (130.8)	483.83 (363.4)
Septicaemia (except in labour)	60	36.78 (8.0)	102.16 (22.2)
Candidiasis	6	25.86 (20.0)	71.84 (55.6)
Cryptococcal meningitis	38	125.48 (41.9)	348.55 (116.5)
Viral infection	9	54.68 (29.8)	151.89 (82.8)
Pneumocystis Carinii Pneumonia	9	69.59 (28.2)	193.30 (78.2)
Malaria	13	124.91 (116.9)	346.97 (324.7)
Kaposi's Sarcoma	20	81.66 (21.5)	226.84 (59.6)
Neoplasms - excluding Kaposi's	8	57.12 (15.7)	158.66 (43.7)
Diabetes mellitus without complications	5	21.63 (10.6)	60.07 (29.6)
Diabetes mellitus with complications	9	220.34 (145.4)	612.05 (404.0)
Anaemia	35	57.20 (10.5)	158.90 (29.2)
Mental Health disorders	9	72.97 (30.3)	202.69 (84.1)
Meningitis (except that caused by TB or Crypto)	37	49.54 (10.3)	137.61 (28.7)
Epilepsy; Convulsions	11	28.05 (18.1)	77.92 (50.4)
Other Neurological Problems	16	32.67 (9.2)	90.75 (25.6)
Cerebrovascular disease	25	42.98 (13.6)	119.39 (37.7)
Hypertension	7	46.52 (24.1)	129.23 (66.9)
Congestive heart failure; non-hypertensive	15	28.02 (7.3)	77.83 (20.2)
Other Cardiovascular Problems	13	49.23 (16.0)	136.76 (44.5)
Pneumonia (except that caused by TB)	93	33.36 (5.6)	92.65 (15.6)
Other Respiratory Problems	11	46.70 (18.5)	129.71 (51.4)
Acute - Intestinal Infection	10	155.70 (53.4)	432.49 (148.3)
Chronic - Intestinal Infection	14	26.29 (9.6)	73.03 (26.7)
Upper gastrointestinal disorders	11	68.22 (41.2)	189.49 (114.5)
Liver disease	14	56.37 (24.4)	156.57 (67.7)
Diseases of the genitourinary system	19	44.09 (13.3)	122.48 (37.1)
Diseases of the musculoskeletal system	6	158.44 (93.6)	440.11 (260.1)
Other Problems (<5 cases)	14	50.22 (15.5)	139.49 (43.1)

Table 50 shows the total societal cost of hospital admission by primary medical diagnosis. For all participants, the mean total societal cost of hospital admission was US\$401.53 (INT\$1031.93).

Participants diagnosed with TB of the meninges and central nervous system had the highest mean total societal cost. The total societal cost for those diagnosed with TB of the meninges and central nervous system was US\$1229.92 (INT\$3308.63). For participants diagnosed with Pulmonary TB, the mean total societal cost was US\$614.46 (INT\$1632.92).

The mean total societal cost of managing Cryptococcal Meningitis was US\$963.40 (INT\$1916.77). The mean total societal cost of managing Pneumocystis Carinii Pneumonia was US\$395.51 (INT\$1043.65). The mean total societal cost of managing Kaposi's sarcoma was US\$313.14 (INT\$837.89).

Table 50: Total societal cost of hospital admission

Primary Medical Diagnosis	2014 US Dollars		2014 INT Dollars
	n	Mean (SE)	Mean (SE)
ALL	660	401.53 (18.6)	1031.93 (47.5)
Pulmonary Tuberculosis	55	614.46 (68.5)	1632.92 (184.7)
Tuberculosis of meninges and central nervous system	17	1229.92 (267.7)	3308.63 (725.1)
Tuberculosis of intestines, peritoneum	9	817.22 (437.2)	2195.39 (1196.1)
Tuberculosis of bones and joint	5	388.43 (130.3)	1055.49 (354.3)
Tuberculosis of other organs	15	794.40 (321.7)	2137.99 (890.6)
Miliary Tuberculosis	17	338.35 (30.3)	889.07 (80.2)
Tuberculosis – Retreatment	6	915.32 (280.4)	2427.58 (744.8)
Septicaemia (except in labour)	60	259.73 (23.4)	685.55 (62.4)
Candidiasis	6	178.94 (58.8)	467.81 (156.7)
Cryptococcal meningitis	38	963.40 (109.0)	1916.77 (197.5)
Viral infection	9	328.00 (86.2)	886.12 (236.2)
Pneumocystis Carinii Pneumonia	9	395.51 (50.6)	1043.65 (139.5)
Malaria	13	303.92 (119.3)	786.85 (328.1)
Kaposi's Sarcoma	20	313.14 (43.3)	837.89 (118.5)
Neoplasms - excluding Kaposi's	8	399.28 (51.1)	1062.26 (143.4)
Diabetes mellitus without complications	5	182.95 (49.3)	470.91 (131.2)
Diabetes mellitus with complications	9	439.64 (157.2)	1192.76 (435.2)
Anaemia	35	309.65 (33.0)	838.73 (90.9)
Mental Health disorders	9	259.61 (53.0)	699.64 (142.8)
Meningitis (except that caused by TB or Crypto)	37	300.48 (23.1)	784.96 (61.5)
Epilepsy; Convulsions	11	214.99 (27.5)	559.74 (73.8)
Other Neurological Problems	16	294.25 (56.0)	773.03 (148.8)
Cerebrovascular disease	25	240.19 (33.9)	643.00 (88.1)
Hypertension	7	281.66 (102.3)	765.79 (276.2)
Congestive heart failure; non-hypertensive	15	266.34 (49.8)	721.17 (138.0)
Other Cardiovascular Problems	13	378.09 (107.0)	988.78 (273.3)
Pneumonia (except that caused by TB)	93	231.59 (18.8)	608.41 (51.9)
Other Respiratory Problems	11	289.97 (59.7)	771.71 (158.9)
Acute - Intestinal Infection	10	406.84 (94.3)	1101.07 (262.6)
Chronic - Intestinal Infection	14	275.78 (64.3)	732.41 (175.6)
Upper gastrointestinal disorders	11	261.85 (58.2)	699.54 (163.3)
Liver disease	14	402.67 (104.1)	1098.61 (287.9)
Diseases of the genitourinary system	19	253.67 (30.3)	679.04 (82.2)
Diseases of the musculoskeletal system	6	492.40 (111.6)	1319.96 (302.8)
Other Problems (<5 cases)	14	228.59 (31.4)	613.33 (80.3)

Table 51 show the results of the multivariable analysis investigating the independent effect of HIV status (incorporating whether the patient on ART) on the mean total health provider costs, and Table 52 shows the multivariable analysis investigating the independent effect of HIV status on mean total societal costs of hospital admission.

In the multivariable analysis (Table 51), after adjusting for individual characteristics (model 2), those who were HIV positive, irrespective of whether they were on ART, had an elevated mean **total health provider cost** compared to those who were HIV negative. In the fully adjusted model (model 3), adjusting for individual characteristics and the primary medical diagnosis, only those who were HIV positive and started on ARVs during their hospital admission had a significantly higher mean total health provider cost compared to those who were HIV negative (US\$363.81, 95%CI: US\$34.09-693.54).

In the multivariable analysis (Table 52), after adjusting for individual characteristics (model 2), those who were HIV positive and not on ART had an elevated mean **total societal cost** of US\$97.60 (95%CI: US\$9.23-US\$185.98) compared to those who were HIV negative. In contrast, those who were HIV positive and being treated with ART before their hospital admission did not have a significantly higher total societal cost of admission (US\$64.95, 95%CI: -US\$1.98, US\$131.89). In all the adjusted models, HIV positive individuals who started ART during their hospital admission had an elevated mean total societal cost.

Table 51: Multivariable analysis exploring relationship between HIV status and anti-retroviral treatment status on the Total Health Provider Costs*

	Total health provider cost (2014 US Dollars)			Total health provider costs (2014 INT Dollars)		
	Model 1 (n=649) Coef (95% CI)	Model 2 (n=617) Coef (95% CI)	Model 3 (n=617) Coef (95% CI)	Model 1 (n=648) Coef (95% CI)	Model 2 (n=770) Coef (95% CI)	Model 3 (n=626) Coef (95% CI)
HIV negative	Ref	Ref	Ref	Ref	Ref	Ref
HIV positive + on ART before admission	47.21 (-3.27, 97.70)	62.21** (13.71, 110.72)	-2.25 (-38.69, 34.19)	78.77 (-44.66, 202.20)	117.53 (-3.11, 238.17)	-12.45 (-109.26, 84.36)
HIV positive + started ART in hospital	509.79** (215.67, 803.92)	465.92** (139.06, 792.77)	363.81** (34.09, 693.54)	1320.32** (554.47, 2086.17)	1222.94** (370.90, 2074.97)	923.45** (88.41, 1758.50)
HIV positive + Not on ART	101.16** (21.40, 180.92)	105.77** (33.34, 178.21)	31.47** (-15.17, 78.10)	175.72** (6.19, 345.26)	202.97** (40.33, 365.61)	66.38 (-55.21, 187.96)
HIV status unknown	-131.65** (-181.36, -81.94)	-138.02** (-188.57, -87.47)	-98.27** (-140.33, -56.21)	-351.63** (-483.10, -220.17)	-368.99** (-499.07, -238.90)	-270.37** (-381.58, -159.15)

Model 1: adjusted for exposure, Age and Sex

Model 2: additionally adjusted for marital status, educational attainment, income and wealth quintile

Model 3: additionally adjusted for primary medical diagnosis

ART: Anti-retroviral therapy

*Findings from Generalized Linear Model with Poisson distribution and Identity link function

** $p < 0.05$

Table 52: Multivariable analysis exploring relationship between HIV status and anti-retroviral treatment status on the Total Societal costs*

	Total health societal costs (2014 US Dollars)			Total societal costs (2014 INT Dollars)		
	Model 1 (n=649) Coef (95% CI)	Model 2 (n=770) Coef (95% CI)	Model 3 (n=617) Coef (95% CI)	Model 1 (n=800) Coef (95% CI)	Model 2 (n=770) Coef (95% CI)	Model 3 (n=626) Coef (95% CI)
HIV and Anti-Retroviral therapy status						
HIV negative	Ref	Ref	Ref	Ref	Ref	Ref
HIV positive + on ART before admission	61.20 (-12.27, 134.68)	64.95 (-1.98, 131.89)	-8.83 (-56.68, 39.02)	119.61 (-72.64, 311.86)	120.51 (-53.03, 294.06)	-30.50 (-158.91, 97.92)
HIV positive + started ART in hospital	950.71** (206.82, 1694.60)	517.95** (103.68, 932.21)	404.19** (46.06, 762.32)	2550.15** (512.87, 4587.43)	1366.58** (252.12, 2481.04)	1028.13** (111.37, 1944.88)
HIV positive + Not on ART	116.10** (15.22, 216.98)	97.60** (9.23, 185.98)	22.63 (-38.75, 84.00)	219.83 (-21.18, 460.84)	185.20 (-31.51, 401.91)	39.55 (-122.94, 202.04)
HIV status unknown	-170.22** (-235.06, -105.37)	-170.61** (-238.13, -103.09)	-123.68** (-180.76, -66.59)	-462.02** (-636.55, -287.50)	-461.95** (-639.51, -284.40)	-341.64** (-494.57, -188.70)

Model 1: adjusted for exposure, Age and Sex

Model 2: additionally adjusted for marital status, educational attainment, income and wealth quintile

Model 3: additionally adjusted for primary medical diagnosis

ART: Anti-retroviral therapy

*Findings from Generalized Linear Model with Poisson distribution and Identity link function

** $p < 0.05$

7.3.5 Health-related quality of life analysis

Table 53 shows the EQ-5D utility scores on admission, the average EQ-5D utility score during the hospital admission, the last recorded EQ-5D utility score prior to discharge and the change in EQ-5D utility score from admission to discharge, by primary medical diagnosis.

For all participants, the mean EQ-5D utility score on admission was 0.484 (SE: 0.01), the average EQ-5D utility score during the hospital admission was 0.498 (SE: 0.01), the last recorded EQ-5D utility score was 0.510 (SE: 0.02) and the change in EQ-5D utility score from admission to discharge or death was 0.024 (SE: 0.02). The mean EQ-5D utility score on hospital admission for those with Pulmonary Tuberculosis was 0.445 (SE: 0.04), for those with Candidiasis was 0.349 (SE: 0.09), for those with Cryptococcal meningitis was 0.483 (SE: 0.04), for those with Pneumocystis Carinii Pneumonia was 0.559 (SE: 0.08) and for those with Kaposi's sarcoma was 0.415 (SE: 0.06).

Participants with a primary medical diagnosis of Diabetes Mellitus without complications experienced the largest improvement in EQ-5D utility score from admission to discharge (mean change: 0.222). Participants with a primary medical diagnosis of Neoplasm other than Kaposi's sarcoma experienced the largest deterioration in EQ-5D utility score (mean change: 0.260; SE: 0.15). The mean change in EQ-5D utility score during hospital admission for those with Pulmonary

Tuberculosis was 0.034 (SE: 0.05), for those with Candidiasis was 0.223 (SE: 0.27), for those with Cryptococcal meningitis was -0.013 (SE: 0.07), for those with Pneumocystis Carinii Pneumonia was -0.058 (SE: 0.16) and for those with Kaposi's sarcoma was -0.018 (SE: 0.07).

Table 54 shows the visual analogue scale (VAS) scores on admission, the mean VAS score during the hospital admission, the last recorded VAS score prior to discharge and the change in VAS score from admission to discharge by the primary medical diagnosis. For all participants, the mean VAS score on admission was 52.8 (SE: 0.8), the mean VAS over the course of the hospital admission was 53.8 (SE: 0.8), the last recorded mean VAS score was 54.0 (SE: 1.6) with participants experiencing a mean improvement in the VAS score of 0.1 (SE: 1.6) during their hospital admission.

Figure 55 compares the EQ-5D utility score, derived from the responses participants gave to the EQ-5D five-dimension descriptive system, to the VAS recorded by participant on the thermometer. The EQ-5D utility scores show a high degree of correlation to the VAS scores. The Pearson's correlation coefficient between the change in EQ-5D utility score and change in VAS was 0.64.

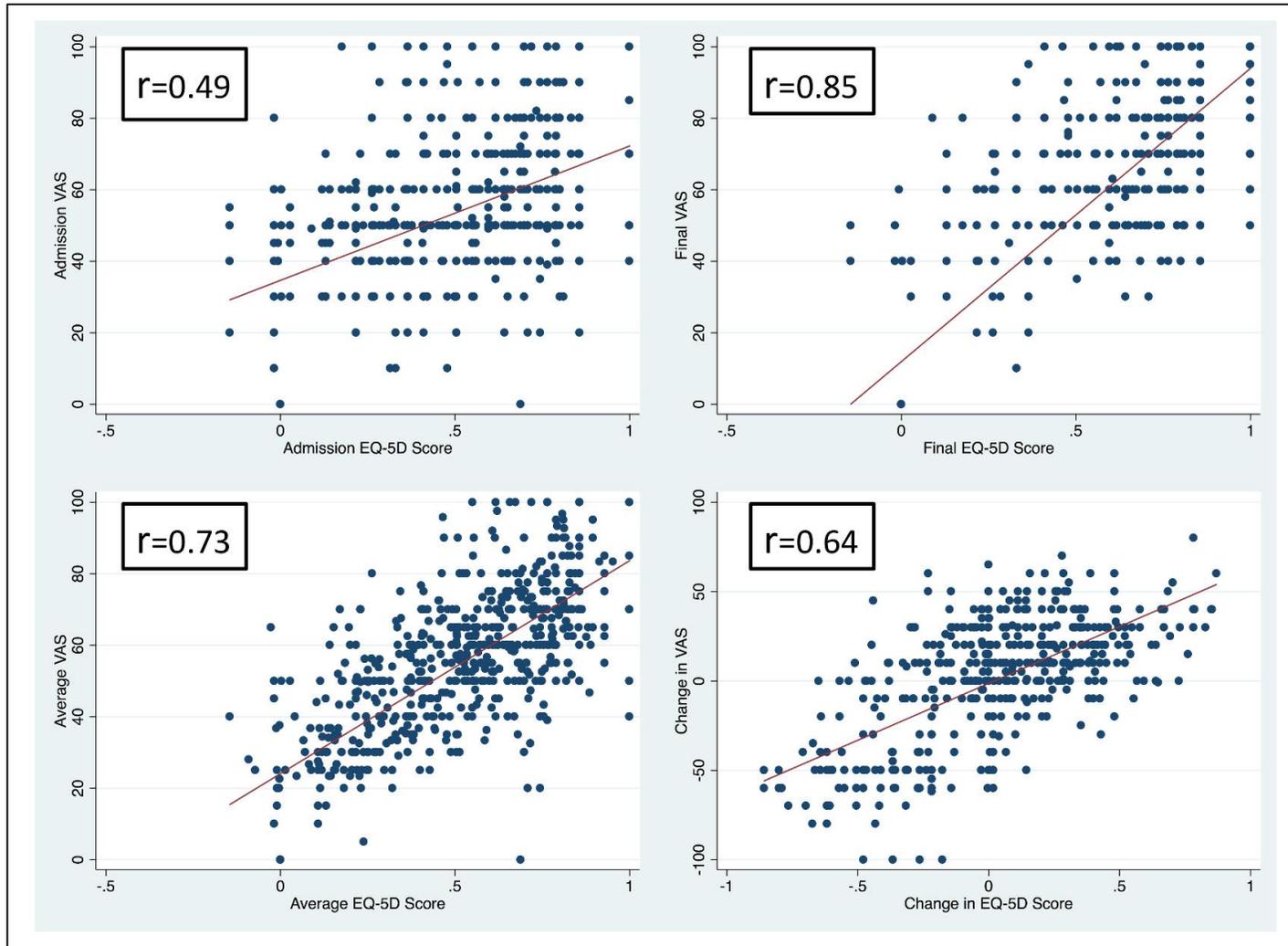
Table 53: EQ-5D utility scores by primary medical diagnosis (Zimbabwean Tariff)

Primary Medical Diagnosis	N	EQ-5D Utility Scores (Zimbabwean Tariff)						
		On Admission		Average during Admission		Pre-Discharge		Mean change (SE)
		n (%)	Mean (SE)	Mean (SE)	n (%)	Mean (SE)		
ALL	661	654 (98.9%)	0.484 (0.01)	0.498 (0.01)	494 (74.7%)	0.510 (0.02)	0.024	
Pulmonary Tuberculosis	55	55 (100%)	0.445 (0.04)	0.465 (0.04)	51 (92.7%)	0.465 (0.04)	0.034 (0.05)	
Tuberculosis of meninges and central nervous system	17	17 (100%)	0.288 (0.08)	0.333 (0.06)	13 (76.5%)	0.333 (0.06)	0.075 (0.15)	
Tuberculosis of intestines, peritoneum	9	9 (100%)	0.524 (0.11)	0.473 (0.09)	8 (88.9%)	0.473 (0.09)	-0.106 (0.07)	
Tuberculosis of bones and joint	5	5 (100%)	0.385 (0.09)	0.257 (0.09)	5 (100%)	0.257 (0.09)	-0.163 (0.10)	
Tuberculosis of other organs	15	15 (100%)	0.542 (0.08)	0.458 (0.08)	13 (86.7%)	0.458 (0.08)	-0.192 (0.11)	
Miliary Tuberculosis	17	17 (100%)	0.393 (0.07)	0.283 (0.06)	15 (88.2%)	0.283 (0.06)	-0.236 (0.08)	
Tuberculosis - retreatment	6	6 (100%)	0.577 (0.15)	0.576 (0.15)	5 (83.3%)	0.576 (0.15)	-0.039 (0.10)	
Septicaemia (except in labour)	60	60 (100%)	0.514 (0.04)	0.549 (0.04)	37 (61.7%)	0.549 (0.04)	0.093 (0.06)	
Candidiasis	6	6 (100%)	0.349 (0.09)	0.382 (0.09)	2 (33.3%)	0.382 (0.09)	0.223 (0.27)	
Cryptococcal meningitis	38	38 (100%)	0.483 (0.04)	0.498 (0.04)	34 (89.5%)	0.498 (0.04)	-0.013 (0.07)	
Viral infection	9	9 (100%)	0.524 (0.11)	0.431 (0.10)	6 (66.7%)	0.431 (0.10)	-0.260 (0.15)	
Pneumocystis Carinii Pneumonia	9	8 (88.9%)	0.559 (0.08)	0.528 (0.09)	8 (88.9%)	0.528 (0.09)	-0.058 (0.16)	
Malaria	13	13 (100%)	0.521 (0.07)	0.518 (0.07)	4 (30.8%)	0.518 (0.07)	-0.021 (0.11)	
Kaposi's Sarcoma	20	20 (100%)	0.415 (0.06)	0.425 (0.05)	15 (75.0%)	0.425 (0.05)	-0.018 (0.07)	
Neoplasms - excluding Kaposi's	8	8 (100%)	0.584 (0.07)	0.484 (0.08)	8 (100%)	0.484 (0.08)	-0.262 (0.10)	
Diabetes mellitus without complications	5	5 (100%)	0.682 (0.06)	0.749 (0.04)	3 (60.0%)	0.749 (0.04)	0.222 (0.10)	
Diabetes mellitus with complications	9	9 (100%)	0.405 (0.09)	0.429 (0.06)	6 (66.7%)	0.429 (0.09)	0.057 (0.11)	
Anaemia	35	35 (100%)	0.558 (0.04)	0.590 (0.04)	30 (85.7%)	0.590 (0.04)	0.032 (0.05)	
Mental Health disorders	9	9 (100%)	0.629 (0.08)	0.658 (0.06)	6 (66.7%)	0.658 (0.06)	0.169 (0.12)	
Meningitis (except that caused by TB or Crypto)	37	36 (97.3%)	0.484 (0.04)	0.561 (0.04)	31 (83.8%)	0.561 (0.04)	0.147 (0.06)	
Epilepsy; Convulsions	11	11 (100%)	0.588 (0.11)	0.588 (0.12)	5 (45.5%)	0.588 (0.12)	-0.003 (0.10)	
Other Neurological Problems	16	15 (93.8%)	0.506 (0.06)	0.510 (0.06)	10 (62.5%)	0.510 (0.06)	0.027 (0.10)	
Cerebrovascular disease	25	23 (92.0%)	0.359 (0.05)	0.399 (0.06)	12 (48.0%)	0.399 (0.06)	0.150 (0.07)	
Hypertension	7	7 (100%)	0.387 (0.13)	0.419 (0.11)	6 (85.7%)	0.419 (0.11)	0.037 (0.13)	
Congestive heart failure; non-hypertensive	15	15 (100%)	0.569 (0.06)	0.524 (0.06)	15 (100%)	0.524 (0.06)	-0.092 (0.09)	
Other Cardiovascular Problems	13	13 (100%)	0.471 (0.08)	0.539 (0.06)	11 (84.6%)	0.539 (0.06)	0.176 (0.12)	
Pneumonia (except that caused by TB)	93	91 (97.8%)	0.501 (0.03)	0.529 (0.03)	57 (61.3%)	0.529 (0.03)	0.084 (0.04)	
Other Respiratory Problems	11	11 (100%)	0.486 (0.08)	0.595 (0.07)	10 (90.9%)	0.595 (0.07)	0.215 (0.09)	
Acute - Intestinal Infection	10	10 (100%)	0.487 (0.10)	0.498 (0.08)	9 (90.0%)	0.498 (0.08)	0.033 (0.11)	
Chronic - Intestinal Infection	14	14 (100%)	0.434 (0.08)	0.443 (0.07)	9 (64.3%)	0.443 (0.07)	-0.054 (0.16)	
Upper gastrointestinal disorders	11	11 (100%)	0.501 (0.06)	0.487 (0.07)	9 (81.8%)	0.487 (0.07)	-0.019 (0.13)	
Liver disease	14	14 (100%)	0.436 (0.09)	0.420 (0.09)	11 (78.6%)	0.420 (0.09)	-0.040 (0.09)	
Diseases of the genitourinary system	19	19 (100%)	0.536 (0.06)	0.576 (0.06)	15 (78.9%)	0.576 (0.06)	0.080 (0.10)	
Diseases of the musculoskeletal system	6	6 (100%)	0.416 (0.09)	0.326 (0.09)	4 (66.7%)	0.326 (0.09)	-0.118 (0.18)	
Other Problems (<5 cases)	14	14 (100%)	0.458 (0.06)	0.502 (0.06)	11 (78.6%)	0.502 (0.502)	0.070 (0.10)	

Table 54: Visual analogue scale scores by primary medical diagnosis

Primary Medical Diagnosis	N	Visual Analogue Scores						
		On Admission		Average during Admission		Pre-Discharge		Mean change (SE)
		n (%)	Mean (SE)	Mean (SE)	n (%)	Mean (SE)		
ALL	661	654 (98.9%)	52.8 (0.8)	53.8 (0.8)	494 (74.7%)	54.0 (1.6)	0.1 (1.6)	
Pulmonary Tuberculosis	55	55 (100%)	55.2 (3.0)	55.9 (3.2)	51 (92.7%)	57.5 (5.8)	-0.9 (4.8)	
Tuberculosis of meninges and central nervous system	17	17 (100%)	42.9 (6.9)	42.2 (7.2)	13 (76.5%)	53.7 (11.2)	-2.5 (11.0)	
Tuberculosis of intestines, peritoneum	9	9 (100%)	50.0 (7.5)	45.9 (7.7)	8 (88.9%)	47.5 (12.4)	-8.8 (12.8)	
Tuberculosis of bones and joint	5	5 (100%)	62.0 (8.0)	46.0 (10.6)	5 (100%)	36.0 (22.3)	-26.0 (14.7)	
Tuberculosis of other organs	15	15 (100%)	51.0 (6.1)	50.2 (6.4)	13 (86.7%)	40.0 (10.9)	-11.2 (12.2)	
Miliary Tuberculosis	17	17 (100%)	38.5 (4.4)	33.4 (4.5)	15 (88.2%)	23.0 (8.4)	-20.0 (9.1)	
Tuberculosis - retreatment	6	6 (100%)	73.3 (7.6)	62.0 (9.6)	5 (83.3%)	51.0 (21.2)	-23.0 (22.8)	
Septicaemia (except in labour)	60	60 (100%)	53.3 (2.8)	54.8 (2.8)	37 (61.7%)	55.0 (6.0)	1.7 (6.3)	
Candidiasis	6	6 (100%)	48.3 (11.7)	48.9 (11.7)	2 (33.3%)	55.0 (5.0)	5.0 (5.0)	
Cryptococcal meningitis	38	38 (100%)	56.8 (3.2)	55.9 (3.2)	34 (89.5%)	51.9 (6.0)	-5.9 (6.6)	
Viral infection	9	9 (100%)	50.0 (10.7)	44.8 (10.5)	6 (66.7%)	42.5 (19.1)	-19.2 (16.1)	
Pneumocystis Carinii Pneumonia	9	8 (88.9%)	55.0 (8.0)	53.4 (8.7)	8 (88.9%)	58.8 (13.3)	3.8 (11.0)	
Malaria	13	13 (100%)	53.2 (6.6)	53.5 (6.5)	4 (30.8%)	62.5 (14.9)	2.5 (4.8)	
Kaposi's Sarcoma	20	20 (100%)	48.3 (3.5)	49.4 (4.4)	15 (75.0%)	48.0 (9.1)	-2.3 (9.4)	
Neoplasms - excluding Kaposi's	8	8 (100%)	52.5 (4.5)	46.8 (5.4)	8 (100%)	38.1 (10.3)	-20.6 (12.0)	
Diabetes mellitus without complications	5	5 (100%)	73.4 (8.1)	76.9 (8.3)	3 (60.0%)	86.7 (13.3)	11.7 (4.4)	
Diabetes mellitus with complications	9	9 (100%)	54.4 (3.4)	55.1 (4.0)	6 (66.7%)	57.5 (8.3)	4.2 (5.5)	
Anaemia	35	35 (100%)	52.5 (3.2)	56.9 (3.1)	30 (85.7%)	57.0 (6.1)	8.1 (6.2)	
Mental Health disorders	9	9 (100%)	61.1 (4.8)	64.0 (5.0)	6 (66.7%)	69.2 (8.4)	12.5 (4.8)	
Meningitis (except that caused by TB or Crypto)	37	36 (97.3%)	49.9 (3.5)	55.0 (3.7)	31 (83.8%)	60.8 (4.6)	11.0 (4.3)	
Epilepsy; Convulsions	11	11 (100%)	59.1 (6.1)	63.9 (5.5)	5 (45.5%)	64.0 (17.5)	14.0 (9.3)	
Other Neurological Problems	16	15 (93.8%)	55.3 (4.1)	57.1 (4.6)	10 (62.5%)	53.3 (8.7)	3.3 (8.7)	
Cerebrovascular disease	25	23 (92.0%)	50.7 (4.9)	51.9 (4.3)	12 (48.0%)	63.8 (7.5)	7.1 (10.7)	
Hypertension	7	7 (100%)	58.6 (2.6)	56.9 (4.2)	6 (85.7%)	49.2 (16.2)	-9.2 (18.7)	
Congestive heart failure; non-hypertensive	15	15 (100%)	57.0 (4.8)	54.1 (5.3)	15 (100%)	49.7 (10.1)	-7.3 (10.6)	
Other Cardiovascular Problems	13	13 (100%)	54.6 (4.4)	55.9 (5.4)	11 (84.6%)	60.9 (10.2)	7.3 (9.0)	
Pneumonia (except that caused by TB)	93	91 (97.8%)	53.3 (2.4)	55.6 (2.6)	57 (61.3%)	58.6 (4.4)	5.0 (4.4)	
Other Respiratory Problems	11	11 (100%)	50.5 (5.7)	54.9 (4.0)	10 (90.9%)	56.5 (8.0)	9.0 (9.1)	
Acute - Intestinal Infection	10	10 (100%)	56.0 (7.3)	52.8 (3.8)	9 (90.0%)	48.9 (7.0)	-8.9 (12.5)	
Chronic - Intestinal Infection	14	14 (100%)	50.0 (2.5)	48.6 (3.9)	9 (64.3%)	40.6 (12.9)	-11.1 (12.8)	
Upper gastrointestinal disorders	11	11 (100%)	52.5 (3.7)	55.2 (5.2)	9 (81.8%)	60.1 (12.0)	6.0 (12.9)	
Liver disease	14	14 (100%)	45.0 (5.9)	45.6 (6.7)	11 (78.6%)	45.5 (11.4)	-4.5 (10.7)	
Diseases of the genitourinary system	19	19 (100%)	53.2 (4.6)	58.7 (4.5)	15 (78.9%)	56.3 (8.6)	9.0 (8.5)	
Diseases of the musculoskeletal system	6	6 (100%)	47.5 (4.4)	53.3 (3.5)	4 (66.7%)	70.0 (4.1)	21.3 (10.1)	
Other Problems (<5 cases)	14	14 (100%)	52.9 (3.4)	55.4 (3.6)	11 (78.6%)	56.8 (8.0)	8.5 (9.3)	

Figure 55: Comparison of EQ5D utility Scores to Visual Analogue Scale Scores



In the multivariable analysis, the model diagnostics revealed the OLS estimator performed as well or better than the other estimators (Table 55 and Table 56). The CLAD estimator performed was marginally more efficient for lower observed EQ-5D utility scores, but less efficient when observed EQ-5D utility scores ranged from 0.4 to <1.0, where the majority of observed scores were.

Table 55: Estimated predicted values compared to actual utility scores

	Model	Obs	Mean	Min	Max	MSE	MAE
	Observed	605	0.503	-0.145	1.000		
Model	OLS	605	0.503	0.242	0.772	0.000	0.199
	TOBIT	605	0.502	0.252	0.759	0.001	0.200
	CLAD*	605	0.489	0.055	1.076	0.015	0.203
	Flogit	605	0.566	0.347	0.795	0.000	0.200

OLS: Ordinary Least Squares
Flogit: Fractional logit
CLAD: Censored least absolute deviations

MSE: Mean Squared Error
MAE: Mean Absolute Error
*No convergence as median EQ-5D score censored at 1.0

Table 56: MSE and MAE for regression models by utility score range

	Observed EQ-5D utility score													
	<0		0 to <0.2		0.2 to <0.4		0.4 to <0.6		0.6 to <0.8		0.8 to <1		1	
Obs	29	44	137	149	179	53	14							
	MSE	MAE	MSE	MAE	MSE	MAE	MSE	MAE	MSE	MAE	MSE	MAE	MSE	MAE
OLS	0.495	0.495	0.355	0.355	0.180	0.180	0.003	0.079	0.178	0.179	0.305	0.305	0.433	0.433
TOBIT	0.500	0.500	0.355	0.355	0.179	0.181	0.002	0.077	0.180	0.180	0.311	0.311	0.415	0.415
CLAD	0.499	0.499	0.331	0.331	0.147	0.160	0.016	0.100	0.181	0.193	0.326	0.327	0.400	0.400
Flogit	0.500	0.500	0.355	0.355	0.180	0.181	0.001	0.077	0.179	0.179	0.308	0.308	0.422	0.422

OLS: Ordinary Least Squares
MSE: Mean Squared Error

Flogit: Fractional logit
MAE: Mean Absolute Error

CLAD: Censored least absolute deviations

Table 57 show the multivariable analysis investigating the independent effect of HIV status (incorporating whether on ART) on the EQ-5D utility score on admission, and the average EQ-5D utility score during hospital admission.

In the multivariable analysis (Table 57), after adjusting for individual characteristics and the primary medical diagnosis (model 3), those who were HIV positive and not on ART had a lower adjusted mean **EQ-5D utility score on admission** of -0.133 (95%CI: -0.206, -0.060) compared to those who were HIV negative. Those who were HIV positive and on ART before their hospital admission had a lower adjusted mean EQ-5D utility score of -0.083 (95%CI: -0.141, -0.025) compared to those who were HIV negative.

In the multivariable analysis (Table 57), the **average EQ-5D utility score during the hospital admission** for those who were HIV positive and not on ART was significantly lower than compared to those who were HIV negative (-0.110, 95%CI: -0.180, -0.040). Finally, those who were HIV positive and on ART before their hospital admission had a lower adjusted 'average' mean EQ-5D utility score of -0.085 (95%CI: -0.141, -0.030) compared to those who were HIV negative.

Table 57: Multivariable analysis exploring relationship between HIV status and anti-retroviral treatment status and the EQ-5D utility scores* derived from the Zimbabwean tariff (Primary analysis)

HIV and Anti-retroviral therapy status	EQ-5D Utility Score on Admission			Average EQ-5D Utility Score during Admission		
	Model 1 (n=646)	Model 2 (n=618)	Model 3 (n=618)	Model 1 (n=646)	Model 2 (n=618)	Model 3 (n=618)
	Coef (95% CI)	Coef (95% CI)	Coef (95% CI)	Coef (95% CI)	Coef (95% CI)	Coef (95% CI)
HIV negative	Ref	Ref	Ref	Ref	Ref	Ref
HIV positive + on ART before admission	-0.068** (-0.118, -0.017)	-0.073** (-0.124, -0.022)	-0.083** (-0.141, -0.025)	-0.069** (-0.118, -0.020)	-0.076** (-0.126, -0.027)	-0.085** (-0.141, -0.030)
HIV positive + started ART in hospital	-0.034 (-0.235, 0.168)	-0.031 (-0.244, 0.182)	-0.018** (-0.206, 0.205)	-0.038 (-0.232, 0.157)	-0.056 (-0.260, 0.149)	-0.063 (-0.275, 0.149)
HIV positive + Not on ART	-0.099** (-0.165, -0.032)	-0.114** (-0.181, -0.047)	-0.133** (-0.206, -0.060)	-0.082** (-0.146, -0.017)	-0.095** (-0.160, -0.031)	-0.110** (-0.180, -0.040)
HIV status unknown	0.014 (-0.138, 0.109)	-0.035 (-0.155, 0.084)	-0.039 (-0.165, 0.088)	-0.010 (-0.129, 0.109)	-0.029 (-0.144, 0.086)	-0.055 (-0.175, 0.065)

Model 1: adjusted for exposure, Age and Sex

Model 2: additionally adjusted for marital status, educational attainment, income and wealth quintile

Model 3: additionally adjusted for primary medical diagnosis

ART: Anti-retroviral therapy

*Findings from OLS estimator

** $p < 0.05$

7.3.5 Findings from sensitivity analysis

Table 58 shows the findings from the sensitivity analysis where the UK tariff was used to estimate the EQ-5D utility scores by the primary medical diagnosis. Using the UK tariff, the mean EQ-5D utility score on admission was 0.267 (SE: 0.02), the mean EQ-5D utility score during the hospital admission was 0.325 (SE: 0.01), the last recorded mean EQ-5D utility score was 0.406 (SE: 0.02) and the mean change in EQ-5D utility score was 0.154.

Figure 56 compares the EQ-5D utility scores derived from the Zimbabwean and UK tariffs. The EQ-5D utility scores estimated using the UK tariff was lower than the EQ-5D utility scores estimated from the Zimbabwean tariff. Figure 56 shows the Pearson's correlation coefficient was >0.9 when the two EQ-5D tariffs were compared.

Table 59 shows the findings from the multivariable analysis investigating the independent effect of HIV status on the EQ-5D utility score on admission, and the average EQ-5D utility score during hospital admission where the EQ-5D utility scores were derived from the UK tariff. The multivariable analysis revealed comparable findings to when the Zimbabwean tariff was used, but with the adjusted EQ-5D utility scores estimated using the UK tariff being systematically lower.

Table 58: Sensitivity analysis: EQ-5D utility scores from UK Tariff by primary medical diagnosis

Primary Medical Diagnosis	EQ-5D Utility Scores						
	N	n (%)	On Admission	Average during admission	Pre-Discharge	Mean change	
			Mean (SE)	Mean (SE)	Mean (SE)	(SE)	
ALL	661	654 (98.9%)	0.267 (0.02)	0.325 (0.01)	494 (74.7%)	0.406 (0.02)	0.154 (0.02)
Pulmonary Tuberculosis	55	55 (100%)	0.205 (0.05)	0.289 (0.04)	51 (92.7%)	0.402 (0.05)	0.190 (0.06)
Tuberculosis of meninges and central nervous system	17	17 (100%)	0.070 (0.10)	0.173 (0.06)	13 (76.5%)	0.314 (0.10)	0.223 (0.18)
Tuberculosis of intestines, peritoneum	9	9 (100%)	0.384 (0.14)	0.339 (0.09)	8 (88.9%)	0.373 (0.11)	-0.059 (0.10)
Tuberculosis of bones and joint	5	5 (100%)	0.089 (0.12)	0.028 (0.09)	5 (100%)	0.100 (0.06)	0.011 (0.09)
Tuberculosis of other organs	15	15 (100%)	0.324 (0.10)	0.287 (0.10)	13 (86.7%)	0.314 (0.12)	-0.017 (0.10)
Miliary Tuberculosis	17	17 (100%)	0.156 (0.10)	0.091 (0.07)	15 (88.2%)	0.112 (0.06)	-0.093 (0.11)
Tuberculosis - retreatment	6	6 (100%)	0.412 (0.22)	0.470 (0.19)	5 (83.3%)	0.509 (0.21)	0.167 (0.12)
Septicaemia (except in labour)	60	60 (100%)	0.306 (0.05)	0.389 (0.05)	37 (61.7%)	0.484 (0.07)	0.270 (0.07)
Candidiasis	6	6 (100%)	0.073 (0.07)	0.126 (0.05)	2 (33.3%)	0.450 (0.26)	0.403 (0.47)
Cryptococcal meningitis	38	38 (100%)	0.244 (0.06)	0.318 (0.05)	34 (89.5%)	0.359 (0.07)	0.122 (0.08)
Viral infection	9	9 (100%)	0.399 (0.10)	0.326 (0.10)	6 (66.7%)	0.421 (0.19)	-0.117 (0.12)
Pneumocystis Carinii Pneumonia	9	8 (88.9%)	0.382 (0.13)	0.381 (0.11)	8 (88.9%)	0.392 (0.17)	0.010 (0.21)
Malaria	13	13 (100%)	0.338 (0.09)	0.332 (0.10)	4 (30.8%)	0.472 (0.25)	-0.037 (0.12)
Kaposi's Sarcoma	20	20 (100%)	0.145 (0.07)	0.204 (0.05)	15 (75.0%)	0.262 (0.09)	0.110 (0.07)
Neoplasms - excluding Kaposi's	8	8 (100%)	0.453 (0.12)	0.292 (0.12)	8 (100%)	0.134 (0.18)	-0.295 (0.15)
Diabetes mellitus without complications	5	5 (100%)	0.610 (0.09)	0.701 (0.05)	3 (60.0%)	0.858 (0.07)	0.301 (0.16)
Diabetes mellitus with complications	9	9 (100%)	0.148 (0.14)	0.184 (0.13)	6 (66.7%)	0.243 (0.14)	0.057 (0.14)
Anaemia	35	35 (100%)	0.355 (0.07)	0.442 (0.06)	30 (85.7%)	0.464 (0.07)	0.160 (0.07)
Mental Health disorders	9	9 (100%)	0.416 (0.12)	0.489 (0.10)	6 (66.7%)	0.669 (0.11)	0.236 (0.21)
Meningitis (except that caused by TB or Crypto)	37	36 (97.3%)	0.294 (0.06)	0.423 (0.05)	31 (83.8%)	0.525 (0.07)	0.261 (0.09)
Epilepsy; Convulsions	11	11 (100%)	0.426 (0.17)	0.444 (0.18)	5 (45.5%)	0.480 (0.31)	0.112 (0.18)
Other Neurological Problems	16	15 (93.8%)	0.308 (0.10)	0.324 (0.09)	10 (62.5%)	0.191 (0.10)	0.090 (0.13)
Cerebrovascular disease	25	23 (92.0%)	0.087 (0.08)	0.151 (0.09)	12 (48.0%)	0.482 (0.14)	0.264 (0.10)
Hypertension	7	7 (100%)	0.132 (0.19)	0.179 (0.14)	6 (85.7%)	0.314 (0.16)	0.133 (0.16)
Congestive heart failure; non-hypertensive	15	15 (100%)	0.371 (0.10)	0.388 (0.09)	15 (100%)	0.416 (0.10)	0.045 (0.10)
Other Cardiovascular Problems	13	13 (100%)	0.270 (0.11)	0.386 (0.09)	11 (84.6%)	0.524 (0.11)	0.330 (0.15)
Pneumonia (except that caused by TB)	93	91 (97.8%)	0.296 (0.04)	0.366 (0.03)	57 (61.3%)	0.492 (0.05)	0.222 (0.06)
Other Respiratory Problems	11	11 (100%)	0.236 (0.12)	0.425 (0.10)	10 (90.9%)	0.594 (0.12)	0.410 (0.13)
Acute - Intestinal Infection	10	10 (100%)	0.292 (0.15)	0.303 (0.12)	9 (90.0%)	0.257 (0.10)	0.044 (0.15)
Chronic - Intestinal Infection	14	14 (100%)	0.170 (0.12)	0.246 (0.10)	9 (64.3%)	0.250 (0.14)	0.162 (0.18)
Upper gastrointestinal disorders	11	11 (100%)	0.286 (0.10)	0.292 (0.09)	9 (81.8%)	0.423 (0.13)	0.055 (0.16)
Liver disease	14	14 (100%)	0.229 (0.11)	0.264 (0.09)	11 (78.6%)	0.374 (0.11)	0.098 (0.11)
Diseases of the genitourinary system	19	19 (100%)	0.299 (0.08)	0.417 (0.07)	15 (78.9%)	0.522 (0.12)	0.269 (0.13)
Diseases of the musculoskeletal system	6	6 (100%)	0.131 (0.10)	0.011 (0.10)	4 (66.7%)	0.069 (0.16)	-0.150 (0.22)
Other Problems (<5 cases)	14	14 (100%)	0.185 (0.10)	0.298 (0.09)	11 (78.6%)	0.360 (0.13)	0.323 (0.11)

Figure 56: Comparison of EQ-5D utility scores estimated from Zimbabwean and UK tariffs

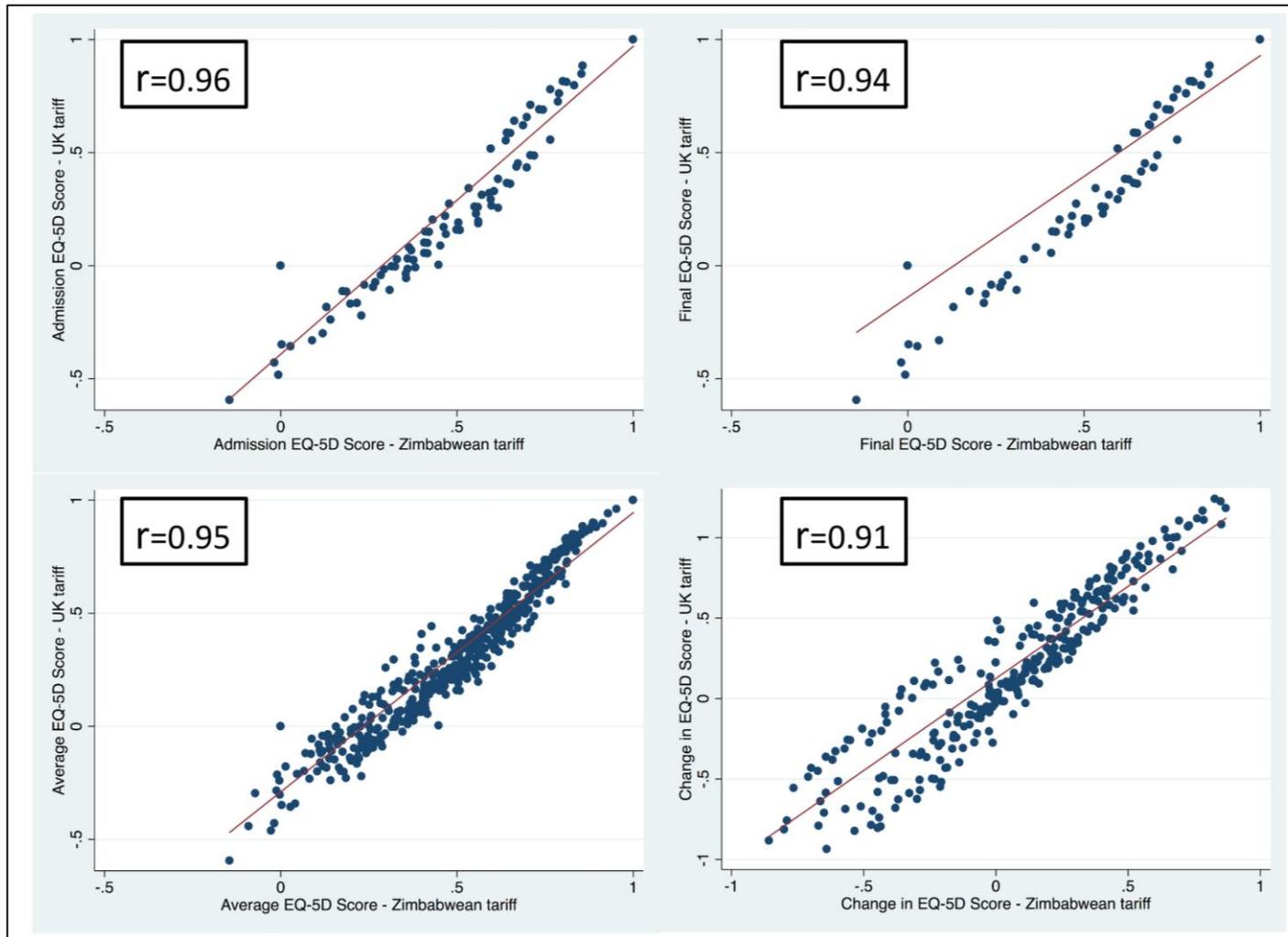


Table 59: Multivariable analysis exploring relationship between HIV status and anti-retroviral treatment status on EQ-5D utility scores derived from the UK tariff (Sensitivity analysis)*

HIV and Anti-Retroviral therapy status	EQ-5D Utility Score on Admission			Average EQ-5D Utility Score during Admission		
	Model 1 (n=646)	Model 2 (n=617)	Model 3 (n=617)	Model 1 (n=646)	Model 2 (n=617)	Model 3 (n=617)
	Coef (95% CI)	Coef (95% CI)	Coef (95% CI)	Coef (95% CI)	Coef (95% CI)	Coef (95% CI)
HIV negative	Ref	Ref	Ref	Ref	Ref	Ref
HIV positive + on ART before admission	-0.100** (-0.173, -0.027)	-0.114** (-0.192, -0.037)	-0.122** (-0.209, -0.034)	-0.085** (-0.149, -0.021)	-0.103 (-0.171, -0.036)	-0.116** (-0.192, -0.041)
HIV positive + started ART in hospital	-0.072 (-0.362, 0.218)	-0.065 (-0.386, 0.257)	-0.053 (-0.390, 0.283)	-0.119 (-0.375, 0.136)	-0.149** (-0.429, 0.130)	-0.177 (-0.466, 0.113)
HIV positive + Not on ART	-0.163** (-0.259, -0.067)	-0.189** (-0.290, -0.088)	-0.210** (-0.321, -0.100)	-0.116** (-0.200, -0.031)	-0.141** (-0.229, -0.053)	-0.162** (-0.257, -0.067)
HIV status unknown	0.025 (-0.202, 0.153)	-0.038 (-0.290, 0.142)	-0.048 (-0.238, 0.142)	-0.032 (-0.188, 0.125)	-0.042 (-0.199, 0.115)	-0.078 (-0.241, 0.086)

Model 1: adjusted for exposure, Age and Sex

Model 2: additionally adjusted for marital status, educational attainment, income and wealth quintile

Model 3: additionally adjusted for primary medical diagnosis

ART: Anti-retroviral therapy

*Findings from OLS estimator

** $p < 0.05$

7.4 Discussion

In this component of the PHD I estimated the total health provider costs, the total societal costs and the EQ-5D utility scores for a range of medical diagnoses for individuals admitted to the medical wards at Queen Elizabeth Central Hospital (QECH).

The study undertaken in this Chapter demonstrates the high health provider costs of managing patients in hospitals and the high costs incurred by those admitted to hospital. Additionally, I show the poor health-related quality of life amongst those admitted to hospital. For example in Chapter 6 of the PhD, I estimated the health provider cost of managing an HIV positive individual on anti-retroviral therapy at the HIV clinic for one year to be approximately 2014 US\$166. In this Chapter, I estimated the average health provider cost of managing an adult on the medical ward during a hospitalisation episode to be approximately 2014 US\$ 315. In Chapter 6 of the PhD, I found that over the first year of accessing anti-retroviral therapy, the total direct non-medical and indirect costs were approximately 2014 US\$9. In this chapter, I found the total direct non-medical and indirect cost during a hospitalisation episode was approximately 2014 US\$87. In Chapter 6 of the PhD I found the mean EQ-5D utility score amongst HIV positive individuals attending the HIV clinic to be assessed for initiation of anti-retroviral therapy to be approximately 0.841. Amongst adults admitted to the QECH the mean EQ-5D utility scores was found to be 0.484.

In this study, the average health provider cost of managing individuals in hospital was approximately US\$314.93. This cost is comparable to previous estimates of health provider costs of providing hospital care in sub-Saharan Africa. In a previous study in Kenya, the average health provider costs was found to be US\$163 (in 2000 prices) (Guinness et al., 2002). In Zimbabwe, the average health provider cost of hospital admission was estimated to range from US\$40 for HIV negative individuals in a district hospital to US\$316 for HIV positive individuals in a central hospital (in 2000 prices) (Hansen et al., 2000). In this study I found the cost of the ward stay (including clinical staff salaries) accounted for approximately 60% of the total health provider cost, whilst the cost of procedures accounted for approximately 35% of the total health provider costs.

Table 60 shows the findings from previous hospital costing studies and the proportion of the total health provider costs accounted for by different resources. The high proportion of the total costs accounted for by investigations and procedures could possibly reflect the fact that this study was undertaken in the main teaching hospital in Malawi. Queen Elizabeth Central hospital (QECH) provides a wider range of laboratory services than district level hospitals in Malawi. Alternatively it may reflect the gradual increase in availability of diagnostic services in the region. Of the three studies shown in Table 60, the most recent study found investigations and procedures accounted for nearly half of the total health provider costs (Tshamba et al., 2014). The relatively lower proportion of the total cost accounted for by drugs is likely to reflect increasing availability of medicines in Africa,

and the work done by International Organisations like the World Health Organisation (WHO). Since 2001, the WHO has implemented the prequalification of medicines programme that aims to ensure high quality drugs enter the African healthcare markets at reasonable prices (WHO, no date-b). The service allows many of the National and International healthcare providers working the region bulk purchase medicines at reduced costs.

Table 60: Distribution of costs by cost category amongst hospitalised medical patients from previous hospital costing studies in the region.

	<i>Guinness et al (Guinness et al., 2002)</i>	<i>Hongoro and McPake(Hongoro and McPake, 2003)</i>	<i>Tshamba et al (Tshamba et al., 2014)</i>
Year of Data Collection	1997	1999	2010
Country of Study	Kenya	Zimbabwe	Dr Congo
HIV Status of sample	Positive	Mixed	Positive
Proportion of total hospital cost			
<i>Hotel/Staff Costs</i>	68%	89%	19%
<i>Investigations/procedures</i>	21%	10%	46%
<i>Medications</i>	11%	1%	35%

In this study, I found the average health provider cost per day of hospital admission to be approximately 2014 US\$32, with patients spending on average 12 days in hospital to receive inpatient care. Table 61 shows the average duration of hospital stay found in previous studies investigation hospital care in Africa. The higher duration of hospital admission in this study could also reflect that fact that QECH is a teaching hospital and consequently is caring for those with more complex medical

conditions, or the gradual improvement in inpatient care available in the region that necessitates longer admissions.

Table 61: Comparison of duration of hospital admission

	Guinness et al (Guinness et al., 2002)		Hongoro and McPake (Hongoro and McPake, 2003)	de Cherif et al (de Cherif et al., 2009)	Olukoga (Olukoga, 2007)	McCarthy et al (McCarthy et al., 2006)	Janson et al (Janson et al., 2012)	Tshamba et al (Tshamba et al., 2014)
Year of Data Collection	1997	1997	1999	2002	2002	2008	2008	2010
Country of Study	Kenya	Kenya	Zimbabwe	South Africa	South Africa	South Africa	South Africa	Dr Congo
HIV Status	Positive	Negative	Mixed	Positive	Mixed	Positive	Mixed	Positive
Average days of admission by Clinical diagnosis								
<i>Acute Gastroenteritis</i>	3.5	4.5						
<i>Acute Pneumonia</i>	6.0	4.0						
<i>Tuberculosis</i>	8.0	8.0	4-10			9.7	9.7	
<i>Clinical enteric illness</i>	10.5	6.5						
<i>Diabetes</i>	4.0	4.0						
<i>Malaria</i>	4.0	3.0	3-6					
<i>Bacterial meningitis</i>	7.0	9.0						
<i>Cryptococcal meningitis</i>						10		
<i>All</i>	7	6		8-9	3-9			7

In this study, the health provider costs were highest for those diagnosed with Cryptococcal Meningitis (US\$837.92), where 20% of the total health provider cost was due to the cost of drugs. In QECH, these individuals received treatment with Amphotericin B and Flucytosine, both of which are very costly drugs. A recent study in Uganda estimated the health provider cost of managing Cryptococcal Meningitis with Amphotericin B with Flucytosine to be approximately US\$467.48 (in 2012 prices) (Rajasingham et al., 2012). However, the study did not involve primary data collection from individuals and primary costing of health services, and consequently

may explain their slightly lower estimate. In comparison, the health provider costs of managing Candidiasis, Pneumocystis Carinii Pneumonia and Kaposi's sarcoma, all of which are also occur with late-stage HIV disease, was comparable to or lower than the average health provider costs of managing inpatients at QECH. In comparison to the average inpatient at QECH, where 3.6% of the total cost of care was for drugs, inpatients with Candidiasis, Pneumocystis Carinii Pneumonia and Kaposi's sarcoma, a smaller proportion of the total health provider cost was spent on drugs. This may reflect the lack of available medicines to care for this patient group in the setting.

Tuberculosis remains one of the commonest reasons for hospital admission and this study highlights the high health provider costs of managing affected individuals (US\$316.08 to US\$743.97). The majority of TB patients in the study were HIV positive, a high proportion of them died, and very few had improvements in health-related quality of life during admission. Previous studies have highlighted the high costs incurred by patients affected by TB needing hospital admission (Floyd et al., 1997, Moalosi et al., 2003, Schnippel et al., 2013). In this study, patients diagnosed with TB had high mean direct non-medical and indirect costs during their hospital admission (US\$73.35 to US\$485.95). The long duration of hospitalisation would explain the high costs, especially for those requiring re-treatment for TB. These costs may be unavoidable after developing TB disease, considering the severity of the illness, but the findings highlight the importance of improving uptake of TB preventative therapy and TB case detection, especially amongst those infected with HIV.

In Malawi, hospital care is provided free but users will inevitably incur some costs in accessing care, ranging from transportation to hospital, to loss of income. The average direct non-medical and indirect costs was approximately US\$86.93. The majority of Malawians live on less than \$2 a day (World Bank), highlighting the catastrophic impact of a hospitalisation on the finances of Malawians. Whilst preventing illness will have a major impact on reducing this burden, decentralising hospital care could avert much of these costs. QECH is the main teaching hospital in Malawi and therefore likely to provide more intensive care than the rural district hospitals where the majority of the population live. Patients may need to spend more money travelling long distances to access care, need a family or carer to accompany them and take more time off from income generating activities than if hospitalised closer to their primary residence. However, the shortage of medical personnel in Malawi and the rest of Africa, and the high cost of laboratory services, impedes the decentralisation of hospital care.

Previous studies have highlighted the impact of HIV on the costs of hospital care and the burden it places on individuals (Guinness et al., 2002, Hansen et al., 2000, Menzies et al., 2012, Hongoro and McPake, 2003, Goudge et al., 2009). In this study, approximately 70% of patients were HIV positive, a finding comparable to previous estimates from a study undertaken in the same hospital (SanJoaquin et al., 2013). HIV status was found to be independently associated with the total health provider and total societal costs of admission. However, after adjusting for the primary medical diagnosis, the association was no longer statistically significant. The findings

would suggest it is the illnesses that HIV causes, specifically the illness associated with late stage HIV disease that places the greatest financial burden on health providers and society. Timely entry into HIV care and initiation of anti-retroviral therapy has been shown to reduce the burden of late-stage HIV diseases (Brinkhof et al., 2007, May et al., 2010a, Sterne et al., 2009), and therefore would likely reduce this financial burden.

The health-related quality of life (HRQoL) of hospitalised individuals in the study was poor. The average EQ-5D utility score amongst inpatients during their hospital admission was 0.498, this compares poorly with the average EQ-5D utility score observed amongst HIV testers in Chapter 5 and HIV positive individuals accessing HIV care in Chapter 6. Of more concern was the minimal improvement in HRQoL from admission to discharge. HIV infection seems to be the main driver of this poor HRQoL, with HIV status being independently associated with the EQ-5D utility scores, even after adjusting for the medical diagnosis. Of note, individuals started onto ART tended to have better HRQoL than HIV positive individuals not yet started therapy, even after adjusting for the primary medical diagnosis.

Previous studies have highlighted the lack of health utility data in the region for the purposes of undertaking cost-utility analyses (Robberstad and Olsen, 2010, Beard et al., 2009). This study provides an extensive catalogue of health utility scores to inform cost-utility analyses for a range of interventions, not just limited to HIV (Guo

et al., 2009, Organization, 2010, Dabhadkar et al., 2011). The findings of this study also suggest the EQ-5D measure provides health state utility scores that correlates to individuals own perception of their health-related quality of life derived from the VAS. The utility scores derived from the 5-dimensions of the descriptive questions individuals answer (on their pain, mobility, self-care, usual activities and anxiety/depression), using the Zimbabwean tariff show a high degree of correlation to the visual analogue scores derived from individuals rating their health on a scale ranging from 0 to 100 (Figure 55). This high correlation was also seen when I examined the change in the EQ-5D utility score and the change in the VAS score.

Of interest is the choice of tariffs used to convert the descriptive responses provided by participants to the EQ-5D measure. In the sensitivity analysis, I examined the EQ-5D utility scores derived using the UK York A1 tariff and compared them to the EQ-5D utility scores derived from the Zimbabwean tariff. The UK York A1 tariff results in systematically lower utility scores than the Zimbabwean tariff, with the change in utility scores found with the two tariffs being greater when the UK tariff was used. The average change in EQ-5D utility score for all participants, measured by the UK tariff was 0.154, whilst using the Zimbabwean tariff was 0.024. As highlighted previously, the UK York A1 tariff translates health states with 'severe' problems in one or more of the five dimensions to lower EQ-5D utility scores than the Zimbabwean tariff. This has important implications for this study where I used a tariff set not derived from the population I was studying. If the Malawian population valued health states more comparably to the UK population than the Zimbabwean

population, then I would potentially undervalue potential gains from interventions improving the health status of those with more severe diseases. Putting this in context, if HIV self-testing were to increase timely uptake of HIV testing amongst those infected with the virus, and consequently reducing the risk of progressing to advanced HIV disease and HIV-associated illness with early initiation of ART, the incremental cost-effectiveness ratio (ICER) estimated using the Zimbabwean tariff set would be higher. In Chapter 8 of the PhD where I estimate the ICER from implementing HIVST, I will explore the impact of using EQ-5D utility scores derived from the UK tariff in the sensitivity analysis.

The findings from this study are primarily limited by the relatively small number of participants recruited for a few of the medical conditions, and the fact that the study was undertaken in a large central teaching hospital which limits generalisability to smaller district hospital settings. In addition the findings may be potentially biased by the high attrition rate (only 80% of eligible participants consented to participate and had their medical notes found). For the majority of these participants it was because their medical notes could not be found. This is a common issue with doing research in resource-poor settings where medical records are not computerised or patients may take them on discharge.

7.5 Summary of Chapter 7

In this chapter I undertook primary data collection from individuals admitted to hospital in Blantyre, Malawi. I collected data on the costs of providing care and health-related quality of life of patients admitted with a range of HIV-related illnesses. In addition, I estimated the total societal costs of medical illnesses needing inpatient management.

In this study I found that approximately 70% of adults admitted to the hospital for the management of medical condition were HIV positive. I show the high mortality rates amongst this cohort, especially amongst those HIV positive. This study highlights the significant financial burden HIV poses on healthcare providers and individuals needing hospital inpatient medical care in Malawi. The high costs of hospital care and the detrimental effects on their health-related quality of life highlight the benefits of early and timely entry into HIV care. Many of the illnesses seen in this study would be potentially avoidable with early uptake of HIV testing and initiation of anti-retroviral therapy.

In the next chapter the economic data collected as part of this study will be used to inform the decision-analytic modeling of the cost-effectiveness of HIV self-testing.

**CHAPTER 8: Cost-utility analysis of
providing HIV self-testing in
addition to facility-based HIV
testing and counselling in Blantyre,
Malawi**

8 Overview of Chapter 8

In this chapter I will aim to investigate the primary objective of my PhD and thereby answer the primary research question.

To undertake a decision-analytic modelling based cost-utility analysis to estimate the incremental cost per quality-adjusted life year (QALY) gained with the provision of HIV self-testing in conjunction with traditional facility-based HIV testing and counselling services in Blantyre, Malawi.

I will provide a brief introduction to the topic, and describe in detail the methods used in undertaking the decision-analytic modeling. I will describe the model structure and the data used to parameterise the model. I will present the findings of the model analysis, including the sensitivity analysis. I will provide a brief discussion of the findings in this Chapter, with a more detailed discussion of findings in the main discussion (Chapter 9).

8.1 Introduction

HIV remains a global health problem, and sub-Saharan Africa has been disproportionately affected by the epidemic (UNAIDS, 2014b). Recent advances in HIV treatment and prevention offers promise (Cohen et al., 2011, Gray et al., 2007a, Group et al., 2015a, Group, 2015b), however for them to be effective individuals will need to be aware of their current HIV status (Granich et al., 2009). Efforts are currently being made to increase provision of HIV testing amongst Africans (UNAIDS, 2014a), with HIV self-testing high on the agenda (WHO, 2015).

HIV self-testing (HIVST) has been found to be a safe and effective strategy for increasing the uptake of HIV testing, and can be delivered by trained health volunteers, with individuals accurately testing themselves (Choko et al., 2015a). Individuals found to be HIV positive are willing to link into HIV treatment services (Choko et al., 2015a, MacPherson et al., 2014). HIVST can be delivered at costs comparable to facility-based HTC; potentially at lower costs should the price of the HIV self-test kits fall (Chapter 5). HIVST saves users significant time and money, which may in part explain the high levels of uptake (Chapter 5). The cost of managing HIV positive individuals identified through HIVST is comparable to those identified through facility-based HIV testing and counseling (HTC), with potential savings during the assessment for ART eligibility (Chapter 6). Additionally, HIVST identifies HIV positive individuals earlier in their disease progression than facility-based HTC (Choko et al., 2015b, Rosen and Fox, 2011), potentially averting some of the cost and health consequences of HIV associated illnesses (Chapter 7).

However, policy makers will need to be aware of the value for money of offering HIVST, if they are to consider prioritising its implementation over other health technologies. Economic evaluations allow us to investigate this issue and provide useful information to policy makers wishing to scale-up HIV self-testing services in their region. Whilst there is a range of approaches to undertaking an economic evaluation, a cost-utility analysis has the advantage of providing economic evidence to policy makers on the value of implementing interventions whilst allowing direct comparisons to be made with intervention targeting other disease areas.

The main aim of the study undertaken was to investigate the cost-effectiveness of providing HIVST in addition to facility-based HTC in Malawi. I used decision-analytic modeling to simulate the costs and health consequences of implementing HIVST, and to estimate the incremental cost per quality-adjusted life gained. I populated the models with primary cost and health-related quality of life data collected from Malawi, and epidemiology data extracted from the literature. I undertook the evaluation from both the health provider and societal perspectives. The findings will help inform policy on the cost-effectiveness of implementing HIVST.

8.2 Methods

8.2.1 Study overview

Decision-analytic modeling was undertaken to perform a cost-utility analysis (Drummond et al., 2005b) to estimate the incremental cost-effectiveness of the HitTB HIV self-testing intervention. In the model I compare the costs and consequences of providing only facility-based HIV testing to providing HIV self-testing (HIVST) in addition to facility-based HIV testing and counseling (HTC). The model examines the costs and consequences for hypothetical adults (aged >15 years) living in Blantyre, Malawi.

The analysis was undertaken from both the health provider and societal perspectives (Drummond et al., 2005b). The primary health outcome was measured in quality-adjusted life years (QALYs). Costs are represented in 2014 US dollars and 2014 International Dollars, and a discount rate of 3% was applied to both costs and health effects (WHO, 2003a). An individual sampling model (Barton et al., 2004) was used, with a one month cycle length, and was run over a time horizon of 20 years in the primary analysis. The model was also run over shorter (10 years) and longer (40 years) time horizons. The model is a static model and assumes there is no interaction between individuals being modeling. The model was built in TreeAge Pro 2015 (TreeAge Software, Williamstown, Massachusetts) and probabilistic sensitivity analysis (PSA) was carried out using Monte Carlo simulation.

8.2.2 Model description

8.2.2.1 Model overview

An individual sampling model (ISM) (Barton et al., 2004) was used to project the health consequences and costs incurred as individuals accessed either modality of HIV testing, accessed HIV care or were admitted to hospital for the management of an HIV associated illness.

An individual sampling model (ISM), which is often referred to as a microsimulation model in the literature (Barton et al., 2004), is comparable to a Markov model but overcomes the Markovian assumption that does not allow transition probabilities and rewards assigned to a health state to be conditional on either the time spent in the health state or characteristics of individuals entering the health state (Barton et al., 2004). Additionally in comparison to a cohort model, the ISM simulates the transitions through the health states in the model for a single individual. Taken together an ISM provided the flexibility needed to model the evaluation of HIV testing and counseling strategies where likelihood of HIV testing depends on past history of HIV testing, and risk of health events, whilst eligibility for anti-retroviral therapy (ART) on an individuals' HIV disease stage.

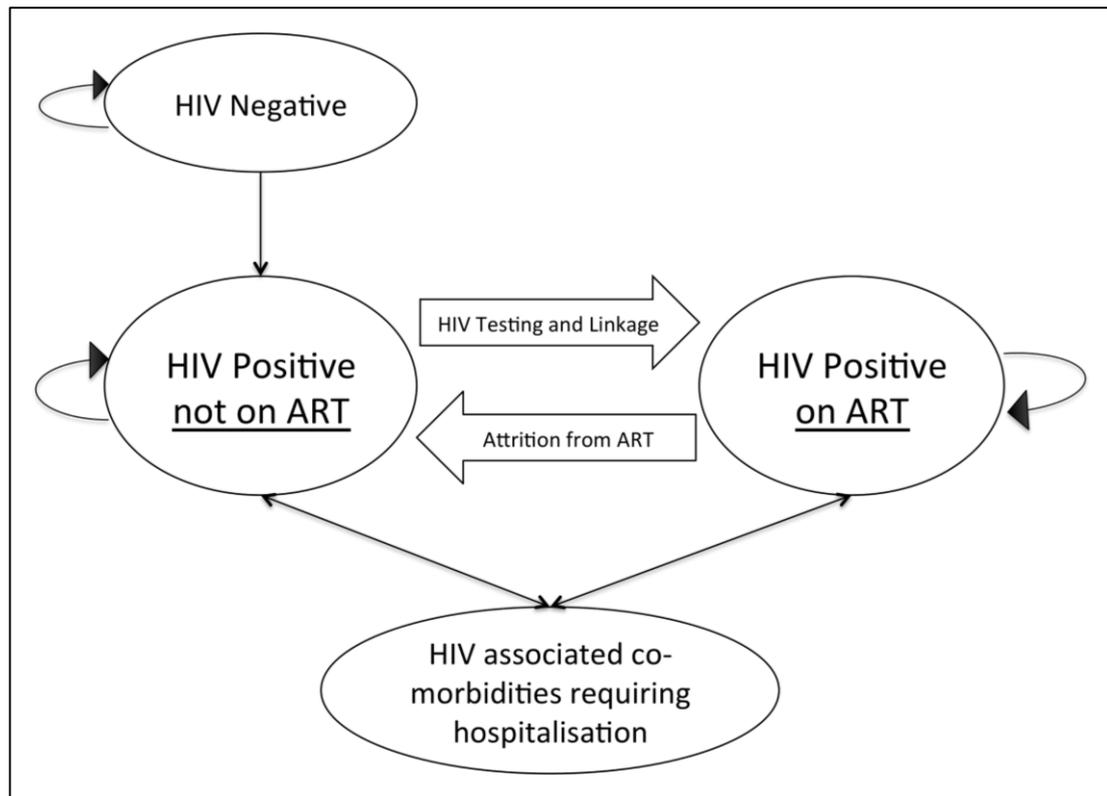
The model projects the costs and consequences of offering HIVST as provided in the HitTB intervention. The characteristics of the population modeled and the costs and impact on HRQoL reflect the HiTTB study population. In the model HIV negative and

HIV positive individuals both access HIV testing services, but only HIV positive individuals may be linked into HIV treatment and start anti-retroviral therapy. In the model HIVST is only available in the intervention strategy. HIV positive individuals may suffer from one of the HIV-associated co-morbidities. HIV negative individuals are not at risk of suffering from one of the HIV associated co-morbidities, but may acquire HIV infection. In the model, eligibility for initiation of ART is based on Malawian National HIV guidelines (MoH, 2014). Figure 57 provides a broad overview of the model structure. The model had 4 main health states; (1) HIV negative; (2) HIV positive and not on ART; (3) HIV-associated co-morbidity; (5) HIV positive and on ART. In addition, all individuals are at risk of dying, resulting in them entering death - an absorbing health state.

In the model there are three modules: (1) HIV disease progression module (Figure 58); (2) HIV testing and linkage module (Figure 59); and (3) HIV treatment module (Figure 60). The modules simulate individuals' HIV disease progression, uptake of HIV testing, entry into HIV care and admission to hospital for the management of an HIV associated illness. The model records and tracks the characteristics of the individuals and these are used to determine likelihood of a range of events. The model tracks the CD4 count and the WHO stage of HIV positive individuals to determine eligibility for ART after HIV testing. The model uses the individual's CD4 count to determine the risk of death, the risk of hospitalisation for a severe HIV associated illness and health outcomes on ART. The model records history of HIV testing to determine uptake of re-testing. The model tracks duration on ART or in pre-ART care to

determine likelihood of retention in care, and the costs and HRQoL changes whilst in care.

Figure 57: Overview of HIV model structure



8.2.2.2 Individual simulation in the model

At the beginning of the simulation, individuals are assigned to either the HIV negative health state or the HIV positive and not on ART health states. Individuals who are HIV negative are at risk of acquiring HIV infection. HIV positive individuals are assigned a CD4 count on entry into the model and also after acquiring HIV infection. The CD4 count assigned determines whether the individual is assigned to

one of five health states; CD4 count >500 cells/ μ l; CD4 count 351-500 cells/ μ l; CD4 count 201-350 cells/ μ l; CD4 count 51-200 cells/ μ l; or CD4 count \leq 50 cells/ μ l. The CD4 count assigned to individuals was randomly chosen between these ranges, with the exception for those assigned to the health state with a CD4 count >500 cells/ μ l.

There is very little certainty in the literature around actual CD4 counts during the early phase on HIV infection, as very few individuals will know precisely when they acquired HIV and therefore unlikely to have had their CD4 count measured soon after infection (Lodi et al., 2011). Therefore, individuals entering the CD4 count >500 cells/ μ l were assigned a CD4 count of 501 cells/ μ l and the literature was used to determine the monthly probability of their CD4 count falling to below 500 cells/ μ l, at which stage they were assigned a CD4 count of 500 cells/ μ l.

Figure 58 provides an overview of the HIV disease progression module. After an individual is assigned a CD4 count (on entry into the model or after acquiring HIV infection), the model simulates their HIV disease progression over time with monthly decrements in their CD4 count. Individual's transition to the health state with the lower CD4 count strata if their CD4 count falls below the defined range.

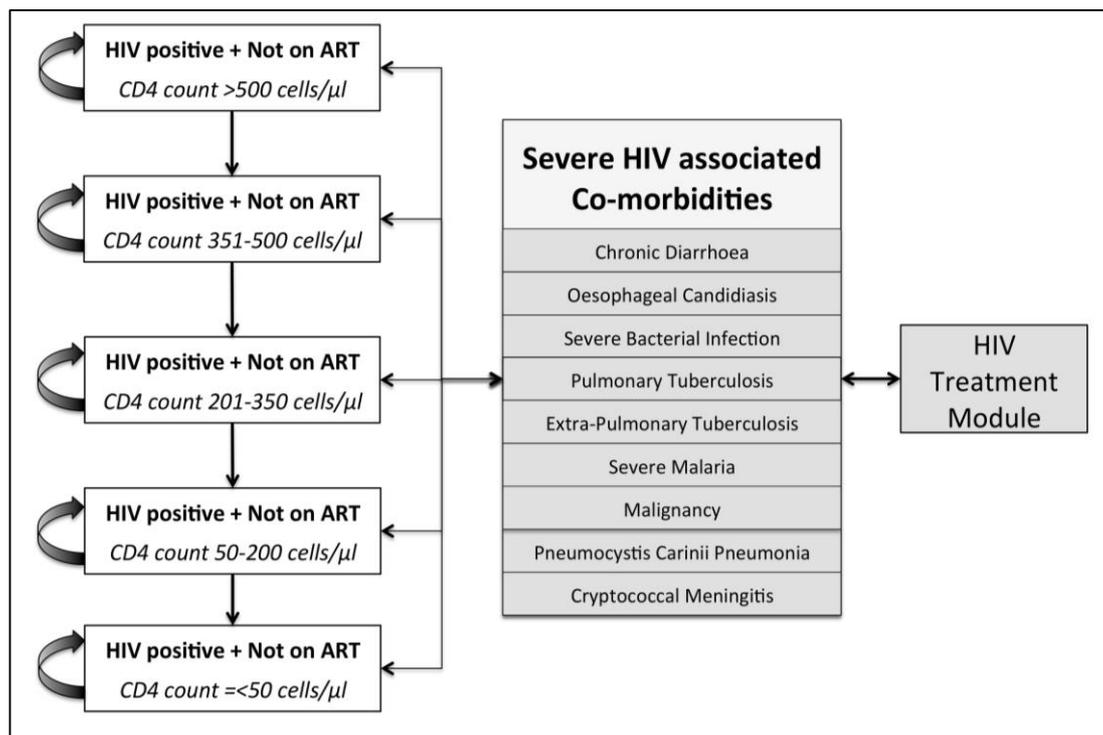
Every month individuals are also at risk of death and risk of suffering from one of the severe HIV associated co-morbidities. The risk of death and severe HIV associated co-

morbidities depends on their CD4 count. In the CD4 count defined health states individuals do not incur any costs, but their HRQoL changes.

If an individual suffers from one of the severe HIV associated co-morbidities, they temporarily transition into those health states incurring additional costs and changes in their health-related quality of life. As the findings in Chapter 7 highlights the majority of hospitalised patients undergo HTC, it was assumed that everyone has an HIV test. However, as I found very few subsequently initiated ART, I assumed everyone would be initiated onto ART if they attended the HIV clinic, and assumed the likelihood of linking into HIV care was comparable to the likelihood of linking into HIV care after facility-based HTC.

In the model there are nine health states representing the severe illnesses that HIV positive individuals are potentially at risk of and that result in hospitalisation (Chronic Diarrhoea; Oesophageal Candidiasis; Severe Bacterial infection; Pulmonary Tuberculosis; Extra-Pulmonary Tuberculosis; Severe Malaria; Malignancy; Pneumocystis Carinii Pneumonia; Cryptococcal meningitis).

Figure 58: Overview of HIV disease progression module



Every month HIV positive and HIV negative individuals may access HIV testing. HIVST is only available in the intervention strategy, whilst facility-based HTC is available in both strategies being investigated. Figure 59 shows the HIV testing and linkage module in the model. HIV negative individuals who access HIV testing will test HIV negative and therefore are not in need of linkage into HIV care. Individuals who test HIV negative are assumed to not re-test for another year in accordance with the WHO's HIV testing guidelines (WHO, 2015). In the HiTTB HIVST intervention, HIVST was only offered to individuals once a year (Choko et al., 2015a), and the model replicates this. HIV positive individuals who test may then link into HIV care or not link into HIV care. If they do not link into HIV care they return to the HIV disease

progression module. If they link into HIV care they enter the HIV treatment module (Figure 60).

Figure 59: Overview of HIV Testing and Linkage module

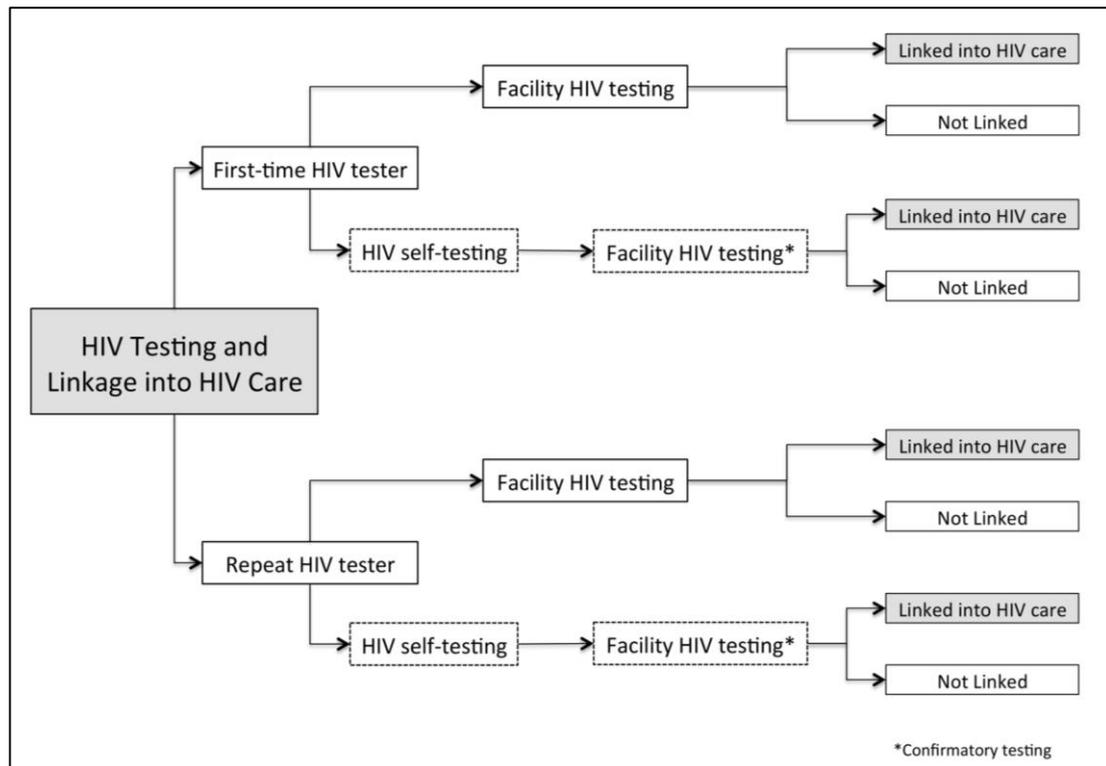


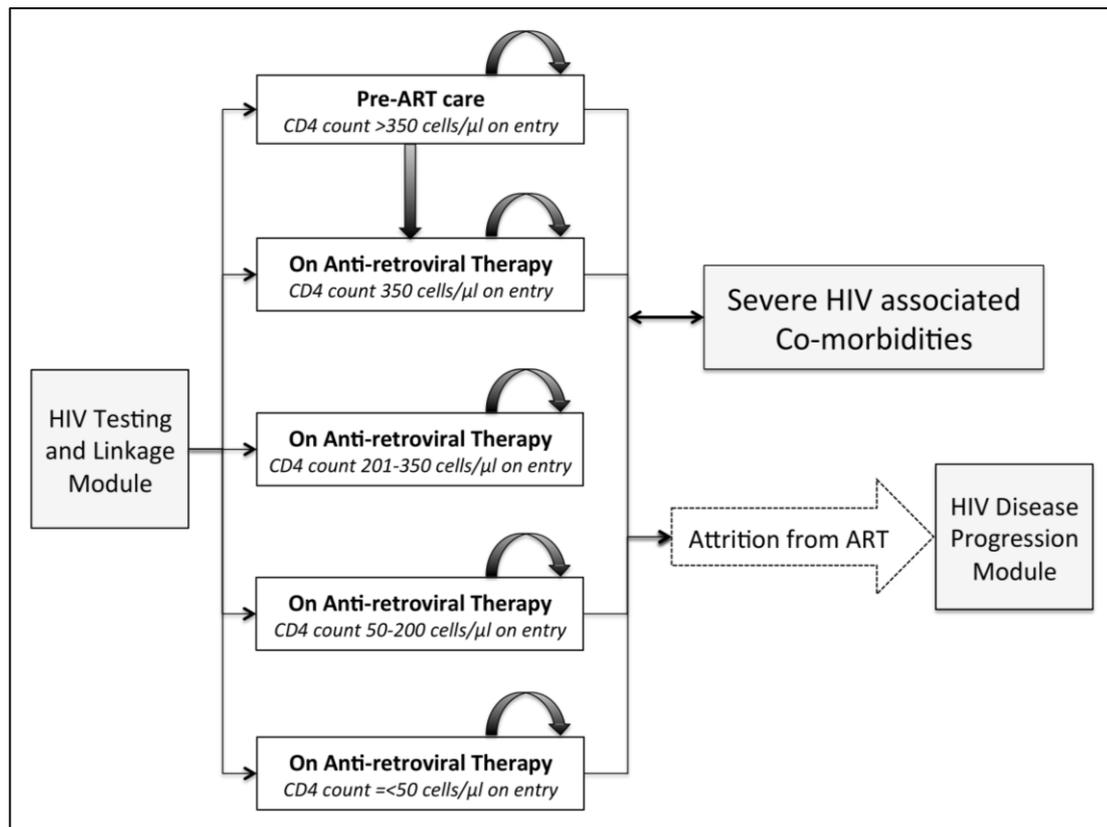
Figure 60 provides an overview of the HIV treatment module. Individuals who access HIV are assessed for eligibility for ART; this involves measuring their CD4 count and clinical assessment of their HIV disease stage. Individuals whose CD4 count is below 350 cells/ μ l are started onto anti-retroviral therapy. Individuals whose CD4 count is greater than 350 cells/ μ l and who have advanced HIV disease (WHO stage 3 or 4) are

started onto ART. Individuals whose CD4 counts are greater than 350 cells/ μ l but do not have advanced disease (WHO stage 3 or 4) enter pre-ART care.

As individuals access ART or pre-ART care they incur costs and their HRQoL may change. In addition, every month individuals are at risk of dying or not returning to continue with their HIV treatment. If they fail to return to continue their HIV treatment (attrition from ART) they re-enter the HIV disease progression module. Individuals on ART are also at risk of suffering from the nine severe HIV associated illnesses that result in hospitalisation.

There are four health states within the HIV treatment module, each defined by the CD4 count on entering HIV treatment. Whilst on treatment their CD4 count may increase and if it does the model updates their CD4 count. If they do not return to continue their HIV treatment, the updated CD4 count determines which health state in the HIV disease progression module they re-enter. The updated CD4 count determines the monthly risk of dying or from suffering one of the severe HIV associated illnesses. However, the CD4 count on entry into ART is used to determine the cost associated with HIV treatment and associated health-related quality of life (to reflect the primary data used in the model). Individuals who enter pre-ART may return for repeat assessment for ART eligibility, incurring additional cost, and potentially becoming eligible for treatment. As they are not on ART, their CD4 count is assumed to continue falling at the same rate.

Figure 60: Overview of HIV treatment module



8.2.3 Model parameters

8.2.3.1 Overview of model parameter synthesis

On entry into the model, the characteristics of the individuals' modeled (HIV status and CD4 count) were chosen to reflect the HitTB study population. At the time of submitting my PhD, the HitTB study was in the process of completing the post-intervention prevalence survey. The HitTB post-intervention prevalence survey was being undertaken in a randomly sampled population of both the intervention and control clusters, and is collecting data on HIV status, ART coverage and CD4 counts.

Once this data becomes available, some of the model parameters will be updated prior to publication of the cost-effectiveness findings.

I used primary data collected during the PhD (Chapters 5, 6 and 7) to define the costs and health utility scores for all the health states in the model. I undertook targeted literature reviews to synthesise transition parameters that were not available from the HitTB study or from primary studies undertaken as part of my PhD. I undertook the targeted literature searches in *Pubmed* and reviewed the references to determine the appropriateness of the data for this model. A targeted literature search provided an efficient approach to obtaining the relevant data (Moher et al., 2007). Where there was more than one data source found I used the inverse variance weight approach (fixed-effects meta-analysis) to pool the data to estimate a weighted mean and standard error of the weighted mean for parameter inputs. The data extracted were all converted to monthly transition probabilities (Briggs et al., 2006).

The primary analysis involves a probabilistic sensitivity analysis and therefore probability distributions were fitted to the parameters used in the model to reflect the underlying uncertainty in the estimates (Briggs et al., 2012b). The beta distribution was fitted to transition probabilities and health state utilities, and the gamma distribution for costs (Briggs et al., 2006). For the mean monthly decline in CD4 count I fitted the normal distribution. To fit the beta distribution, either the

primary observed data (numbers experiencing the event and not experiencing the event) was used to determine the alpha (events) and beta (non-events) values, or the method of moments was used estimate the alpha and beta values from the mean and standard errors (Briggs et al., 2006). The method of moments approach was also used to determine the alpha and beta values to fit the gamma distribution for the cost parameters (Briggs et al., 2006). To fit the normal distribution the mean and standard error was used. When primary data from outputs of a multivariable analysis was used, I took into account the covariance between regression coefficients in determining the standard errors (Briggs et al., 2006, Briggs et al., 2012b).

Table 62 to Table 67 show the parameters used in the primary analysis. The low and high values reflect the 95% confidence intervals (CIs) for the parameters in the model, and are provided for transparency in the data utilised and replication of model analysis (Briggs et al., 2012b, Eddy et al., 2012). The 95% CIs are presented for ease of understanding parameters used, and reflect either the primary data, or are from 5000 simulations of the applied probability distributions. The following sections provide a more detailed description of how the model parameters were obtained.

8.2.3.2 Initial characteristics of individuals modeled.

The impact of HIV testing is only on those who are HIV negative and on those who are HIV positive and not on ART. Therefore on model entry individuals are assigned

one of two health states (HIV negative; HIV positive not on ART). The proportion of those already on ART was not taken into account, as it does not impact on the proportion of those who are HIV negative (see equations below). I used the HIV prevalence observed in the Blantyre study population (Choko et al., 2011) to determine the likelihood of which of these two health states to assign an individual to.

$$p_{HIV\ negative} = 1 - (p_{HIV\ positive} * (1 - p_{OnART})) - (p_{HIV\ positive} * p_{OnART})$$

$$p_{HIV\ negative} = 1 - p_{HIV\ positive} + p_{HIV\ positive} * p_{OnART} - p_{HIV\ positive} * p_{OnART}$$

$$= 1 - p_{HIV\ positive}$$

A targeted literature search was undertaken to identify the appropriate parameter values to determine the CD4 count of HIV positive individuals living in sub-Saharan Africa not yet receiving ART (Table 68). A previous literature review and modeling study had been undertaken in 2006 that investigated the CD4 counts of populations in HIV prevalent countries in sub-Saharan Africa (Williams et al., 2006). These studies were excluded as the large-scale introduction of anti-retroviral therapy at the population level will impact on the CD4 count distribution amongst HIV positive individuals not on ART as those with lower CD4 counts are more likely to be receiving treatment. Three studies were identified that investigated the CD4 count amongst a randomly sampled population in a sub-Saharan African country (Kranzer et al., 2013, Maman et al., 2015, Malaza et al., 2013). The data presented in these studies were

incomplete and therefore the authors of the studies were contacted; data was subsequently obtained from only one study (Kranzer et al., 2013). This data was used to determine whether individuals had a: CD4 count >500 cells/ μ l; CD4 count 351-500 cells/ μ l; CD4 count 201-350 cells/ μ l; CD4 count 51-200 cells/ μ l; or CD4 count \leq 50 cells/ μ l; on entry into the model. The CD4 count assigned to individuals was randomly chosen between these ranges. Table 62 shows the parameters used to determine the initial characteristics of individuals modeled.

8.2.3.3 Transition probabilities

8.2.3.3.1 HIV incidence

Evidence from the literature highlights that the risk of an HIV positive individual transmitting their infection to uninfected individuals (predominantly through unprotected sexual contact in sub-Saharan Africa) depends mainly on the stage of their infection (Powers et al., 2011b), gender (Glynn et al., 2001), whether circumcised (Gray et al., 2007a) and whether on anti-retroviral therapy (Cohen et al., 2011). The model was a static model and therefore does not take into account the changing risk of HIV negative individuals acquiring HIV infection through increased population ART coverage (Granich et al., 2009). I therefore undertook a targeted search of the literature to identify studies that have estimated the HIV incidence in African population since the introduction of ART (Table 68).

Of the nine studies identified, one study was undertaken before or in the early stages of scale-up of ART in Africa (Rehle et al., 2010) and another study undertaken in a population sub-group (women) and not representative of the general population (Karim et al., 2011). One study was a systematic review of 12 modeling studies investigating impact of ART on HIV incidence (Eaton et al., 2012), with a further five modeling studies identified that were undertaken after the publication of the systematic review (Alsallaq et al., 2013, Mossong et al., 2013, Cori et al., 2014, Shafer et al., 2014, Murray et al., 2014). One study was an observation study undertaken in a cohort of 16,667 HIV negative individuals in South Africa and examined risk of HIV infection during a period of comparable ART coverage to Malawi (Table 63) (Tanser et al., 2013).

8.2.3.3.2 Changes in CD4 counts amongst those not on ART

I undertook targeted literature searches to obtain the necessary data to quantify the monthly decrements in individuals' CD4 counts, the risk of suffering from one of the nine severe HIV-associated co-morbidities and the risk of death at differing CD4 counts (Table 68).

The evidence in the literature suggests that the CD4 count falls rapidly after HIV seroconversion and then decreases linearly over time (Williams et al., 2006). On searching the literature I found seven studies describing changes in CD4 counts in HIV positive individuals living in Africa who had not started ART. One study only

provided a description of modeling approaches to estimate changes in CD4 counts (Williams et al., 2006) and two studies provided mean changes in CD4 counts for the entire sample not disaggregated by CD4 count strata (Mbotto et al., 2009, Katubulushi et al., 2005). Consequently the data from these three studies were not utilised. One study investigated the time from HIV infection to the CD4 count falling below 500 cells/ μ l (Lodi et al., 2011) and three studies provided relevant information on changes in CD4 counts (Martinson et al., 2014, May et al., 2009, Holmes et al., 2006). The data provided in the three studies (Martinson et al., 2014, May et al., 2009, Holmes et al., 2006) were pooled using inverse variance weight (Sutton et al., 2000) to determine monthly decrements in CD4 counts (Table 63).

8.2.3.2.3 Risk of mortality and HIV associated co-morbidities

A targeted literature search revealed four studies that investigated mortality amongst HIV positive individuals before starting anti-retroviral therapy by their CD4 count (Anglaret et al., 2012, Badri et al., 2006a, Jaffar et al., 2004, Geng et al., 2013). Only one study provided detailed mortality rates disaggregated by the multiple CD4 count strata used in the model (Anglaret et al., 2012). The data used to model the risk of death for those on ART are shown in Table 63. For the risks of co-morbidities two studies were found in the literature (Anglaret et al., 2012, Holmes et al., 2006), with one providing the detailed risks of illnesses by CD4 counts (Anglaret et al., 2012). In addition this study was also used to determine HIV associated mortality and the risk of progression to WHO stage 3 or 4 amongst HIV positive individuals (Anglaret et al., 2012). The parameters used in the model to estimate the risk of HIV associated

co-morbidities and overall likelihood of progression to WHO stage 3 or 4 estimated from this study is shown in Table 64. I did not apply distributions (for the PSA) for the risk of these events. For readability (as the risks are very low) I have provided the monthly probability used in the model as percentages.

Four published studies were found that estimated the mortality rate amongst adults in Malawi from non-HIV associated reasons (Jahn et al., 2008, Streatfield et al., 2014, Glynn et al., 2014, Chihana et al., 2012). All these studies were undertaken in the Karonga district in Malawi where a large sample of the community is actively followed as part of a demographic surveillance site. The data presented in the studies are all from the same source and therefore the most recent data and the data that allowed estimation of non-HIV associated mortality rate was used (Chihana et al., 2012).

8.2.3.2.3 Uptake of HIV testing and linkage

The Malawian HIV programme data was used to determine likelihood of accessing facility-based HTC (MoH, 2014). For the intervention strategy, the likelihood of accessing HIVST was based on observed data from the HiTTB study (Choko et al., 2015a). The model recorded when individuals had accessed either modality of HIV testing. Chapter 5 of the PhD thesis suggested that HIVST is complimentary to facility-based HTC; I assumed that individuals might access either modality of HIV testing.

A prospective cohort study was undertaken in the two main health facilities serving the HitTB study population before the introduction of HIVST (MacPherson et al., 2012a). The study estimated the proportion of facility-based HIV testers linking into HIV care, and consequently this data was used to estimate the probability of linkage after facility-based HTC. Of note a systematic review was recently undertaken that estimated linkage into HIV care after facility-based HTC in sub-Saharan Africa (Rosen and Fox, 2011). In the review, they estimated approximately 59% (range 35% to 88%) of facility-based HIV testers linked to the HIV clinic for assessment for ART eligibility (Rosen and Fox, 2011), comparable to the estimate from the study in Malawi (MacPherson et al., 2012a).

The probability of linking into HIV care after HIVST was based on observed data from the HiTTB study (Choko et al., 2015a). In that study, which I co-authored, there were two estimates of linkage into HIV care after HIVST. The first estimate (524 of the 930 sampled individuals linked into HIV care) excluded those who were already on anti-retroviral therapy. The second estimate (524 of the 1257 sampled individuals linked into HIV care) included those already on ART. As the model simulates linkage after HIV positive individuals not on ART access HIVST, I used the first estimate in the base-case analysis (Table 63) and investigate the impact of a lower rate of linkage (the second estimate) in the sensitivity analysis.

8.2.3.2.4 Outcomes of HIV care

I undertook a targeted literature search to identify studies that had investigated retention in care amongst those who are not eligible for ART. In the literature a systematic review of this topic had recently been published (Plazy et al., 2015). I reviewed the papers in the review (Clouse et al., 2013, Hassan et al., 2012, Honge et al., 2013, Kranzer et al., 2010, Lessells et al., 2011, Namusobya et al., 2013), excluding those undertaken amongst pregnant women. Two additional papers not included in the review were found (Geng et al., 2013, Larson et al., 2010) to obtain the probability of individuals in pre-ART care returning for repeat assessment for ART eligibility.

Since the population scale-up of anti-retroviral therapy in the region, large cohorts of individuals in different countries in sub-Saharan Africa have been followed up as part of the International Epidemiologic Databases to Evaluate AIDS (IeDEA) collaboration (formerly called ART-Linc) (IeDEA, no date). The collaboration has published several publications on the outcomes of HIV positive individuals on ART. The publications will often use the same cohorts, with longer follow-up, to provide an updated understanding of outcomes for ART patients. Their database of publications relating to Southern Africa was reviewed to obtain the most recent publication (relating to the most recent data), with the longest follow-up and with data on mortality disaggregated by CD4 count.

The data obtained to estimate the probability of death by CD4 count was obtained from one of the studies undertaken using multiple cohorts in South Africa (Hoffmann et al., 2013). The study excluded pregnant women and provided data on the risks on mortality in the first three years after starting ART disaggregated by the current CD4 count (Hoffmann et al., 2013). In addition, the study estimated the increase in CD4 count whilst on ART (Hoffmann et al., 2013). A recent systematic review and meta-analysis was found in the literature that examined the retention rates in HIV treatment for those who initiated ART (Fox and Rosen, 2010). The data was used to estimate the monthly probability of loss to follow-up from HIV treatment (Table 63).

A literature search did not reveal any studies that provided the risks of severe HIV associated illnesses by CD4 counts for those started on ART. However, a study in South Africa compared the risk of hospitalisations amongst those on ART and those not on ART (Badri et al., 2006b). The study provided odds ratios for the risk of hospitalisations amongst HIV positive patients on ART relative to HIV positive patients not receiving ART. I therefore multiplied the derived probability from the odds ratios (Table 63) by the associated risks estimated for those not on ART (Table 64) to determine likelihood of being admitted to hospital for the nine severe HIV-associated illnesses in the model.

The model does not take into account the impact of ART treatment failure amongst HIV positive individuals on ART. A recent analysis of HIV positive patients on anti-

retroviral therapy in 16 countries in sub-Saharan Africa, with a total of 297 825 patients with 782 412 person-years of follow-up, found only 3% switched to a second-line anti-retroviral therapy regimen (Haas et al., 2015).

8.2.3.4 Health provider and societal costs

All cost estimates used in the model were derived from the primary studies undertaken as part of the PhD. The cost of facility-based HTC and HIVST were derived from the study undertaken in chapter 5 of the PhD. The cost of assessing individuals for ART eligibility and the cost of providing ART were derived from Chapter 6 of the PhD.

The cost of hospitalisation for the nine severe HIV associated illnesses modeled in the cost-utility analysis were derived from Chapter 7 of the PhD. Table 65 shows the cost parameters (in 2014 US and INT Dollars) used in the model for analysis from the health provider perspective. Table 66 shows the cost parameters used in the model for analysis from the societal perspective.

8.2.3.5 Health state utility scores

The health utility scores for the health states in the model were derived from the studies undertaken in the PhD. The utility score for the HIV positive individuals not yet on ART were derived from the pre-ART observation period in the study

undertaken in Chapter 6 of the PhD. The health utility scores for those who start ART and the change in utility scores with time on ART were derived from the ART observation period in the study undertaken in Chapter 6 of the PhD.

The health utility scores for those who suffered from one of the nine severe HIV associated illnesses were derived from Chapter 7 of the PhD. Table 67 shows the utility parameters, derived from the EQ-5D measure using the Zimbabwean tariff, that were used in the primary analysis.

Table 62: Parameters used to determine baseline characteristics of individuals in model

		Parameters to determine Individual characteristics on entry into model				
		Base case	Low	High	Distribution	Reference
HIV Prevalence		0.185	0.140	0.234	Beta	(Choko et al., 2011)
CD4 count on entry into model amongst HIV positive individuals	>500 cells/ μ l	0.363	0.292	0.439	Beta	(Kranzer et al., 2013)
	351-500 cells/ μ l	0.244	0.182	0.312	Beta	
	201-350 cells/ μ l	0.263	0.201	0.332	Beat	
	51-200 cells/ μ l	0.107	0.065	0.157	Beat	
	=< 50 cells/ μ l	0.024	0.006	0.051	Beat	

Table 63: Monthly transition probabilities in model

Parameter	Parameter Values			Distribution	Reference
	Base case	Low	High		
HIV incidence		0.00219	0.00208	0.00231	Beta (Tanser et al., 2013)
Probability of CD4 count falling to 500 cells/μl		0.011	0.009	0.011	Beta (Lodi et al., 2011)
Monthly fall in CD4 count (cells/μl)	351-500 cells/ μ l	2.37	2.12	2.61	Normal (Martinson et al., 2014, May et al., 2009, Holmes et al., 2006)
	201-350 cells/ μ l	1.74	1.45	2.03	
	51-200 cells/ μ l	4.42	3.98	4.86	
Mortality for HIV positive and not on ART	>500 cells/ μ l	0.0005	0.0001	0.0017	Beta (Anglaret et al., 2012)
	350-500 cells/ μ l	0.0013	0.0007	0.0025	
	200-349 cells/ μ l	0.0035	0.0023	0.0047	
	100-199 cells/ μ l	0.0142	0.0109	0.0177	
	50-99 cells/ μ l	0.0266	0.0219	0.0394	
	<50 cells/ μ l	0.0563	0.0454	0.0670	
Uptake of Facility-based HIV Testing and counselling		0.0256	0.0254	0.0257	Beta (MoH, 2014)
Uptake of HIV Self-testing		0.143	0.138	0.149	Beta (Choko et al., 2015a)
Linkage into HIV care	Facility-based HTC	0.5070	0.4505	0.5642	Beta (MacPherson et al., 2012a)
	HIV self-testing	0.5633	0.5322	0.5945	Beta (Choko et al., 2015a)
Retention in care for Pre-ART		0.57	0.56	0.58	Beta (Clouse et al., 2013, Geng et al., 2013, Hassan et al., 2012, Honge et al., 2013, Kranzer et al., 2010, Larson et al., 2010, Lessells et al., 2011, Namusobya et al., 2013, Plazy et al., 2015)
Mortality on ART by CD4 count on initiation of treatment	>350 cells/ μ l	0.00117	0.00101	0.00133	Beta (Hoffmann et al., 2013)
	201-350 cells/ μ l	0.00208	0.00188	0.00229	
	101-200 cells/ μ l	0.00416	0.00387	0.00446	
	\leq 100 cells/ μ l	0.01159	0.01119	0.01200	
Weekly increase in CD4 count on ART (cells/μl)		1.3	1.1	1.5	Normal (Hoffmann et al., 2013)
Lost to follow-up from ART	Months 0 to 6	0.0246	0.0222	0.0275	Beta (Fox and Rosen, 2010)
	Months 7 to 12	0.0101	0.0085	0.0113	
	Months 13 to 24	0.0035	0.0023	0.0048	
	After month 24	0.0032	0.0024	0.0043	
Probability multiplier for risk Severe HIV associated illness on ART		0.2248	0.1870	0.2647	Beta (Badri et al., 2006b)

Table 64: Monthly risk of Severe HIV associated illness and HIV disease progression by current CD4 count

	Monthly risk by current CD4 count						Ref
	>500 cells/ μ l	350-500 cells/ μ l	200-349 cells/ μ l	100-199 cells/ μ l	50-99 cells/ μ l	<50 cells/ μ l	
Chronic Diarrhoea	0.00%	0.00%	0.01%	0.03%	0.10%	0.18%	
Oesophageal candidiasis	0.00%	0.00%	0.01%	0.03%	0.10%	0.17%	
Invasive bacterial diseases	0.20%	0.18%	0.52%	0.97%	1.07%	0.96%	(Anglaret et al., 2012)
Pulmonary TB	0.03%	0.03%	0.11%	0.26%	0.40%	0.13%	
Extra-pulmonary TB	0.02%	0.02%	0.10%	0.09%	0.16%	0.09%	
Malaria	0.09%	0.14%	0.19%	0.26%	0.30%	0.40%	
Malignancy (KS/Lymphoma)	0.00%	0.00%	0.01%	0.01%	0.03%	0.05%	
Pneumocystis Pneumonia	0.00%	0.00%	0.03%	0.05%	0.05%	0.67%	
Cryptococcal Meningitis	0.00%	0.00%	0.03%	0.04%	0.18%	0.54%	
Overall monthly progression to WHO stage 3	0.61%	0.66%	-	-	-	-	(Anglaret et al., 2012)
Overall monthly progression to WHO stage 4	0.02%	0.12%	-	-	-	-	

Table 65: Health provider costs for model (2014 US and INT Dollars)

Cost Parameter	Health Provider Costs						Distribution	
	2014 US Dollars			2014 INT Dollars				
	Base case	Low	High	Base case	Low	High		
HIV testing at Health Facility	8.90	7.53	10.57	20.44	20.25	25.18	Gamma	
HIV self-testing	8.78	7.78	10.46	17.25	14.25	22.42		
Assessment for ART eligibility after facility HTC (CD4 >350 cells/μl)	31.91	26.10	33.44	80.77	26.10	33.44		
Assessment for ART eligibility after facility HTC (CD4 <350 cells/μl)	22.03	19.85	24.22	59.79	54.34	65.24		
Assessment for ART eligibility after HIVST (CD4 >350 cells/μl)	23.63	18.24	29.03	60.90	49.07	72.74		
Assessment for ART eligibility after HIVST (CD4 <350 cells/μl)	21.51	19.04	23.97	57.78	51.74	63.82		
HIV treatment: Month 1 after Facility HTC	19.51	17.71	21.31	33.03	28.78	37.28		
Cost of ART: Month 2 onwards after Facility HTC	14.41	13.17	15.65	19.22	16.53	21.91		
Cost of ART: Month 1 after HIVST	16.23	13.99	18.48	25.04	20.31	29.76		
Cost of ART: Month 2 onwards after HIVST	13.84	12.49	15.19	18.28	15.32	21.25		
Cost of hospital admission for severe HIV associated illness	Chronic Diarrhoea	233.06	99.08	367.04	609.07	243.19		974.94
	Oesophageal candidiasis	153.08	69.03	237.13	395.98	170.12		621.84
	Invasive bacterial diseases	226.88	203.64	250.13	591.03	529.02		653.05
	Pulmonary TB	438.99	341.45	536.53	1151.13	891.00		1411.25
	Extra-pulmonary TB	492.25	390.55	593.95	1288.55	1027.30	1549.79	
	Malaria	199.63	111.34	287.93	488.44	256.78	720.09	
	Malignancy (KS/Lymphoma)	243.35	195.28	291.41	638.36	517.23	759.49	
	Pneumocystis Pneumonia	325.92	270.34	381.50	850.35	700.83	999.88	
Cryptococcal Meningitis	837.92	651.27	1024.57	1568.22	1299.65	1836.79		

Table 66: Societal costs for model (2014 US and INT Dollars)

Cost Parameter	Societal Costs						Distribution	
	2014 US Dollars			2014 INT Dollars				
	Base case	Low	High	Base case	Low	High		
HIV testing at Health Facility	10.68	9.91	11.45	26.78	24.94	28.63	Gamma	
HIV self-testing	8.85	7.97	9.72	17.62	15.09	20.16		
Assessment for ART eligibility after facility HTC (CD4 >350 cells/μl)	36.27	30.52	42.02	92.44	78.50	106.39		
Assessment for ART eligibility after facility HTC (CD4 <350 cells/μl)	23.04	20.19	25.89	62.39	54.98	69.80		
Assessment for ART eligibility after HIVST (CD4 >350 cells/μl)	24.96	16.71	33.21	64.19	44.40	83.98		
Assessment for ART eligibility after HIVST (CD4 <350 cells/μl)	22.36	18.49	26.23	59.81	49.77	69.85		
Cost of ART: Month 1 after Facility HTC	21.40	19.10	23.69	38.26	32.49	44.03		
Cost of ART: Month 2 onwards after Facility HTC	14.39	12.84	15.95	19.17	15.46	22.88		
Cost of ART: Month 1 after HIVST	17.87	14.85	20.89	29.60	22.24	36.95		
Cost of ART: Month 2 onwards after HIVST	13.93	12.18	15.69	18.54	14.26	22.82		
Cost of hospital admission for severe HIV associated illness	Chronic Diarrhoea	260.90	117.88	403.93	686.42	288.95		1083.89
	Oesophageal candidiasis	178.94	57.65	300.24	467.81	149.47		786.16
	Invasive bacterial diseases	268.80	237.55	300.04	707.46	619.21		795.71
	Pulmonary TB	580.78	433.99	727.58	1545.00	1160.15		1929.85
	Extra-pulmonary TB	764.94	524.73	1005.14	2046.00	1400.56	2691.43	
	Malaria	358.45	53.43	663.47	929.60	137.93	1721.27	
	Malignancy (KS/Lymphoma)	317.45	241.01	393.89	844.20	638.28	1050.12	
	Pneumocystis Pneumonia	395.51	291.58	499.44	1043.65	761.95	1325.35	
Cryptococcal Meningitis	963.40	746.68	1180.12	1916.77	1541.48	2292.06		

Table 67: EQ-5D Utility scores for model (Zimbabwean and UK tariff)

Utility Parameters		Utility scores						Distribution
		Main analysis (Zimbabwean Tariff)			Sensitivity analysis (UK Tariff)			
		Base case	Low	High	Base case	Low	High	
HIV Negative individuals		1.000	1.000	1.000	1.000	1.000	1.000	Beta
HIV positive not on ART	CD4>200 cells/μl	0.897	0.816	0.977	0.855	0.737	0.973	
	CD4 51 to 200 cells/μl	0.850	0.768	0.931	0.796	0.676	0.916	
	CD4 count <=50 cells/μl	0.668	0.565	0.771	0.481	0.329	0.633	
Monthly improvement on Anti-retroviral therapy		0.008	0.007	0.010	0.011	0.009	0.012	
Hospital admission for severe HIV associated illness	Chronic Diarrhoea	0.476	0.318	0.634	0.213	0.036	0.466	
	Oesophageal candidiasis	0.349	0.168	0.530	0.073	0.001	0.282	
	Invasive bacterial diseases	0.495	0.454	0.536	0.283	0.224	0.343	
	Pulmonary TB	0.426	0.346	0.505	0.175	0.069	0.281	
	Extra-pulmonary TB	0.391	0.306	0.477	0.167	0.061	0.273	
	Malaria	0.567	0.411	0.722	0.403	0.205	0.602	
	Malignancy (KS/Lymphoma)	0.420	0.321	0.520	0.159	0.028	0.289	
	Pneumocystis Pneumonia	0.559	0.399	0.718	0.382	0.125	0.638	
Cryptococcal Meningitis	0.483	0.399	0.568	0.244	0.114	0.373		

Table 68: Targeted literature search findings for synthesis of parameters in model

HIV incidence	Search strategy	((HIV incidence[Title/Abstract]) AND Africa[Title/Abstract]) AND antiretroviral therapy
	Publications identified	44
	Relevant publications	9
Population CD4 count distribution	Search strategy	((HIV[Title/Abstract]) AND CD4[Title/Abstract]) AND Africa[Title/Abstract]
	Total references	1802
	Relevant publications	4
CD4 count decline	Search strategy	((HIV[Title/Abstract]) AND CD4[Title/Abstract]) AND Africa[Title/Abstract]
	Total references	1802
	Relevant publications	7
HIV mortality before starting anti-retroviral therapy	Search strategy	((HIV[Title/Abstract]) AND Africa[Title/Abstract]) AND death[Title/Abstract]
	Total references	1182
	Relevant publications	4

8.2.4 Model validation

The model was validated using three broad approaches: (1) face validity; (2) model verification; and (3) external validity (Eddy et al., 2012). The face validity of the model was undertaken by reviewing the literature around economic evaluation of HIV interventions (Chapter 4 of PhD) to determine best practices and approaches to modeling HIV interventions. Discussion with experts in the field of HIV were undertaken to determine appropriate clinical pathways for HIV disease progression and outcomes of undergoing HIV testing and HIV treatment.

I undertook model verification and examined the external validity of the model by examining components of the model and comparing outputs from the model with findings in the literature. I evaluated the model predicted uptake of both facility HTC and HIVST, and the HIV prevalence amongst HIV testers to findings from the HiTTB study and published findings from the region. I compared the model outputs pertaining to linkage into HIV treatment and outcomes of those on HIV treatment to previous studies to ensure the calculations being undertaken in the model reflect real world findings. Model verification was also used to make modifications to the model structure and pathways in the model (Briggs et al., 2012b). As previously mentioned the model verification will be repeated once the observed findings from the HiTTB study become available. This will allow the model to be calibrated to reflect the outcomes of the HiTTB study. The findings were not available at the time of PhD submission, but will be utilised prior to publication of findings in peer-reviewed journals.

8.2.5 Sensitivity analysis

A range of sensitivity analyses was undertaken to evaluate the effects of alternative plausible parameter input on the findings of the model. I undertook sensitivity analyses to evaluate the impact on alternative model parameter values on the primary outcome, namely the incremental cost-effectiveness ratio (ICER). The range of sensitivity analyses undertaken included:

- I. Utilising the EQ-5D utility scores derived from the UK tariff set (data shown in Table 67).
- II. Alternative discount rates: *0% and 6%* (WHO, 2003a)
- III. Lower HIV prevalence: *10% and 5%*
- IV. Higher cost of providing HIVST: *50% higher; 25% lower; 50% lower*
- V. Lower rates of linkage into HIV treatment after HIVST: *50% lower*
- VI. Lower cost of providing HIV treatment: *25% lower*
- VII. Impact of rate of HIV disease progression (measured by CD4 count) for those not yet receiving ART: *50% faster and 50% slower monthly rate of decline*
- VIII. Lower uptake of HIVST in those who are HIV positive but not yet aware of their infection: *20% lower uptake*

8.2.6 Alternative model scenarios

The WHO now recommends that HIV positive individuals are started onto ART when their CD4 count falls to 500 cells/ μ l (WHO, 2014). The Malawian MoH has not yet adopted this practice, and during the HitTB study individuals were started onto ART when their CD4 count fell below 350 cells/ μ l (or WHO stage 3 or 4). In addition, there is emerging evidence that suggest HIV positive individuals would benefit with initiation of ART as soon as they are aware of their HIV status (Group, 2015a, Group, 2015b). As either of these changes may soon become practice, I evaluated the cost-effectiveness of offering HIVST in addition to facility-based HTC under these scenarios (Table 69).

Table 69: Alternative model scenarios evaluated

Current scenario	Facility HTC + ART initiation at CD4 350 cells/μl or WHO stage 3 or 4
Alternative scenario	Facility HTC + ART initiation at CD4 500 cells/ μ l or WHO stage 3 or 4
	Facility HTC + Immediate ART initiation
	HIVST + Facility HTC + ART initiation at CD4 350 cells/μl or WHO stage 3 or 4
	HIVST + Facility HTC + ART initiation at CD4 500 cells/ μ l or WHO stage 3 or 4
	HIVST + Facility HTC + Immediate ART initiation

8.2.6 Decision rules

The WHO suggests that interventions where the ICER is less than the GDP per capita should be interpreted as *very cost-effective*, whilst interventions that are less than three times the GDP per capita should be interpreted as *cost-effective* (WHO, 2001, WHO, 2003a). The World Bank estimates for the GDP per capita in Malawi is approximately \$250. These decision rules were applied in my analyses.

8.3 Results

8.3.1 Findings from model validation

Table 70 and Table 71 show the findings from the model validation checks. Table 70 shows that in the model simulations, the proportion of the total population who access facility-based HTC over the first three years was 22.9% to 28.1%, and comparable to that observed in the study population prior to implementing HIV self-testing (22.6%). In the model simulations, the uptake of HIVST in the model over the first year (77.4%) was comparable to that observed in the HiTTB HIV self-testing study (76.5%). The uptake of HIVST in the model simulations over the subsequent years were higher than that observed in the HiTTB HIV self-testing study. The model simulation shows the HIV prevalence amongst facility HTC clients was comparable to that observed in the study population. In the model simulation, the HIV prevalence amongst HIV self-testers was higher than that observed in the HiTTB study.

Table 71 shows the model validation checks on the CD4 count at initiation of antiretroviral therapy simulated by the model and that observed in the real world. The model predicts the CD4 count of facility HIV testers and HIV self-testers that link into HIV treatment services to be marginally higher than that observed in Blantyre, and in the HiTTB study.

Table 70: Findings from model validation for outcomes of offering HIV testing

Findings from model simulation		Data from Blantyre, Malawi	
		Study	Observed data
Annual uptake of Facility HTC (Current strategy)	Year 1: 28.1% Year 2: 23.4% Year 3: 22.9%	Choko et al (2011)	22.6%
Proportion of population ever tested (Current strategy)	After Year 1: 28.1% After Year 2: 51.0% After Year 3: 58.8%	Choko et al (2011) MacPherson et al (2012)	61.8% (Population) 37.1% (HTC clients)
Population uptake of HIVST (Intervention strategy)	Year 1: 77.4% Year 2: 58.4% Year 3: 51.6%	Choko et al (2015)	Year 1: 76.5% Year 2: 74.4%
HIV prevalence amongst Facility HTC (Current Strategy)	Year 1: 18.8% Year 2: 20.1% Year 3: 20.7%	MacPherson et al (2012)	18.5%
HIV prevalence amongst HIVST (Intervention strategy)	Year 1: 18.4% Year 2: 12.0% Year 3: 12.3%	Choko et al (2015)	Year 1: 10.1% to 11.8% Year 2: 6.8% to 7.3%
CD4 count amongst Facility HTC Clients at ART assessment (Current Strategy)	Median: 417 cells/ μ l Mean: 369 cells/ μ l	MacPherson et al (2012)	Median: 294 cells/ μ l (All) Median: 240 cells/ μ l (men and non-pregnant women)
CD4 count amongst HIVST Clients at ART assessment (Intervention strategy)	Median: 445 cells/ μ l Mean: 388 cells/ μ l	Choko et al (2015)	Median: 250 cells/ μ l
Proportion of HIV positive Facility HTC clients starting ART (Current Strategy)	Year 1: 22.8% Year 2: 22.3% Year 3: 21.3%	MacPherson et al (2012)	31.1%
Proportion of HIV positive HIVST clients starting ART (Intervention strategy)	Year 1: 26.2% Year 2: 13.1% Year 3: 9.9%	Choko et al (2015)	29.6% (HIVST clients attended clinic and had CD4 count <350 cells μ l)

Table 71: Findings from model validation for outcomes on Anti-retroviral therapy

CD4 count at ART initiation	Percentage of those Initiated who die in the first year	
	Model simulation	Observed data (May et al., 2010b)
>=200 cells/ μ l	2.3%	5.1%
100-199 cells/ μ l	7.3%	5.5%
50-99 cells/ μ l	13.6%	8.7%
25-49 cells/ μ l	20.7%	16.6%
<25 cells/ μ l	16.4%	21.4%

8.3.2 Primary findings

Table 72 shows the discounted costs in 2014 US dollars, effectiveness estimate and ICER estimate of offering HIVST and facility-based HTC versus offering just facility-based HTC over a 20-year time horizon (primary analysis).

The projected mean discounted incremental cost per person over the 20-year time horizon from implementing HIVST was US\$167.03 and US\$175.14 from the health provider perspective and societal perspectives, respectively. The model estimated a mean discounted health gain of 0.53 QALYs per person over the 20-year time horizon. When the model was run over a 20-year time horizon the ICER from the health provider perspective was US\$316.18 per QALY gained. The ICER from the societal perspective was US\$332.05 per QALY gained. Table 73 shows the findings when the costs were estimated in 2014 International Dollars.

Figure 61 **and** Figure 62 shows the cost-effectiveness plane for the model simulations from the health provider and societal perspective, respectively. Figure 63 **and** Figure 64 shows the cost-effectiveness acceptability curves (CEAC) for the primary analysis from the health provider and societal perspective, respectively. At a willingness to pay (WTP) threshold of three times the GDP for Malawi (<US\$750 per gain in QALY), the intervention would be considered cost-effective from both the health provider and societal perspectives.

The model predicts the probability of the intervention being cost-effective at a WTP threshold of US\$ 250 per gain in QALY to be 0.09 and 0.08 from the health provider and societal perspectives, respectively. The CEAC shows that all model simulations predict the ICER to be below US\$670 from the health provider perspective, and below US\$610 from the societal perspective.

Table 72: Cost-effectiveness findings from primary analysis (2014 US Dollars)

Perspective	Strategy	Discounted Mean costs and QALYS per person				ICER (2014 US\$ per QALY)
		2014 US Dollars		QALYs		
		Mean Cost	Incremental cost	Mean Effectiveness	Incremental Effectiveness	
Health Provider	Facility HTC	435.34	-	13.85	-	316.18
	HIVST + Facility HTC	602.36	167.03	14.38	0.53	
Societal	Facility HTC	491.68	-	13.85	-	332.05
	HIVST + Facility HTC	666.82	175.14	14.38	0.53	

Table 73: Cost-effectiveness findings from primary analysis (2014 INT Dollars)

Perspective	Strategy	Discounted Mean costs and QALYS per person				ICER (2014 INT\$ per QALY)
		2014 INT Dollars		QALYs		
		Mean Cost	Incremental cost	Mean Effectiveness	Incremental Effectiveness	
Health Provider	Facility HTC	811.64	-	13.85	-	502.36
	HIVST + Facility HTC	1077.89		14.38	0.53	
Societal	Facility HTC	976.09	-	13.85	-	549.06
	HIVST + Facility HTC	1265.03	288.94	14.38	0.53	

Figure 61: Cost-effectiveness plane showing incremental costs and effectiveness of offering HIVST (Health provider perspective)

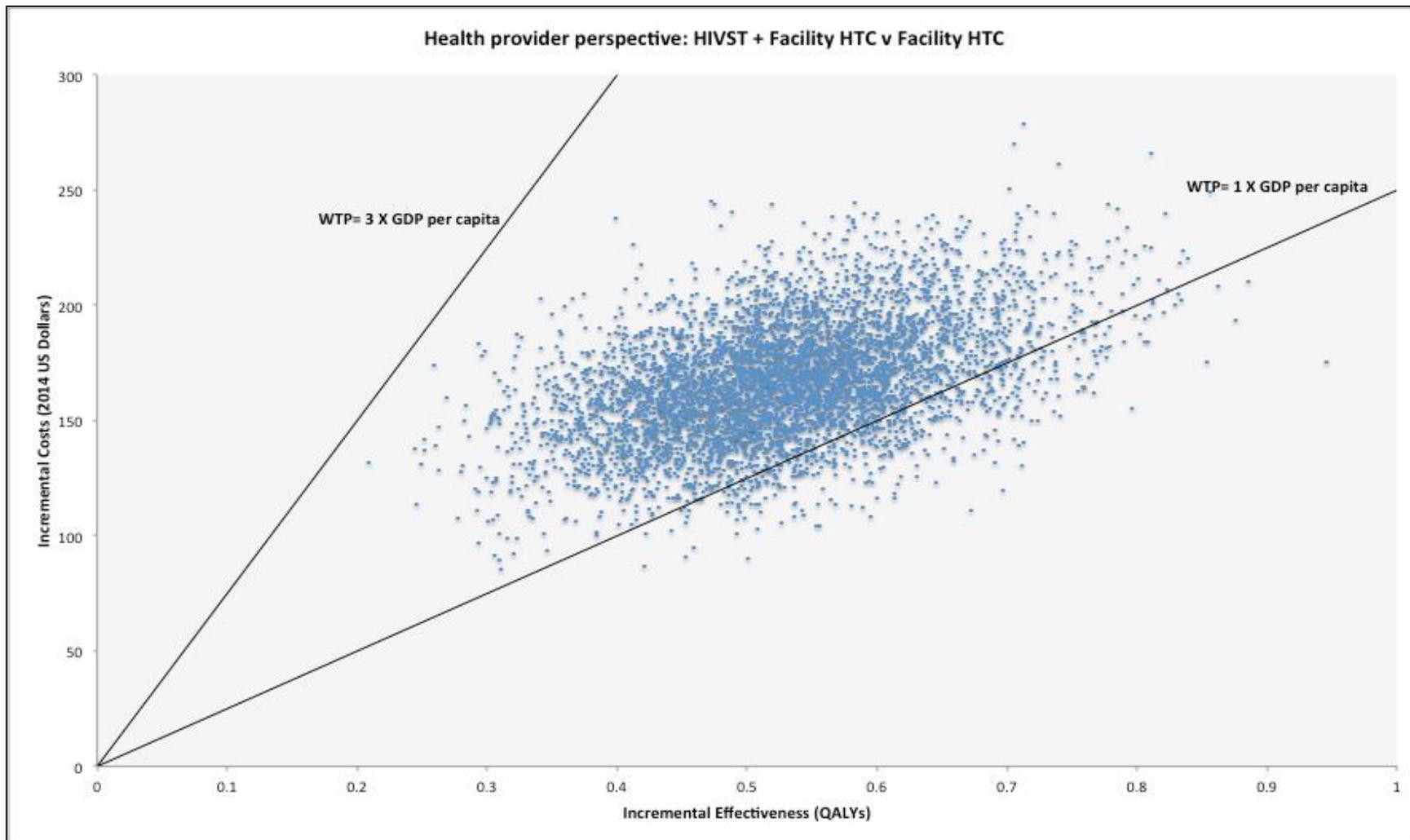


Figure 62: Cost-effectiveness plane showing incremental costs and effectiveness of offering HIVST (Societal perspective)

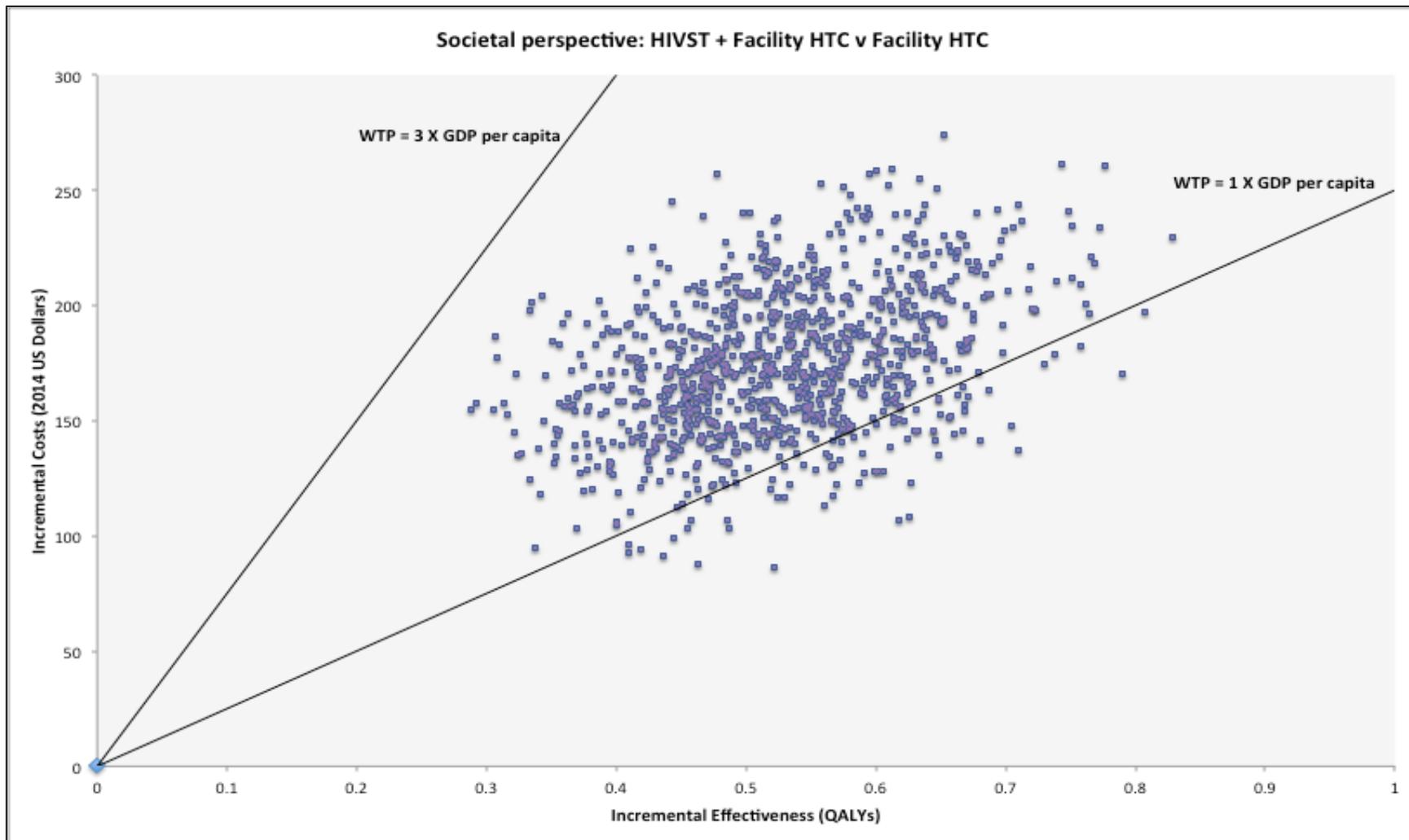


Figure 63: Cost-effectiveness acceptability curve – Health provider perspective

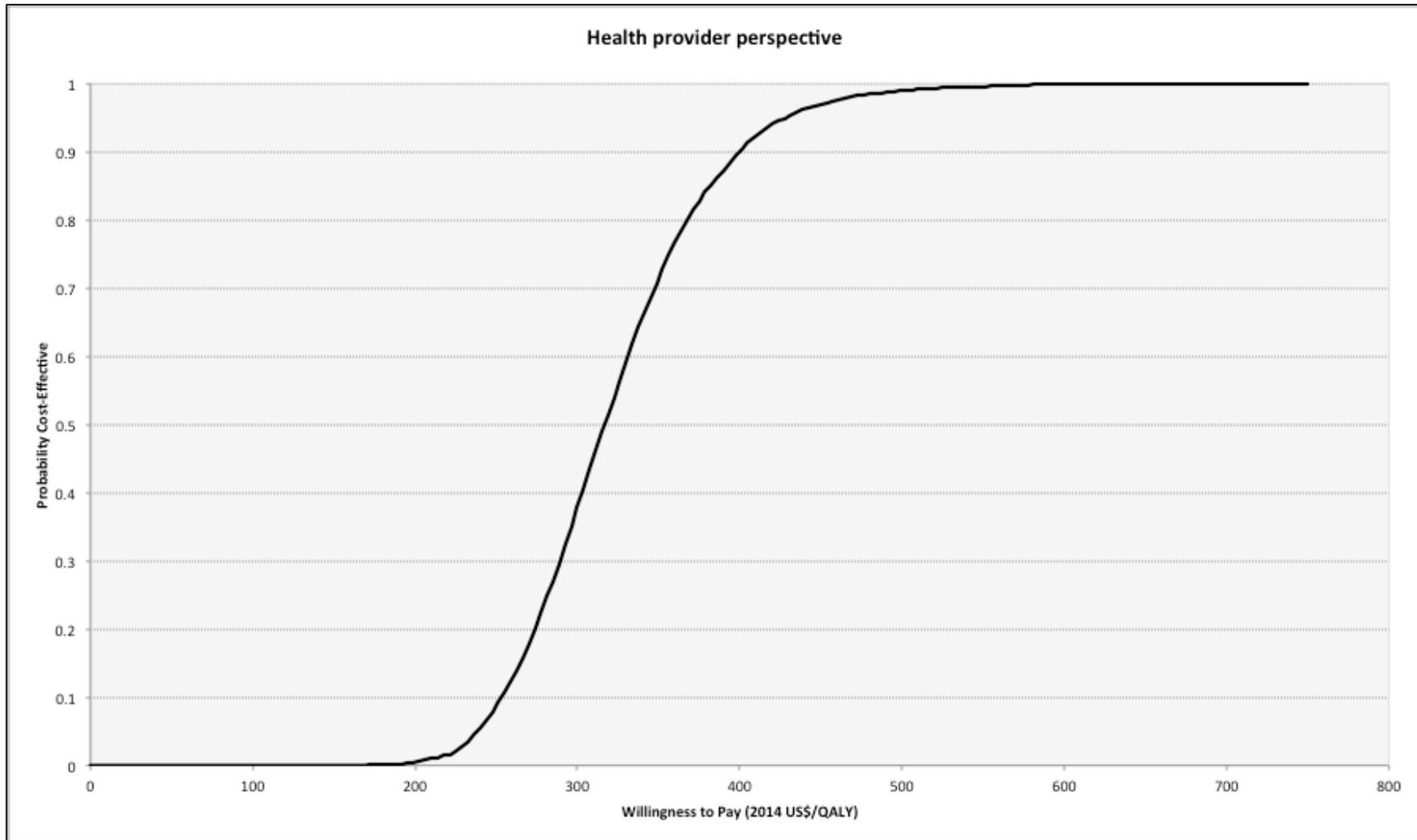
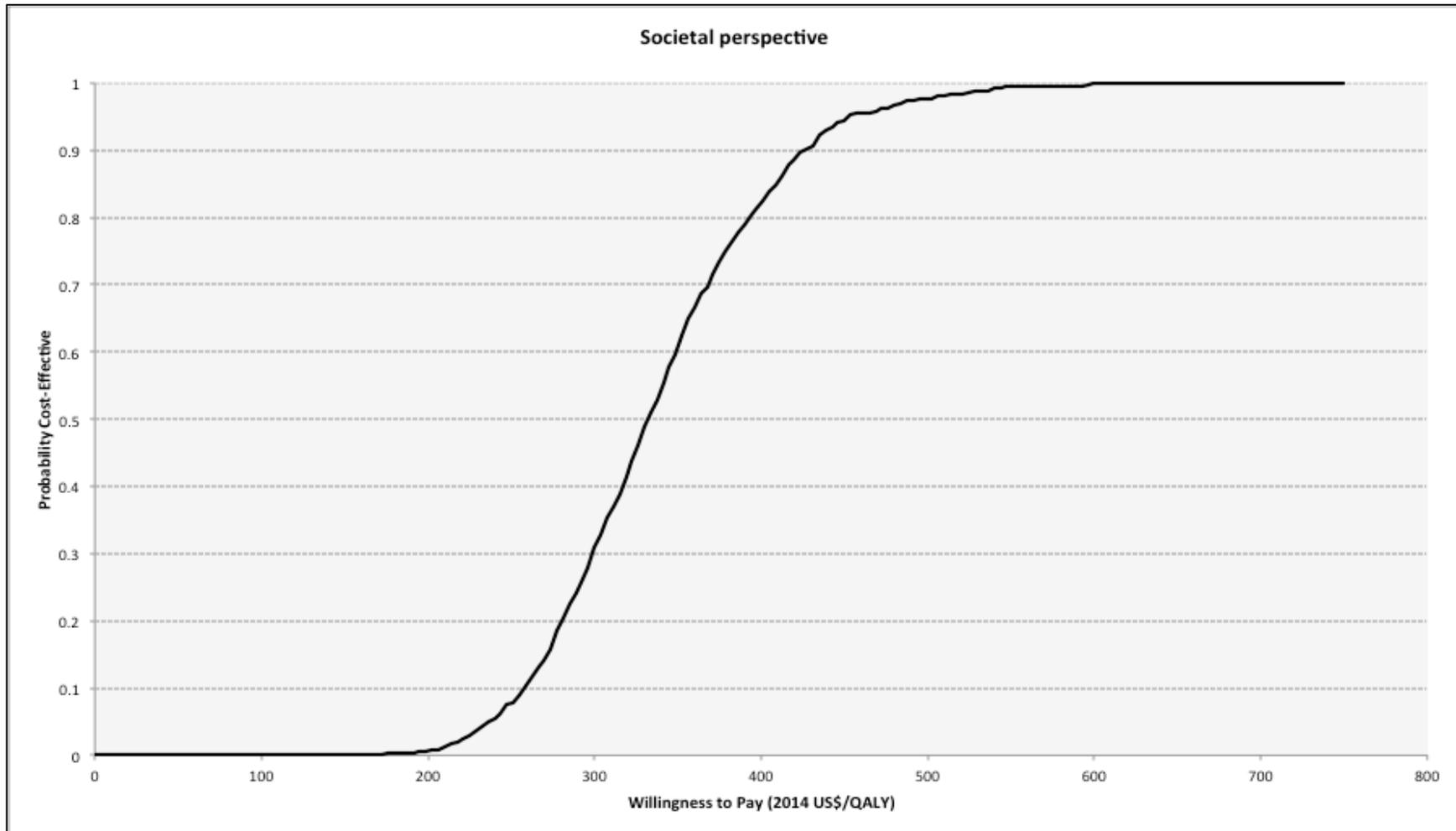


Figure 64: Cost-effectiveness acceptability curve – Societal perspective



8.3.3 Findings over different time horizons

Table 74 shows the findings from the health provider perspective and costs in 2014 US Dollars when the model was run over a 10-year and 40-year time horizon. The projected mean discounted incremental cost per person was US\$90.44 and US\$269.39 over a 10-year and 40-year time horizons, respectively. The model estimated a mean discounted health gain of 0.15 QALYs and 1.77 QALYs per person over a 10-year and 40-year time horizon, respectively. When the model was run over a short time horizon of 10 years, the ICER was US\$ 598.56 per QALY gained. When the model was run over a longer time horizon of 40 year, the ICER was US\$ 151.81 per QALY gained. Over a longer time-horizon of 40 years, the model predicts the probability of the intervention being cost-effective at a WTP threshold of US\$ 250 per gain in QALY to be 0.998 from the health provider perspective (Table 75).

8.3.3 Sensitivity analysis

Figure 65 shows ICERs for the different scenarios investigated in the sensitivity analysis undertaken. Table 75 shows incremental costs in 2014 US dollars from the health provider perspective, incremental effectiveness estimate, ICER estimate, and the probability of offering HIVST and facility-based HTC being cost-effective at the two willingness to pay thresholds of one times the GDP and three times the GDP per capita of Malawi. All the scenarios investigated suggest that the intervention would remain cost-effective is our willingness to pay for a gain in QALY was below three times the GDP of Malawi.

Table 75 shows that in comparison using a discount rate of 3%, discounting costs and health benefits at a rate of 6%, results in a lower incremental cost, higher incremental effectiveness, with the probability of implementing HIVST being cost-effective at a willingness to pay threshold of US\$ 250 per gain in QALY was higher at 0.895.

In comparison to using the Zimbabwean tariff to derive the EQ-5D utility scores, using the UK tariff results in the probability of implementing HIVST being cost-effective at a willingness to pay threshold of US\$ 250 per gain in QALY to be higher at 0.115 (Table 75). If the HIV prevalence in the population offered HIVST was lower at 5% or 10%, the sensitivity analysis shows the ICER estimate to be higher at US\$ 476.04 per QALY gained and US\$394.25 per QALY gained.

The sensitivity analysis shows that if the cost of an HIV self-test episode was 25% or 50% lower the probability of the intervention being cost-effective at the lower willingness to pay threshold of US\$ 250 per gain in QALY to be 0.220 and 0.496, respectively (Table 75). The sensitivity analysis shows that if the cost of delivering HIVST was 50% higher, providing HIVST would still be considered *cost-effective*.

Table 74: Cost-effectiveness findings from primary analysis over different time horizons (2014 US Dollars)

Perspective	Time Horizon	Strategy	Discounted Mean costs and QALYS per person				ICER (2014 US\$ per QALY)
			2014 US Dollars		QALYs		
			Mean Cost	Incremental cost	Mean Effectiveness	Incremental Effectiveness	
Health Provider	10 years	Facility HTC	170.63	-	8.09	-	598.56
		HIVST + Facility HTC	261.07	90.44	8.24	0.15	
Health Provider	20 years	Facility HTC	435.34	-	13.85	-	316.18
		HIVST + Facility HTC	602.36	167.03	14.38	0.53	
Health Provider	40 years	Facility HTC	928.61	-	22.29	-	151.81
		HIVST + Facility HTC	1198.00	269.39	24.06	1.77	

Figure 65: Tornado diagram showing findings from sensitivity analysis

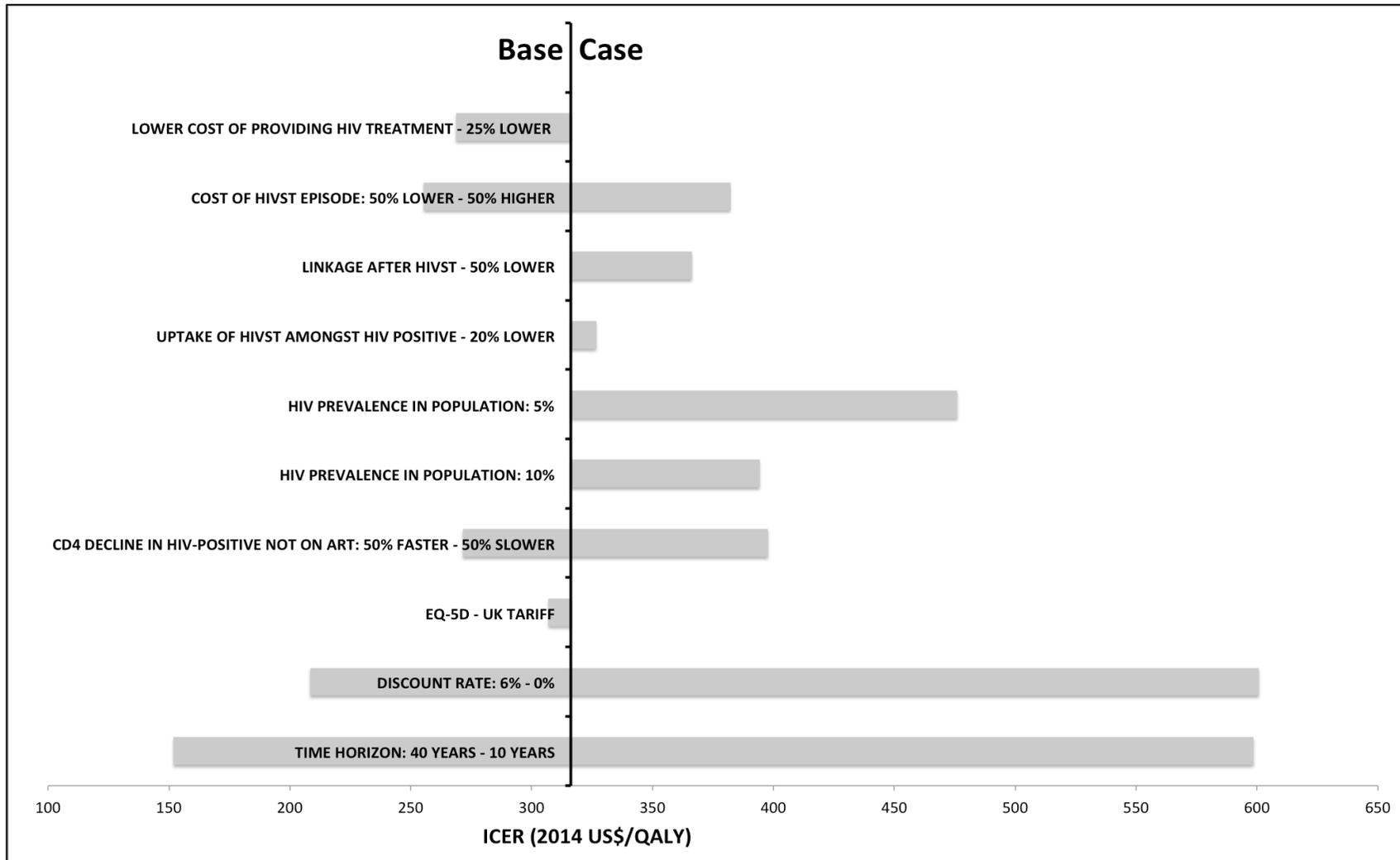


Table 75: Findings from sensitivity analysis and different time horizons, including probability of intervention cost-effective

	Incremental cost (2014 US Dollars)	Incremental effectiveness (QALYs)	ICER (2014 US\$ per QALY)	Probability cost-effective	
				1X GDP/capita	3 X GDP/capita
Base Case Scenario - 20 year time horizon	167.03	0.53	316.18	0.087	1.000
Base Case Scenario - 40 year time horizon	269.39	1.77	151.81	0.998	1.000
Base Case Scenario - 10 year time horizon	90.44	0.15	598.56	0.000	0.807
Discount rate 0%	224.64	0.37	600.73	0.000	0.778
Discount rate 6%	129.52	0.62	208.41	0.895	1.000
EQ-5D - UK Tariff	166.80	0.54	306.92	0.115	1.000
Faster CD4 decline amongst HIV positive individuals not on ART (50% faster)	177.45	0.65	271.50	0.292	1.000
Slower CD4 decline amongst HIV positive individuals not on ART (50% slower)	155.68	0.39	397.75	0.006	0.995
HIV prevalence in population: 5%	130.78	0.27	476.04	0.000	0.967
HIV prevalence in population: 10%	143.87	0.36	394.25	0.004	0.998
Uptake of HIVST amongst HIV positive - 20% Lower	160.44	0.49	326.67	0.053	1.000
Linkage after HIVST - 50% lower	122.35	0.33	366.21	0.034	0.994
Higher cost of HIVST - 50% higher	198.59	0.52	382.18	0.003	0.999
Lower cost of HIVST - 25% lower	150.78	0.52	288.08	0.220	1.000
Lower cost of HIVST - 50% lower	134.23	0.53	255.42	0.496	1.000
Lower cost of providing HIV Treatment - 25% lower	141.86	0.53	268.77	0.318	1.000

ICER: Incremental cost-effectiveness ratio

GDP: Gross Domestic Product

8.3.4 Public health impact of offering HIVST

Table 76 shows the potential public health impact of providing HIVST over the 20 years the model was run. Provision of HIVST would result in a 284.6% increase in the number of HIV testing episodes and a 143.2% increase in the months of ART provided. There would potentially be a 47.3% reduction in the number of hospitalisations amongst HIV positive individuals for Pneumocystis Pneumonia, and a 73.7% reduction in admission for pulmonary Tuberculosis. There would potentially be 79.2% fewer HIV infected individuals dying over the 20 years after HIVST was implemented.

Table 76: Public health Impact of implementing HIV self-testing

	Percentage change over 20 years of providing HIVST	
HIV testing episodes	284.6%	
Months of ART provided	143.2%	
Hospitalisations	Chronic Diarrhoea	55.1%
	Oesophageal candidiasis	62.4%
	Invasive bacterial diseases	77.3%
	Pulmonary TB	73.7%
	Extra-pulmonary TB	69.1%
	Malaria	82.8%
	Malignancy (KS/Lymphoma)	63.9%
	Pneumocystis Pneumonia	47.3%
Cryptococcal Meningitis	47.5%	
HIV related deaths	79.2%	

8.3.4 Alternative scenarios – Earlier initiation of ART

Table 77 shows the incremental costs in 2015 US dollars, incremental effects and ICERs for the cost-effectiveness analysis of HIVST under alternative thresholds for eligibility for ART initiation. Figure 66 shows the cost-effectiveness plane comparing the alternative strategies to the current strategy of providing facility-based HTC and initiation of ART when individuals CD4 count falls below 350 cells/ul (or WHO Stage 3 or 4).

Table 77 shows that in comparison to the current strategy of providing only facility-based HTC and ART, the ICER for providing HIVST and immediate of ART was US\$ 345.85 per QALY gained and would be a *cost-effective* strategy for Malawi.

The strategies for earlier initiation of ART with only providing facility-based HTC were dominated by strategies for earlier initiation of ART with the additional provision of HIVST. In addition, providing HIVST under current guidelines for ART initiation were dominated by strategies with earlier initiation of ART with the additional provision of HIVST. Figure 67 shows the cost-effectiveness acceptability frontier (CEAF) with the optimal strategies by increasing willingness to pay thresholds. The current strategy remains optimal up to a WTP threshold of US\$310 per QALY gained. At WTP thresholds above US\$310 per QALY gained, providing HIVST and earlier initiation of ART are the optimal strategies.

Table 77: Cost-effectiveness findings for alternative scenario from the health provider perspective (20 year time horizon)

HIV Testing strategy	ART Initiation Strategy	Discounted Mean costs and QALYS per person				ICER	
		2014 US Dollars		QALYs		(2014 US\$ per QALY gained)	
		Mean Cost	Incremental cost	Mean Effectiveness	Incremental Effectiveness		
Facility HTC	CD4 <=350 cells/ μ l or WHO stage 3 or 4	434.38		13.87			
Facility HTC	CD4 <=500 cells/ μ l or WHO stage 3 or 4	490.26	55.89	14.04	0.17	329.17	Extended dominance
Facility HTC	Immediate ART initiation (Test and Treat)	591.14	156.76	14.26	0.39	402.43	Extended dominance
Facility HTC + HIVST	CD4 <=350 cells/ μ l or WHO stage 3 or 4	603.75	169.38	14.39	0.53	322.34	Extended dominance
Facility HTC + HIVST	CD4 <=500 cells/ μ l or WHO stage 3 or 4	684.43	250.05	14.66	0.79	316.63	
Facility HTC + HIVST	Immediate ART initiation (Test and Treat)	823.45	389.07	14.99	1.12	345.85	

Figure 66: Cost-effectiveness plane showing incremental costs and effectiveness for alternative scenarios (Health provider perspective)

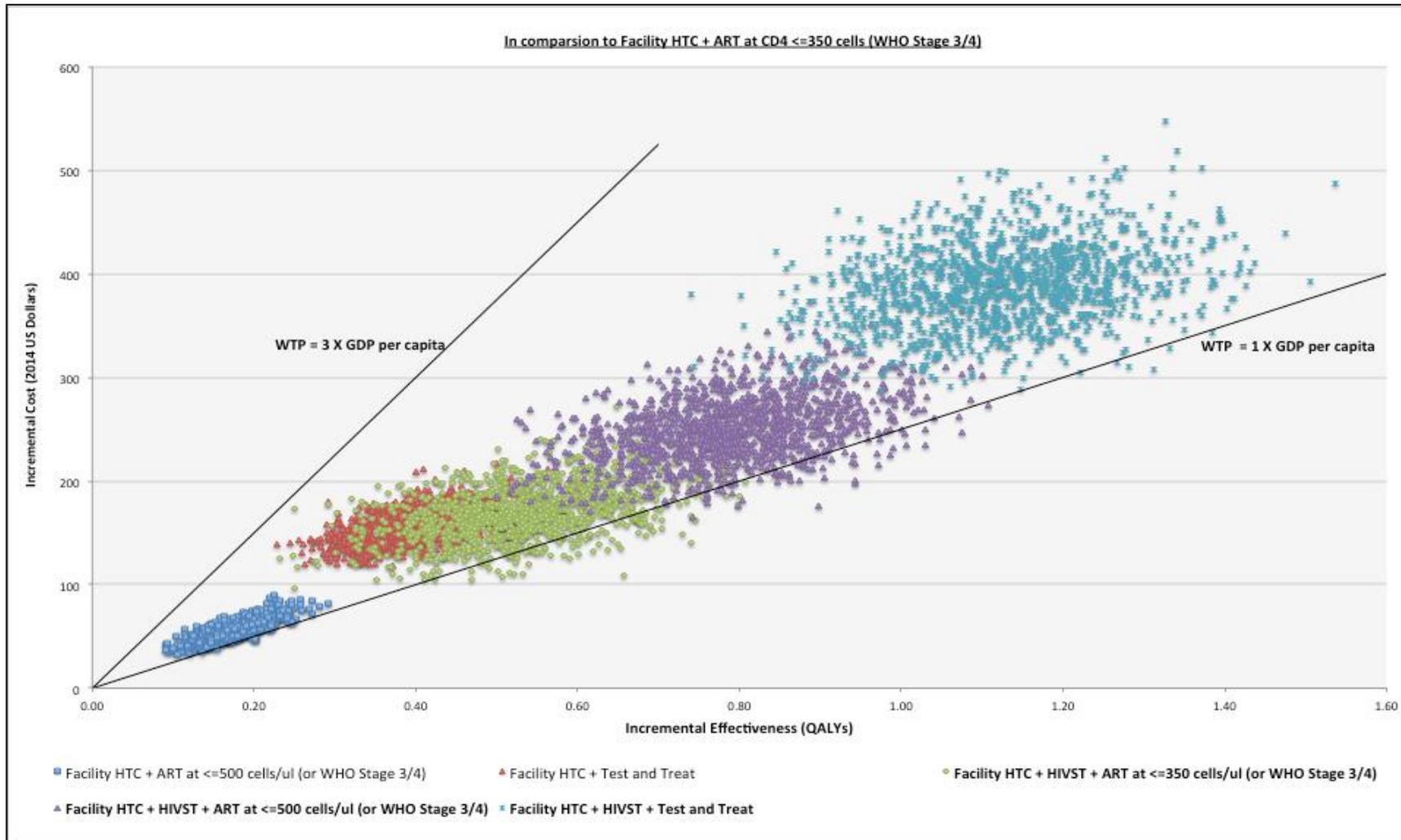
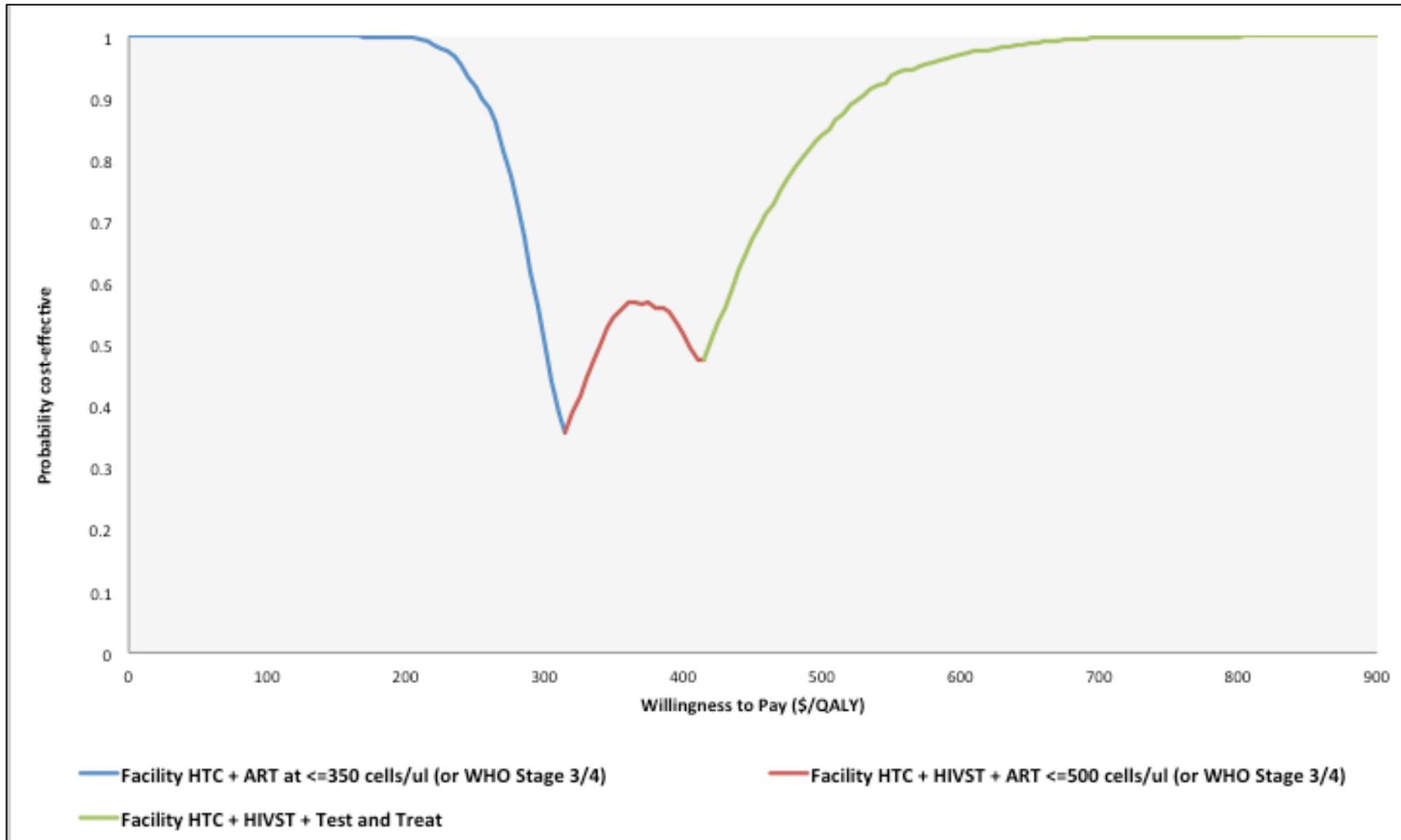


Figure 67: Cost-effectiveness acceptability frontier for alternative scenarios (Health provider perspective)



8.4 Discussion

In this chapter of the PhD, I found that implementing HIVST would be a *cost-effective* health strategy for Malawi, potentially *very cost-effective* if the decision was considered over a longer time horizon of 40 years. Additionally, I found the implementing HIVST would have a significant public health impact by reducing the burden of HIV associated illnesses that require hospital care. Implementing HIV self-testing would result in an increase in spending from the health provider but also a gain in quality adjusted life years. The analysis over the shorter (10-year) and longer (40-year) time horizons suggests that much of the additional costs would be incurred in the first few years of implementing HIVST, and much of the health benefits would not be realised till later. The ICER estimate was considerably lower when future costs and health gains were not discounted, and considerably higher when they were discounted at a higher rate of 6%.

The cost of providing HIVST and HIV treatment were important drivers of costs and cost-effectiveness. HIVST would remain *cost-effective* if the cost of delivering self-testing was higher. However, the ICER estimates would be lower if the cost of providing HIVST or HIV treatment were lower, increasing the likelihood the strategy would be considered *very cost-effective*, whilst making implementation more affordable. These scenarios could be achieved through market-based strategies to increase the competition and reduce barriers to market access for HIV self-test kits and generic anti-retroviral drugs. The former is currently being investigated through a large UNITAID grant that I am involved in, and involves working with healthcare

providers and manufacturers of HIV self-test kits to investigate alternative lower cost approaches to delivering HIVST, and providing regulatory support for current and future manufactures of HIV self-test kits to enter the African market. One of the aims of the project is to bring down the price of the Oral HIV self-test kit (US\$4.80 including shipping) to a price comparable to the rapid finger prick HIV test kits used in health facilities (US\$0.69). This would potentially lower the cost of delivering HIVST by 25-50%. Further cost reductions could be achieved if alternative approaches to delivering HIVST prove effective. The cost of providing HIV treatment has historically fallen, as HIV programmes grew in size and matured, and the prices for anti-retroviral drugs fell (Menzies et al., 2012, Tagar et al., 2014). It is possible this trend will continue with earlier initiation of ART in HIV positive individuals.

The HIV prevalence in Malawi varies, with higher prevalence reported in the urban cities and lower in rural villages (Chihana et al., 2012, MoH, 2014, WHO, no date-a). In addition, the HIV prevalence in other countries in sub-Saharan Africa has also been reported as lower than the 18.5% assumed in the primary model analysis (UNAIDS, 2013a). The findings from the CUA suggest that implementing HIVST would remain a cost-effective strategy if the HIV prevalence in the population offered the service were lower. However, implementing HIVST in other settings may be associated with higher or lower costs than that estimated in Blantyre. This should be taken into account, and further work is needed before the findings can be generalised.

The incremental cost-effectiveness ratio (ICER) of implementing HIVST estimated from the societal perspective was comparable to that estimated from the health provider perspective. In Chapters 5-7 I found the direct non-medical and indirect costs were considerable. Although HIVST is associated with minimal direct non-medical and indirect costs, accessing HIV treatment is not. HIVST will increase the number of HIV positive individuals accessing HIV treatment and thereby placing additional costs on them. Moving HIV testing closer to individual's homes saves users time and money, and this may also be possible with HIV treatment. Assessing individuals for initiation of ART and providing HIV treatment in people's homes have proved effective (Jaffar et al., 2009, MacPherson et al., 2014, Wringe et al., 2010), but will come at a cost but may still be cost-effective for healthcare providers.

In the cost-effectiveness analysis undertaken I have assumed the incidence of HIV amongst HIV-negative individuals would remain constant over time and would not differ across the two strategies examined. Implementing HIVST will increase the proportion of HIV-positive individuals on ART, and may reduce the HIV incidence over time. This would have a beneficial impact on health outcomes and costs of providing HIV care, as fewer and fewer individuals would become infected with HIV and need costly treatment with anti-retroviral drugs. Taking into account the impact on HIV transmission would likely result in a lower ICER.

In the study I undertook a range of model validation checks to compare the outputs of the model to outcomes observed in the real world. For this I predominantly used

findings observed in the study population from which the majority of my model parameter estimates were derived from. The validation checks suggest the model could be further optimised and this will be possible once the findings from HiTTB cluster randomised trial become available. Two potential issues found from the model validation related to the HIV prevalence amongst HIV self-testers in the model were higher than that found in the HiTTB study, and the higher CD4 counts observed amongst both HIV self-testers and facility-based testers who link into HIV treatment services. The sensitivity analysis suggests that the ICER estimate remained comparable if we assumed a lower uptake of HIVST amongst those who were HIV positive but not yet aware of their status, and if we assumed a faster decline in CD4 counts amongst HIV positive individuals not on ART.

In Chapters 5, 6 and 7 I found the EQ-5D utility scores derived from the UK tariff were systematically lower than the scores derived in the primary analysis using the Zimbabwean tariff. In the sensitivity analysis in this chapter I found the ICER estimate was only marginally lower when the EQ-5D utility scores derived from the UK tariff was used to populate the model. This would suggest that if Malawians were to value health in a comparable way to the UK population, placing lower values for health states associated with 'severe problems' in one or more of the five dimensions of health enquired in the EQ-5D measure, the conclusions around cost-effectiveness would not change. However, as the model shows more gains when run over a 40-year time horizon, it may still be valuable to consider deriving an EQ-5D tariff set for Malawi.

8.5 Summary of Chapter 8

In this chapter, I undertook a cost-utility analysis to investigate my primary research question. I used decision-analytic modelling and provide a description of the modelling approach and structure of the model. I describe the parameters used to populate the model and the sensitivity analysis undertaken. I found implementing HIVST would be a cost-effective option for Malawi, potentially very cost-effective. I show that this conclusion would not change if we used alternative parameters in the model or a shorter time horizon. I provide a brief discussion of the findings.

In the final chapter (Chapter 9) I will provide a more detailed discussion of the findings from the PhD, the implications for policy and research, and the strengths and limitations of the analyses undertaken in the PhD.

CHAPTER 9: Discussion of Findings

9 Overview of Chapter 9

In this chapter I provide a final discussion of my PhD thesis. I begin by summarising the primary issues relating to HIV and HIV testing in sub-Saharan Africa and Malawi. I then summarise the main findings of my PhD; how my findings relate to previous findings in the area; and the strengths and limitations of the PhD. I summarise the implications of my findings for policy, and the original contribution to research made by this PhD. I discuss potential areas for future research relating to HIVST, reflect on the research training and experiences during the course of my study, and finish with a brief conclusion to the thesis.

9.1 Introduction

HIV self-testing (HIVST) is a potential solution to help increase awareness of HIV status amongst Africans (Choko et al., 2015b), promote timely access to anti-retroviral therapy (ART) and biomedical prevention strategies, and consequently limit a regional epidemic (Granich et al., 2009, Gray et al., 2007a, Cohen et al., 2011, Grant et al., 2010). However, for policy makers to consider implementation, evidence is needed on the cost and cost-effectiveness of HIVST used within a regional context.

In 2014, over 35 million people were living with HIV, with over 2 million people becoming infected every year and nearly 2 million people dying from the infection (UNAIDS, 2014b). Sub-Saharan African has been worst hit by the epidemic, accounting for nearly three quarters of the global burden (UNAIDS, 2014b). In Malawi there are approximately one million adults living with HIV, and despite of efforts to increase the provision of HIV testing and treatment services, less than half of adults are aware of their HIV status, and less than half of those in need of ART are receiving therapy (UNAIDS, 2013a, MoH, 2014, Staveteig et al., 2013, UNAIDS, 2015).

In Africa, HIV testing and counselling (HTC) has traditionally been provided through health facilities. Individuals either access them voluntarily or are offered the option when accessing other forms of medical care. Facility-based HTC has been found to be unpopular amongst Africans, especially amongst men (Hensen et al., 2012,

Jurgensen et al., 2012, Kalichman and Simbayi, 2003, Macpherson et al., 2012c, Weiser et al., 2006). Health facilities offering HTC often lack privacy and confidentiality and may require individuals to take time of work or incur other personal costs (Kalichman and Simbayi, 2003, Wolff et al., 2005, Morin et al., 2006, Wringe et al., 2009, Angotti et al., 2009, Kwapong et al., 2014, Musheke et al., 2013). As a consequence HIV positive individuals have been found to enter HIV treatment services late; reducing survival, increasing burden of HIV associated illnesses and increasing the risk of transmission to their sexual partners.

Community-based HIV testing strategies, including home-based and mobile HTC, have been found to be popular offering those wishing to test privacy and convenience (Suthar et al., 2013, Sabapathy et al., 2012). In comparison to facility-based HTC, the cost of community-based HTC is high (Menziés et al., 2009, Grabbe et al., 2010), but economic evaluations suggest they are cost-effective (Smith et al., 2015, Bassett et al., 2014). However, in sub-Saharan African very few healthcare providers have implemented them (Staveteig et al., 2013), with concerns over their cost and human resource needs of scaling them up (Sabapathy et al., 2012).

HIVST involves individuals using an oral self-test kit to test in private and provides a potential approach for delivering community-based HTC services (WHO, 2013b, WHO, 2015, UNAIDS, 2013b). HIVST can be safely delivered by trained volunteers, achieving high rates of HIV testing and re-testing, reaching hard-to-reach groups like

men, and achieves high rates of linkage into HIV treatment services amongst those testing HIV positive (Choko et al., 2011, Choko et al., 2015b, MacPherson et al., 2014).

Economic evaluation provides a rigorous approach to comparing the costs and consequences of alternative health technologies, with the evidence informing policy on how to best use limited resources (Drummond et al., 2005b). In resource-constrained settings like Malawi this information can be extremely useful. There has been an increase in the number of economic evaluations in Africa (Creese et al., 2002, Walker, 2003, Scotland et al., 2003b, Uthman et al., 2010, Galarraga et al., 2009, Gomez et al., 2013, Sweeney et al., 2012, Johri and Ako-Arrey, 2011, Remme et al., 2014, Santa-Ana-Tellez et al., 2011), with development of guidelines for their undertaking (UNAIDS, 2011, WHO, 2003a). However, there are concerns about the methodologies used (Galarraga et al., 2009, Walensky et al., 2010a, Loubiere et al., 2010, Uthman et al., 2010, Beck et al., 2010) and data used (Galarraga et al., 2009, Kahn et al., 2011, Creese et al., 2002, Beck et al., 2010, Meyer-Rath and Over, 2012). This has potentially hindered their use in informing policy making (Beck et al., 2010).

The main objective of this PhD was to undertake a cost-utility analysis (CUA) from the health provider and societal perspective to estimate the incremental cost per quality-adjusted life year (QALY) when providing HIVST in addition to current approaches to providing facility-based HIV testing. Three observational studies were

conducted to collect primary cost and health-related quality of life data from HIV testers, individuals accessing HIV treatment and HIV positive individuals admitted to hospital for the management of HIV associated diseases. A decision-analytic modelling framework was used to undertake a CUA. Decision models were parameterised with the economic data collected and data extracted from the scientific literature.

9.2 Main findings of PhD

The main finding from the PhD was that implementing HIVST is a cost-effective strategy in Blantyre, Malawi. The CUA estimated the incremental cost per QALY gained from implementing HIVST in addition to the current strategy of facility-based provision of HTC to be 2014 US\$316.18 (2014 INT\$502.36) and 2014 US\$332.05 (2014 INT\$549.06) over a 20-year time horizon from the health provider and societal perspectives, respectively. When the decision was evaluated over a longer time horizon of 40 years, the incremental cost-effectiveness ratio (ICER) from the health provider perspective was 2014 US\$151.81 per QALY gained. The World Health Organization (WHO) interprets interventions where the ICERs are below one times the gross domestic product (GDP) per capita to be *very cost-effective* and interventions below three times the GDP per capita to be *cost-effective*. The GDP per capita in Malawi is approximately US\$250. Depending on the time horizon HIVST is cost-effective or very cost-effective. Additionally, taking into account the impact of increased coverage of HIV testing and HIV treatment amongst HIV-positive individuals through the implementation of HIVST will likely result in a lower ICER. This will result in implementation being more cost-effective than that found in this analysis.

The sensitivity analysis found that implementing HIVST would still be considered cost-effective if the decision was considered over a shorter time horizon of 10 years, if the cost of a HIV self-test episode was higher, if there was lower rates of linkage into HIV treatment services after HIVST, if the HIV prevalence in the general

population offered HIVST or in those who self-tested was lower, and if future costs and health outcomes were undiscounted.

Implementing HIVST will result in increased healthcare spending by Malawian healthcare providers. However, HIVST could be provided at a cost comparable to facility-based HTC (Chapter 5). The cost of per individual tested through HIVST was estimated to be approximately 2014 US\$8.78, comparing favourably to facility-based HTC (2014 US\$7.53 to US\$10.57). In the sensitivity analysis undertaken in Chapter 8, I found that as the cost per HIVST episode was lowered by 25% and 50%, the probability of the intervention being very cost-effective (ICER<US\$250 per QALY) improved from 0.09 to 0.220 and 0.496, respectively. The sensitivity analysis suggests that the cost of providing HIVST is an important driver of cost-effectiveness.

One of the main consequences of providing HIVST is the increased numbers of HIV positive individuals entering HIV treatment services and therefore needing life-long anti-retroviral therapy (ART). In Chapter 6 I estimated that it costs approximately 2014 US\$27.28 to assess an individual for eligibility to initiate ART, and for those who start treatment, approximately 2014 US\$166.20 per annum to provide care through a health facility. Over the next 20 years of implementing HIVST, there will be approximately 1.5-fold increase in the provision of ART (Chapter 8). The annual cost of providing ART is twenty times as much as the cost of an episode of HIV testing (in the model individuals were limited to one HIV test episode per annum). If the cost of

providing HIV treatment (including anti-retroviral drugs) were 25% lower, the probability the intervention would be considered very cost-effective would increase to 0.318 (Chapter 8). The findings highlight the impact the cost of providing HIV treatment on the cost-effectiveness of implementing HIVST.

An interesting finding was the lower health provider cost per patient identified eligible for ART through HIVST when compared to facility-based HTC. However users of the two services may not be entirely comparable. Some facility-based HIV testers may have been seeking medical care for other medical reasons, related to progressive HIV disease, having been referred by the health provider for HIV testing under the umbrella of provider-initiated testing and counselling (PITC). Importantly, the health provider and societal cost of providing HIV treatment after initiating ART was not associated with the modality of HIV testing received.

In the PhD I used the EuroQoL EQ-5D-3L measure to ask participants about their HRQoL. Those accessing HIVST reported better HRQoL than those accessing facility-based HTC (Chapter 5); whilst amongst those who accessed HIV treatment those with more advanced HIV disease (measured by CD4 count) reported poorer HRQoL (Chapter 6). I found there was a significant relationship between utility scores and HIV disease stage, measured by CD4 count (Chapter 6). HIV positive individuals with lower CD4 counts had lower mean adjusted EQ-5D utility scores. For HIV positive individuals, utility scores increased after starting ART, with the majority of

participants recruited in the study reporting perfect health (EQ-5D utility score of 1.0) after being on ART for one year. The findings highlight the beneficial impact of timely initiation of ART on an individual's HRQoL and support the importance of taking into account HRQoL in economic evaluations. Individuals who started ART were also found to have a gradual improvement in their EQ-VAS scores (Chapter 6). The VAS score reflects self-reported HRQoL, with individuals rating their own health on a scale between zero and hundred. The findings suggest that individuals themselves report improvements in HRQoL once they start ART. Importantly, I did not find that the EQ-5D utility scores amongst HIV positive individuals varied significantly either before or after starting ART according to the method of HIV testing used.

A questionnaire was developed to ask participants about the direct non-medical costs they incurred and their loss of income as a consequence of accessing medical care. HIVST was found to be associated with lower direct non-medical and indirect costs than facility-based HTC (2014 US\$2.93 lower), however, implementing HIVST increases the numbers of HIV positive individuals entering HIV treatments services. The total direct non-medical and indirect costs associated with a HIV positive individual accessing HIV treatment in the first year was approximately 2014 US\$8.98. Thus the ICERs estimated from health and societal perspectives were similar.

The decision-analytic model shows the impact of implementing HIVST, reducing the risk of hospitalisations for HIV associated illnesses (Chapter 8). Many of these illnesses are seen exclusively (e.g. Cryptococcal meningitis, Pneumocystis Pneumonia) or predominantly (e.g. Tuberculosis) in those who are HIV positive. Approximately 70% of adults admitted to Queen Elizabeth Central hospital (QECH) are HIV positive (Chapter 7), with high mortality rates and poor HRQoL amongst hospitalised patients, and high health provider, direct non-medical and indirect costs of hospitalisation. Approximately one in five adults admitted to QECH for medical reasons died during their hospitalisation, the mean EQ-5D utility score amongst hospitalised patients was 0.484 and the mean total health provider cost was 2014 US\$314.92. By comparison, the mean EQ-5D utility score amongst those who started ART (Chapter 6) was 0.845 and the mean annual health provider cost of managing a HIV positive individuals in a primary health facility (including providing anti-retroviral drugs) was 2014 US\$166.20.

In September 2015, the WHO released a press statement advising immediate initiation of ART in all those infected with HIV. The Malawi Ministry of Health (MoH) is in the progress of reviewing these guidelines and planning to implement them in 2016. In the CUA (Chapter 8) I investigated implementing HIVST in the context of earlier (CD4 falls below 500 cells/ μ l) and immediate initiation of ART. Earlier initiation of ART only providing facility-based HTC was extended dominated by earlier initiation of ART with the additional provision of HIVST. Extended dominance means that the ICER for earlier ART initiation with only facility-based HTC is higher

than for earlier initiation of ART with the provision of both facility-based HTC and HIVST, but the latter comes at greater cost. A move towards earlier initiation of ART, would provide better money for value if additionally implementing HIVST. Earlier initiation of ART would result in a further reduction in HIV incidence at the population level, improving the cost-effectiveness of implementing HIVST.

The CUA suggests that in comparison to ART initiation when CD4 falls below 350 cells/ul with the provision of only facility-based HTC, immediate ART initiation with the additional provision of HIVST would be a 'cost-effective' option for Malawi. The estimated ICER from the health provider perspective was US\$345.85 per QALY gained.

9.3 Comparison to previous findings

The findings from the PhD suggest that implementing HIVST would be a cost-effective strategy in Malawi. A recent economic evaluation of HIVST in Zimbabwe found HIVST would be cost-effective, potentially cost saving (Cambiano et al., 2015). In addition, recent economic evaluations of home and mobile HIV testing, using finger-prick rapid HIV testing providing by HIV counsellors, would be a cost-effective strategy for South Africa (Bassett et al., 2014, Smith et al., 2015).

The recent economic evaluation of HIVST in Zimbabwe investigated a range of hypothetical scenarios relating to the cost of implementing HIVST, uptake of HIVST, linkage into HIV treatment services, and ART eligibility criteria on the incremental cost-effectiveness on implementing HIVST (Cambiano et al., 2015). The analysis was undertaken prior to availability of real-world outcome data relating to HIVST. Similarly to findings presented in this thesis, the cost of delivering HIVST was a major determinant of cost-effectiveness (Cambiano et al., 2015), although the authors found that implementing HIVST would be cost saving if it could be delivered at a cost of US\$3, and only cost-effective at ICER thresholds above US\$10,000 per DALY averted if the cost of providing each episode was above US\$9 (their estimate of facility HTC was US\$9/subject). In the analysis, ART was initiated once individuals CD4 count fell below 500 cells/ μ l and a transmission dynamic model was used undertake the modelling. This may in part explain the differences in the findings. Using a transmission model to undertake the cost-effectiveness analysis will capture additional health gains and cost savings through potential reductions in HIV

incidence. Initiating HIV-positive individuals earlier onto ART will reduce HIV transmission, and result in additional health gains and cost saving over time.

In South Africa implementing mobile HTC, in addition to facility-based HTC, was associated with an ICER of 2012 US\$2,400 per year of life saved (Bassett et al., 2014), whilst implementing home-based HTC (counsellor provided finger-prick HTC) was associated with an ICER of 2014 US\$1090 per DALY averted (Smith et al., 2015). The higher estimates are likely to reflect the higher cost of goods in South Africa, and the fact HIV care is doctor-led. The similar ICER estimates would suggest that community-based provision of HTC is cost-effective.

The advantage HIVST offers is the lower cost of delivering HIV testing in the community. I estimated the cost of testing an individual through HIVST to be approximately 2014 US\$8.78. This compares favourably to previous estimates of community-based HIV testing strategies (US\$7.77 to US\$33.54 in 2012 prices) that utilised standard finger-prick RDT kits (Chapter 3) (Suthar et al., 2013). In the previous economic evaluations of home-based and mobile HTC, the cost per individuals tested used in the model analysis was over US\$20.

In the CUA, I found the ICER for changing eligibility for ART initiation from ≤ 350 cells/ μ l to ≤ 500 cells/ μ l, with only provision of facility-based HTC, to be

approximately 2014 US\$329.16 per QALY gained. Previous studies have estimated the ICER to be 2012 \$273 to \$1691 per DALY averted in South Africa, and 2012 \$749 per DALY averted in Zambia (Eaton et al., 2014). Additionally, I found the ICER for moving to immediate ART initiation, with only provision of facility-based HTC, to be approximately 2014 US\$402.43 per QALY gained. Previous studies have estimated the ICER to range from 2012 US\$170 per life year saved (Hontelez et al., 2013) to 2013 US\$408 per QALY gained (Alistar et al., 2014). The comparability of findings would suggest external validity in the ICERs estimated in the PhD.

The cost of providing HIV treatment was an important determinant of cost-effectiveness. I found that the yearly cost of providing anti-retroviral drugs and HIV care (US\$166.20) was comparable with recent estimates in Malawi (US\$136 in 2011 prices), Kenya (US\$230 to US\$288 in 2009 prices), Zambia (US\$198 to US\$278 in 2011 prices), Ethiopia (US\$186 to US\$216 in 2011 prices), Rwanda (US\$232 in 2011 prices) and Lesotho (US\$261 to US\$345 in 2010 prices) (Larson et al., 2013, Johns et al., 2014, Scott et al., 2014, Tagar et al., 2014, Bratt et al., 2011, Jouquet et al., 2011). In comparison to previous studies, I did not find the cost of providing HIV care, including anti-retroviral drugs, to be associated with the HIV disease stage of individuals when they entered care (Leisegang et al., 2009, Harling and Wood, 2007). This is likely because in estimating HIV treatment costs I only included the costs of medical resources used directly during an individual's visit to the HIV clinic.

In the PhD I found the HRQoL was poorer amongst those with more advanced HIV disease and in those suffering from HIV-associated illnesses requiring hospital admission. Additionally I found HRQoL improved in HIV positive individuals who initiated anti-retroviral therapy. Like previous studies, I found HRQoL was poorer amongst those with more advanced HIV disease, and much of the improvement in HRQoL occurred in the first few months after starting ART (Pitt et al., 2009, Jelsma et al., 2005, Stangl et al., 2007, Beard et al., 2009). However, only a few studies undertaken in sub-Saharan Africa have used the EQ-5D tool to measure HRQoL in HIV infected individuals (Beard et al., 2009, Robberstad and Olsen, 2010, Bhargava and Booyesen Fle, 2010, Gow et al., 2013), and even fewer have used the tool to investigate the impact of HIV associated illness (like Tuberculosis) (de Grass et al., 2015). A potential barrier to the use of the EQ-5D tool in sub-Saharan Africa is the limited number of population tariff sets for countries in the region from which to derive EQ-5D utility scores. However, the EQ-5D tool has been found to demonstrate reliability, discriminative validity and responsiveness to change in HIV infected individuals, including after initiation of ART (Tran et al., 2012, Tran et al., 2015).

In the PhD I found the direct non-medical and indirect costs associated with accessing HIV testing, HIV care and hospital care were high. Previous studies have highlighted the direct non-medical costs of accessing HIV care (Rosen et al., 2007, Bisson et al., 2006, Chimbindi et al., 2015), or that these costs are barriers to individuals accessing HIV services (Fox et al., 2010, Hardon et al., 2007, Tuller et al., 2010, Zachariah et al., 2006).

9.4 Strengths and limitations of PhD

In the PhD I undertook three observational studies to collect primary cost and HRQoL data relating HIV testing and HIV management. I undertook a CUA using decision-analytic modelling to estimate the incremental cost-effectiveness of implementing HIVST in addition to current facility-based provision of HTC. The research undertaken in the PhD has several strengths and limitations.

The main strength of the PhD are that the research question was answered by undertaking a CUA, with the analysis undertaken from both the societal and health provider perspective, incorporating a wide range of costs and consequences from accessing the two different approaches to HIV testing, with the costs adjusted and presented to a common price year and currency, and the economic data prospectively collected and driven by the modelling needs (Drummond et al., 2005b, Briggs et al., 2008, Petrou and Gray, 2011b).

A CUA offers a systematic approach to comparing the costs and consequences of implementing new health technologies, aiding policy decisions concerned with allocative efficiency (Drummond et al., 2005b). Measuring health outcomes in QALYs, allows consideration of the impact of implementing HIVST on both mortality and morbidity (Mehrez and Gafni, 1989, La Puma and Lawlor, 1990, Loomes and McKenzie, 1989, Weinstein et al., 2009).

I undertook decision-analytic modelling to investigate the cost-effectiveness of implementing HIVST. HIVST was being provided in Blantyre as part of a randomised controlled trial, and it might be considered a missed opportunity not to ‘piggy back’ an economic analysis onto the trial (Petrou and Gray, 2011a, Glick et al., 2014). However, in this instance, I consider this as one of the strengths of the PhD. The HitTB study was a cluster-randomised trial with the intervention provided over two years and follow-up assessed linkage into HIV treatment and mortality outcomes. Under this scenario I considered decision-analytic modelling unavoidable (Buxton et al., 1997). Decision-analytic modelling allowed me to consider all the cost implications and health outcomes of implementing HIVST at a population level, including long-term costs and consequences of accessing HIV treatment and impact on suffering HIV associated illnesses. The findings from the trial are yet to be published, and it is likely the cost-effectiveness findings from the PhD will be published around the same time, aiding timely dissemination for research and policy.

The structure of the decision-analytic model was influenced by previous evaluations of HIV interventions (Chapter 4) and by clinical doctors working in HIV (Roberts et al., 2012). The cost and HRQoL data were collected to meet the model requirements and not vice-versa (Caro et al., 2012). The studies undertaken in Chapters 5, 6 and 7 were designed and undertaken in such a way as to provide relevant cost and HRQoL data to parameterise the model, including recruiting participants who were residents of the HitTB study. The transition probabilities used in the model were obtained either from the HitTB study, or from undertaking targeted literature searches and fixed-

effects meta-analysis to pool data (Caro et al., 2012). The model underwent standard validation checks, and probabilistic sensitivity analysis was undertaken to reflect the uncertainty in the estimates used to parameterise the model (Briggs et al., 2012b, Eddy et al., 2012). Sensitivity analysis was also undertaken to investigate the impact of using alternative model parameters on conclusions drawn, including implications of changes in costs of delivering HIVST and HIV treatment.

The analysis was undertaken from the health provider and societal perspectives, thereby allowing consideration of the allocative efficiency of implementing HIVST at both the health provider and societal levels (Drummond et al., 2005b, Johannesson and O'Connor, 1997a). I undertook primary observational studies to estimate the direct health provider cost, and the direct non-medical and indirect costs. This provided estimates from both the health provider and societal perspectives for use in the CUA.

In Chapter 5 I estimated the cost of providing HIVST in Africa, the first time this has been done. In Chapter 6 I estimated the costs of providing HIV care, including ART, to HIV positive individuals with findings comparable to previous estimates from Malawi and regionally (Tagar et al., 2014, Scott et al., 2014, Bikilla et al., 2009, Menzies et al., 2012, Marseille et al., 2012). In Chapter 7 I estimated the costs of managing a range of health conditions in adults needing hospital admission, and used medical doctors to extract medical resource use data from the medical notes after discharge. In all

these three studies I prospectively collected healthcare use at the patient level, and undertook primary costing of the resources used to estimate the direct health provider costs. I followed international costing guidelines to cost the healthcare resources (UNAIDS, 2011), with the same methods used across all three observational studies. I interviewed key personnel at each of the healthcare organisations, and collecting the same categories of resource inputs (e.g. Staff salaries and training, consumables, equipment) (NICE, 2008). The use of a combination of a top-down and bottom-up costing methodology depending on the healthcare resource being costed, provided efficiency and accuracy (Beck et al., 2012). Collecting prospectively at the patient level reduces the risk of bias.

I followed standard guidelines for annuitization of equipment costs (WHO, 2003a), and presented costs in both US and International dollars and adjusted to a common price year (WHO, 2003a, Drummond et al., 2009, Drummond et al., 2005a). Providing estimates in both US and International dollars, as advocated by the WHO (WHO, 2003a), aids interpretation of findings in Malawi and Internationally by taking into account differences in purchasing power parity between countries (Shemilt et al., 2010).

In order to estimate the direct non-medical and indirect costs, I developed and pilot tested data collection tools, and prospectively collected economic data from participants. The direct non-medical costs considered were adapted to the setting

and population interviewed (e.g. for hospitalised patients I additionally considered costs incurred from overnight stay). The comparability in the methods, and items considered across the three studies provides rigour, and aides their use in the cost-effectiveness analysis. Importantly, these costs have been considered important deterrents to accessing HIV care in Africa, but have rarely been fully quantified.

In order to undertake the CUA I collected primary HRQoL data directly from participants exposed to the intervention. I used the Chichewa version of the EQ-5D tool that had undergone the EuroQol group's translation and validation process (EuroQol, no date). As there was a lack of a Malawian tariff set to derive the EQ-5D utility scores, I used the Zimbabwean tariff set to derive the EQ-5D utility scores. This is a potential limitation, however, in the sensitivity analysis of all the studies (Chapters 5-8) I investigated the impact of using the UK tariff set to derive EQ-5D utility scores. The UK tariff set equates poor health states to lower EQ-5D utility scores than the Zimbabwean tariff. In the studies described in Chapter 5, 6 and 7 I found the EQ-5D utility scores lower but these did not impact on the multivariable analysis undertaken in the respective chapters. Additionally, using the UK tariff to derive EQ-5D utility scores for the cost-utility analysis did not impact on my final conclusion regarding the cost-effectiveness of implementing HIVST. I also showed that the EQ-5D tool seems to be performing well in this setting, correlating well with the VAS and responses to self-assessed health.

There are five important limitations of the cost-effectiveness analysis and modelling approach used. Firstly, I did not consider the impact of HIV transmission. Secondly, the model was parameterised by predominantly observational data. Thirdly, I did not consider the impact of individuals failing to suppress their HIV infection on anti-retroviral drugs. Fourthly, I only considered the impact of HIV associated illnesses that required hospitalisations, and did not take into account the other illnesses that are managed in the community or at primary health clinics. Fifthly, I did not consider the impact of adverse drug reactions to ART. In the following text I interpret the potential implications of each of these limitations.

Implementing HIVST will potentially increase the proportion of HIV positive individuals on ART, increasing the proportion of HIV positive individuals whose HIV viral load is suppressed by the anti-retroviral drugs, reducing HIV incidence within the population (Tanser et al., 2013). This beneficial effect on HIV incidence will be greater through implementing HIVST. As fewer individuals will acquire HIV, there will be additional cost savings and reduced mortality and morbidity, potentially making HIVST more cost-effective than found in my analysis. I used an individual sampling model (ISM) to undertake the decision-analytic modeling. In previous analysis undertaken in HIV, researchers using ISM have either used a constant risk of HIV transmission/acquisition (Hallett et al., 2011) or not incorporated the impact on HIV transmission (Losina et al., 2009, Walensky et al., 2012, Walensky et al., 2009, Walensky et al., 2010b, Walensky et al., 2011, Goldie et al., 2006, Bendavid et al., 2011, Bendavid et al., 2008, Gray et al., 2007b). An alternative modelling approach

that incorporates changes in HIV incidence over time would be through the use of transmission dynamic modelling or discrete event simulation (Barton et al., 2004). A disadvantage of using a transmission dynamic model would be that I would not have been able to model events based on individual level characteristics and keep the number of health states to a manageable quantity (Barton et al., 2004). Discrete event simulation would have allowed this, but with added computational burden. The primary model simulation took approximately twelve hours to run.

Previous economic evaluations of community-based HIV testing strategies have used both transmission dynamic modelling (Cambiano et al., 2015, Smith et al., 2015) and individual sampling models (Bassett et al., 2014). However, they found that National guidelines determining the CD4 count threshold at which individuals were eligible for ART initiation which drove the beneficial impact on HIV incidence (Smith et al., 2015, Cambiano et al., 2015). HIV positive individuals not receiving ART are at highest risk of transmitting HIV to an uninfected sexual partner in the first six months to a year after they become infected, when their HIV viral load is high (Hollingsworth et al., 2008, Powers et al., 2011a, Blaser et al., 2014). Increasing uptake of HIV testing and entry into HIV treatment through HIVST is unlikely to have major impact HIV incidence, and therefore cost-effectiveness, under current ART initiation threshold of CD4 count ≤ 350 cells/ μl . In the context of immediate initiation of ART in HIV infected individuals, there will potentially be a significant beneficial impact on HIV incidence (Granich et al., 2009).

The findings are also limited by the fact that the cost and HRQoL data used to parameterise the model were obtained from observational studies and therefore are potentially vulnerable to bias. In addition, some of the transition probabilities used in the decision-analytic model were also extracted from observational studies. In the studies undertaken in Chapters 5 and 6 I recruited a convenience sample of HIV testers and HIV positive individuals, respectively. There is a potential risk of selection bias, with recruited participants not representing the HitTB study population (Cochran, 2007). In the study undertaken in Chapter 7, I recruited one in five adults admitted to the medical wards at QECH, in addition to those who had a preliminary medical diagnosis of the rarer HIV associated illnesses I was interested in obtaining economic data to parameterise the model. Additionally there was considerable attrition from initial recruitment into the hospital cohort after hospital admission, to the medical data extraction stage in the study. These all could potentially bias the findings from each of the studies, and the final ICER estimate. In the studies in Chapters 5 and 6 I undertook multivariable analysis to adjust for individual-level characteristics, but the sample sizes in the study undertaken in Chapter 7 did not allow for this. I also represented the uncertainty in the parameter estimates by incorporating the standard errors of the estimated sample means in fitting the distributions, and took into account possible correlations (Briggs et al., 2008). Despite these procedures, there may still be potential biases in the final ICER estimates, and whether they result in the ICER being underestimated or overestimated is not predictable (Philips et al., 2004).

The findings are also limited by the fact that I did not consider the impact of individuals failing ART in the cost-effectiveness analysis. Individuals on ART are often monitored at regular intervals to detect whether the anti-retroviral drugs they are prescribed are suppressing their HIV viral load. If anti-retroviral drugs fail to suppress the HIV viral load their HIV disease will progress. This will increase their risk of HIV associated mortality and morbidity. Incorporating HIV viral load monitoring and switching anti-retroviral drug regimens if individuals fail therapy will increase the costs of providing HIV treatment. Individuals would require additional visits to the HIV clinic, second-line anti-retroviral drug regimens are more costly, and the cost of performing HIV viral load assessments is high (estimated to be US\$26.96 in Chapter 7). Consequently it is possible the ICER for implementing HIVST would be higher as this strategy would result in more individuals on ART, increasing the additional costs of providing HIV treatment. At the time of undertaking the analysis and collection of data in the primary observational study described in Chapter 6, the Malawi health service had not implemented routine monitoring of HIV viral load for patients on ART, and therefore primary healthcare resource use relating to monitoring ART failure was not possible. Additionally, a recent study that observed nearly 300,000 Africans on ART, with over 780,000 person-years of follow-up, found that only 3% were switched onto a second-line anti-retroviral drug regime (Haas et al., 2015). Importantly, there is some evidence that suggests delayed ART initiation is associated with higher likelihood of failing first-line anti-retroviral drug regimes (Vanobberghen et al., 2015, Tran et al., 2014). Implementing HIVST is likely to result in more timely ART initiation. These issues would suggest the likely impact of

considering failure of ART would have been minimal, especially as most of the costs would be incurred in the future.

The CUA did not consider the impact of implementing HIVST on the costs and consequences of suffering HIV associated illness that are managed in primary health clinics or in the community. Previous economic evaluations of HIV interventions have also predominantly focussed on HIV associated illnesses requiring hospitalisation without considering impact on other illnesses that do not require hospitalisation (Badri et al., 2006b, Bendavid et al., 2011, Goldie et al., 2006, Hamers et al., 2012, Walensky et al., 2011, Waters et al., 2011, Walensky et al., 2013). HIV positive individuals are at risk of a range of co-morbidities that require medical care, many of these do not require hospital admission. Considering this issue in the economic analysis would potentially result in HIVST being more cost-effective. HIVST will increase the proportion of HIV positive individuals accessing HIV treatment and initiating ART, thereby reducing their risk of suffering from these co-morbidities and the cost of managing them.

The findings are also limited by the fact that I did not consider the impact of adverse drug reactions to anti-retroviral drugs in the CUA. Individual's prescribed anti-retroviral drugs are at a significant risk of adverse drug reactions including lipodystrophy, peripheral neuropathy and liver damage (Eluwa et al., 2012, Subbaraman et al., 2007). These may potentially impact on the ART adherence and

HRQoL of those treated (Duval et al., 2004, Colebunders et al., 2005). In the CUA, I incorporated the beneficial impact of timely entry into HIV treatment through implementing HIVST. The negative impact of adverse drug reactions to ART will likely reduce the incremental cost-effectiveness of HIVST.

Taken overall the summary effect of these limitations is difficult to gauge. However in many respects they are likely to underrepresent the cost-effectiveness of HIVST. In addition they give useful pointers for future research which could be undertaken in this area.

9.5 Policy implications

The findings from the PhD imply that implementing HIVST in Malawi will be a cost-effective, and potentially a very cost-effective strategy for the Ministry of Health. Policy makers in Malawi have already show a keen interest in HIVST, being one of the first countries in sub-Saharan Africa to investigate the legal and policy issues relating to the provision of HIV self-testing (SAT, 2015), and supporting several research studies in the area. The evidence from research studies highlights that HIVST can be delivered safely; users accurately learn their HIV status and there is a major impact on increasing population coverage of HIV testing and linkage into HIV services for those testing positive (Choko et al., 2011, Choko et al., 2015b, MacPherson et al., 2014, Pant Pai et al., 2013, Mavedzenge et al., 2015, Ngunjiri et al., 2014). The findings from the PhD add to this growing evidence by highlighting that implementing HIVST is a cost-effective intervention in Malawi, with the cost of provision comparable to current facility-based HIV testing.

In the PhD, I estimated the incremental cost per additional quality-adjusted life year gained from implementing HIVST in addition to facility-based HTC. In interpreting whether this strategy was cost-effective, I compared this estimate to thresholds commonly used to conclude cost-effectiveness in international health economics and policy (WHO, 2001, WHO, 2003a). However, this does not necessary imply the intervention offers the most efficient use of resources or that it should be implemented. Policy decisions will take into account other issues including whether implementation is equitable, affordable or feasible. An intervention that is cost-

effective may not be equitable, as it may benefit certain individuals more than others. An intervention that is cost-effective may not be affordable or feasible, as it may require financial, human or capital resources that may not be available in countries like Malawi. Interpretation of cost-effectiveness in resource-constrained settings may also be complicated by the lack of cost-effectiveness data for other interventions to make comparisons against. In addition, healthcare in countries like Malawi receives significant funding from external donors, often provided vertically for specific healthcare services, and therefore thresholds of cost-effectiveness may vary depending on the health service being considered. Policy makers will also need to consider these other issues when interpreting whether implementing HIVST is a cost-effective strategy.

The World Health Organisation (WHO) and the United Nations Programme on HIV/AIDS (UNAIDS) both support the implementation of HIV self-testing in sub-Saharan Africa (Johnson et al., 2014, WHO, 2015, UNAIDS, 2013b). The majority of countries in East and Southern Africa face comparable HIV disease burdens, poor uptake of HIV testing and sub-optimal population coverage of ART (UNAIDS, 2014b, UNAIDS, 2015). In the region, international and national policy makers are aiming to increase awareness of HIV status, ensuring that at least 90% of those HIV positive are aware of their infection, and 90% of HIV positive individuals are being treated with anti-retroviral therapy, potentially bringing an end to the HIV epidemic in the region by 2030 (UNAIDS, 2014a). HIVST offers a potential solution to achieving these goals, and the findings in the PhD (ICER: 2014 INT\$549.06 per QALY gained) suggest

that HIVST would be potentially cost-effective in these other countries, especially as the majority have larger HIV budgets and stronger economies.

HIV testing has been offered in health facilities for over a decade but uptake remains low (Staveteig et al., 2013). Community-based HIV testing strategies have been found to be popular and cost-effective but not widely implemented. They require trained healthcare professions, operating during standard working hours and extensive resources to transport equipment and consumables to the community in order to deliver the service (Suthar et al., 2013). HIVST offers a potential solution to increasing the feasibility of delivering community-based HIV testing. It can be delivered by trained volunteers, with users accessing the service at times that are convenient to them and delivered with minimal infrastructure and service delivery support. One of the main deterrents to accessing facility and community HIV testing services, especially by men, is the lack of privacy and confidentially offered an HIV testing process that requires another person to communicate the result. HIVST does not require this. Policy makers in the region will need to seriously take on board this issue and the potential solution HIVST offers if they are to increase uptake of HIV testing and re-testing.

The cost of HIV self-test kits remains high in comparison to the rapid finger-prick test kits used in health facilities. Additionally, I found the price of delivering HIV self-testing had an impact on its cost-effectiveness. Lowering the cost of HIVST kits would

also make implementation more affordable option for policy makers in the region. Over 100 million HIV tests are performed every year in Africa (WHO, 2011), the potential market for HIV self-test kits is large. Manufacturers of HIV self-test kits need to be aware that bringing easily useable and disposal kits into the market, at prices comparable to current finger-prick test kits, could have massive potential. Alternatively, International donors may need to consider subsidising the costs of HIV self-test kits or negotiating lower prices from manufactures through bulk procurement for low- and middle-income countries. If the cost of HIV self-test kits were 50% lower, the cost of delivering HIVST would fall to US\$6.72 per individual tested. The cost-effectiveness of HIVST would improve, and the cost of implementing the service will increase substantially.

Policy makers wishing to implement HIVST will need to be aware of the knock-on effects on HIV treatment services, with more individuals needing anti-retroviral therapy. Considering the financial implications of HIV testing without taking into account the impact on HIV treatment services would have grave consequences. Overcrowded, poorly functioning and poor quality HIV treatment services could in the long term have negative effects on individuals desire to learn their HIV status, since desire to learn one's HIV status will be in part driven by awareness of HIV services available. Of more concern could be the negative consequences of poorly provided HIV treatment services that could potentially impact on adherence and response to ART, potentially resulting in increased numbers defaulting treatment

after initiation and therefore at increased risk of developing resistance to the few anti-retroviral drug regimens available in the region.

Not all policy makers in sub-Saharan Africa support the provision of HIVST (Napierala Mavedzenge et al., 2011). There are concerns that without healthcare professionals being directly involved in the counselling and consenting before offering HIV testing, some individuals, especially women, may be coerced into testing, or that individuals may test but not link into HIV treatment services (Napierala Mavedzenge et al., 2011, Walensky and Bassett, 2011). HIVST is a relatively novel technology, and healthcare providers are still learning how to implement the service in Africa. Further work is needed to consider these issues, and whether alternative service delivery models may reduce potential risks whilst still being cost-effective. It is likely that as healthcare professionals become more experienced with HIVST, and if less restricted distribution models with HIV counselling provided through alternative approaches (e.g. mobile telephones) prove safe and effective, the costs of providing HIVST could also be substantially lower.

Awareness of HIV status is currently low in Malawi and in the other countries in the region. Implementing HIVST would increase awareness, but in the long-term would reduce the yield of HIV positives identified through an HIV self-testing service. As much of the benefit comes from detecting HIV positive individuals and timely entry into HIV treatment, the cost-effectiveness of HIVST will fall over time. Also over time

healthcare providers who implement HIVST will need to consider approaches to targeting their services to ensure that higher-risk and never previously tested individuals are reached.

HIVST is not intended to replace facility-based HTC strategies. Facility-based HTC will continue to be an important route to offering HTC, primarily because health facilities are attended by sicker populations (e.g. TB patients) and pregnant women (Hensen et al., 2012), who require access to HTC. The need to undertake confirmatory HIV testing and to link individuals into HIV treatment and prevention services (Choko et al., 2015a, MacPherson et al., 2014) suggests the optimal role of HIVST is to detect HIV infection earlier and to bring individuals into treatment before they are affected by an HIV associated illness like Tuberculosis (UNAIDS, 2013b, WHO, 2013b). HIVST could also complement facility-based HTC by improving uptake of testing amongst health facility attendees or utilising them as a route for reaching higher risk individuals, both of which are poorly done at present (MacPherson et al., 2012b, Byamugisha et al., 2011).

9.6 Original contribution to research from PhD

My PhD makes several important contributions to research. This is the first economic evaluation of HIVST undertaken in Malawi. In addition this is the first analysis of HIVST that uses real world health outcome and cost data. In the PhD I estimated the cost-effectiveness of implementing HIVST, undertook primary costing studies to estimate the real-world costs of providing HIVST and investigated the HRQoL of those who underwent HIV testing.

My PhD involved the development of a Chichewa version of the EuroQol EQ-5D tool. Chichewa is the predominant language in Malawi, and the development of a language appropriate tool will allow further cost-utility analyses to be undertaken in the region. In addition, I estimated a catalogue of EQ-5D utility scores for individuals affected by HIV and other medical conditions for use in cost-utility analysis, something that is currently lacking.

In the PhD I estimated the health provider costs of managing a range of health conditions in Queen Elizabeth Central hospital, Malawi. There has been no previous hospital costing study undertaken in the region. The estimates will be valuable for health economists wishing to undertake cost-effectiveness studies relating to a wide range of health conditions that result in hospital admission. The cost estimates from the PhD and data collection tools developed to extract medical resource use have been and are being used in a range of economic evaluation in Malawi.

9.7 Recommendations for future research

HIV self-testing is a new health technology globally and in sub-Saharan Africa. There is on going research in Malawi, which I am involved in, and in sub-Saharan Africa investigating alternative models of delivering HIVST, targeting specific populations (e.g. sex workers, sexual partners of antenatal clinic attendees) or exploring alternative approaches to increasing linkage into HIV treatment (e.g. financial incentives). These models could potentially deliver HIVST at lower costs, more effectively reach HIV positive individuals who are not aware of their HIV status, be associated with higher rates of linkage into HIV treatment services, or offer linkage into HIV prevention services (e.g. voluntary male medical circumcision) amongst those who test HIV negative. These alternative models will need to undergo cost-effectiveness analysis, and in some scenarios, will need to be compared to the HIVST delivery model evaluated in this PhD.

The majority of the HIVST research has been undertaken in Malawi, and further research is needed in other African countries. There are concerns regarding generalising the cost-effectiveness findings from one country to another (Drummond et al., 2009). Countries in East and Southern Africa have been most affected by the HIV epidemic and face comparable disease burdens. HIV services in the region, with the exception of South Africa, are delivered in comparable approaches and face similar financial and human resource constraints to those which Malawi faces. However, the populations may differ in their willingness to access HIVST, link into HIV treatment and prevention services or in the costs of delivering services. In

addition, policy makers may have differing willingness to pay thresholds for gains in health. Economic evaluations, along with research into effectiveness and impact on social harms, of HIVST may be needed in other countries in the region to better inform policy makers on the implications of implementing HIVST in their country.

Primary costing studies are often a necessity in resource-poor settings. National healthcare providers in sub-Saharan Africa often do not have the resources to undertake costing studies or the financial systems in place to provide cost estimates for policy making or researchers looking at undertaking economic evaluations. The WHO provides cost estimates for a range of healthcare resource use inputs from which economic evaluations can be performed (WHO-CHOICE). However, healthcare services are continually changing and newer health technologies are becoming increasingly available in the region. UNAIDS provides costing guidelines to assist researchers planning to cost HIV services (UNAIDS, 2011). In the PhD I estimated the unit costs for a range of healthcare resources, but further research is needed to estimate other health resources and to be done in different healthcare and country settings. This will allow further consideration of developing cost databases that could potentially be updated at regular intervals. Importantly, costing health resources requires further research to investigate whether services are being provided efficiently. A range of research methods is available to investigate the cost efficiency of healthcare provision, investigating the links between resource inputs and healthcare outputs. These will also have added value in provision of health services. For example in the studies undertaken in the PhD I make the assumption that

services are being provided in the most efficient manner. However, it is possible there may be financial gains for healthcare providers from economies of scale and scope. The next 10 years will see a large increase in the numbers of HIV positive individuals on anti-retroviral therapy, and the number of individuals who will have been on treatment for several years. Further research is needed to investigate how to provide these services at either lower cost or at higher quality. This may positively impact on the cost-effectiveness of implementing HIVST.

Health interventions should aim to tackle mortality and improve quality of life. There are increasing resources available to measure and monitor quality of life outcomes. The EQ-5D tool is one such measure and is one of the more widely used tools in the region. It has already been translated and approved by the EuroQol group for use in over 5 African languages. However its use in economic evaluations in the region is still limited. One reason is the lack of population tariff sets from which to derive EQ-5D utility scores from responses given by individuals to the descriptive component of the tool. A local population tariff set has the advantage that it reflects the preferences of the population who will ultimately benefit from the decisions regarding what health services to implement. There is no current Malawian population tariff set and undertaking research to develop one is a research priority. Importantly, it may encourage health economists and grant funders to increase the number of economic evaluations that are performed in the country. Additionally having additional tariff sets for countries in the region will allow investigation of whether populations in the region value health outcomes in similar ways. If so, it

might suggest that a regional tariff, or the use a tariff set performed in another country would be fit for use in a country that lacks a tariff set (Norman et al., 2009).

The realisation that there is a link between individual treatment and population transmission risks (Tanser et al., 2013) and that link depends on the strategy employed at the individual-level (Granich et al., 2009) necessitates further examination of optimal modelling approaches to incorporate both the individual and population consequences of different strategies. Dynamic transmission models will often show that interventions are more cost-effective when targeting communicable diseases than static models. This is mainly because dynamic models represent the impact on reduction of future infections more thoroughly (Jit and Brisson, 2011). They will capture the additional health gains and cost savings through reductions in the future incidence of the infection. In sub-Saharan Africa where resources are especially limited, representing this reduction of future infections is essential to aid optimal use of resources. The management of HIV in sub-Saharan Africa has entered a new phase with optimism surrounding the potential role of anti-retroviral drugs to treat individuals, and to prevent transmission (Cohen et al., 2011). In order to provide policy makers with robust estimates of an increasing number of potential strategies HIV cost-effectiveness modelling approaches need to incorporate all possible recent evidence on costs and consequences of these different interventions.

9.8 Reflection of research training during PhD

The PhD allowed me to develop a range of research skills including experience in undertaking public health and health economics research in resource-poor settings, managing a research team consisting of nine personnel, and further developing my research skills in writing, oral presentation, econometrics and decision-analytic modelling.

During the PhD I managed a team of nine Malawian staff for two years. They were responsible for recruitment and follow-up of research participants, including interviewing participants to complete data collection tools. I gained experience in training and managing research personnel. In addition, I developed and piloted a range of data collection tools (shown in Appendix). An important lesson I learned was that I could have undertaken the research at lower cost and more efficiently. The significant proportion of the data collected had little value in answering the objectives of the PhD. In addition I could have undertaken the study with fewer research personnel.

One of the most important lessons learned during the PhD was the need to be adaptive. The hospital cohort study presented in Chapter 7 of the PhD was not part of the original PhD research objectives. Initially I had planned to collect hospital resource use data from the HIV treatment cohort (Chapter 6) but the small sample sizes meant there would be too few occurrences of these events to obtain

meaningful data. Additionally, non-medical personnel asking participants detailed questions about their hospital admission was not found reliable. The hospital cohort study was developed to resolve these two issues, and resulted in more precise estimates of hospital care.

An important lesson learned about undertaking research in resource-poor settings related to the difficulty of following up participants in the community. The HIV treatment cohort (described in Chapter 6) was recruited at the primary health clinics and seen on each visit to the clinic. Of those who started ART, 33% were lost to follow-up and 7% had their care transferred to another clinic. In the study I recorded a number of contact details for participants, and made three attempts to contact them. The high attrition rate for community-based studies in Malawi is unavoidable because the population are mobile, often for employment and unemployment reasons. In retrospect I probably would have recruited a larger sample for the study to ensure more individuals had at least one year of follow-up on ART.

9.9 Conclusion

In conclusion I found implementing HIV self-testing in Malawi is a cost-effective strategy, supporting other research showing it to be an effective approach to increasing uptake of HIV testing and timely entry into HIV care. I found HIVST to be delivered at comparable cost to facility-based HTC. I estimated the costs of providing HIV treatment and found that overall there were no differences between those who had previously accessed HIVST and those who had accessed facility-based HTC. I found that individuals with advanced HIV disease report poorer quality of life, and that individuals improve once they start anti-retroviral therapy. I also demonstrate the high costs of providing hospital care and the poor quality of life in HIV positive individuals suffering HIV associated illnesses. The cost-effectiveness findings of the PhD provide valuable information to policy makers in Malawi, and potentially in sub-Saharan Africa, on the value of implementing HIVST, and indicate a number of areas for on-going research.

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APPENDIX I: Malawi and Warwick
Ethics committee approval
documents



CERTIFICATE OF ETHICS APPROVAL

This is to certify that the College of Medicine Research and Ethics Committee (COMREC) has reviewed and approved a study entitled:

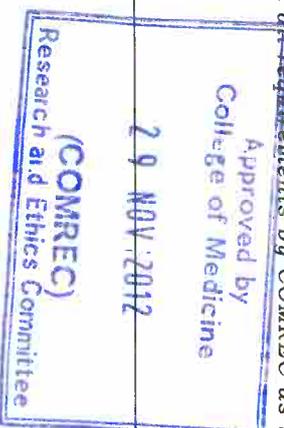
P.08/12/1272 – Cost-effectiveness of Home based HIV testing and Counseling in Blantyre, Malawi by Dr. H. Maheswaran

On 29 November 2012

As you proceed with the implementation of your study, we would like you to adhere to international ethical guidelines, national guidelines and ~~other~~ requirements by COMREC as indicated on the next page

Dr. G. Kalanda- Chairperson (COMREC)

A handwritten signature in blue ink, appearing to be 'G. Kalanda'.



Date 29 November 2012

21st February 2013

Warwick
Medical School

PRIVATE

Dr Hendramoorthy Maheswaran
Health Sciences
WMS
University of Warwick
Coventry
CV4 7AL

Dear Maheswaran,

Study Title and BSREC Reference: *Cost-effectiveness of home-based HIV testing and counselling in Blantyre, Malawi (Cost-HTC)*, REGO-2013-061

Thank you for submitting the above-named project to the University of Warwick Biomedical and Scientific Research Ethics Sub-Committee for Chair's approval.

I am pleased to confirm that your application meets the required standard which means that full approval is granted and your study may commence.

I take this opportunity to wish you success with the study and to remind you any substantial amendments require approval from the committee before they can be made. Please keep a copy of the original signed version of this letter with your study documentation.

Yours sincerely,



Dr David Davies
Chair
Biomedical and Scientific
Research Ethics Sub-Committee

**Biomedical and Scientific
Research Ethics Subcommittee**
Enquiries: Amy Ismay
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APPENDIX II: WHO and CDC
classification of HIV clinical stage

WHO Clinical Staging, 2007	CDC
<p style="text-align: center;"><u>Clinical Stage 1</u></p> <ul style="list-style-type: none"> -Asymptomatic -Persistent generalized lymphadenopathy <li style="text-align: center;">+ <li style="text-align: center;"><u>Either</u> -CD4+ T-lymphocyte count of ≥ 500 cells/μL -CD4+ T-lymphocyte % of total lymphocytes of ≥ 29 	<p style="text-align: center;"><u>Category A</u></p> <ul style="list-style-type: none"> -Asymptomatic -Acute HIV -Persistent Generalised Lymphadenopathy
<p style="text-align: center;"><u>Clinical Stage 2</u></p> <ul style="list-style-type: none"> -Moderate unexplained weight loss (<10% of body weight) -Recurrent respiratory infections -Herpes zoster -Angular cheilitis -Recurrent oral ulceration -Papular pruritic eruptions -Seborrheic dermatitis -Fungal nail infections <li style="text-align: center;">+ <li style="text-align: center;"><u>Either</u> -CD4+ T-lymphocyte count of 200--499 cells/μL -CD4+ T-lymphocyte % of total lymphocytes of 14--28. 	<p style="text-align: center;"><u>Category B</u></p> <ul style="list-style-type: none"> -Bacillary angiomatosis -Oropharyngeal candidiasis -Vulvovaginal candidiasis, persistent or resistant -Pelvic inflammatory disease (PID) -Cervical dysplasia/cervical carcinoma in situ -Hairy leukoplakia, oral -Herpes zoster involving two or more episodes or at least one dermatome -Idiopathic thrombocytopenic purpura -Constitutional symptoms, such as fever (>38.5°C) or diarrhea lasting >1 month -Peripheral neuropathy
<p style="text-align: center;"><u>Clinical Stage 3</u></p> <ul style="list-style-type: none"> -Unexplained severe weight loss (>10% of body weight) -Unexplained chronic diarrhea for >1 month -Unexplained persistent fever for >1 month -Persistent oral candidiasis (thrush) -Oral hairy leukoplakia -Pulmonary tuberculosis (current) -Severe presumed bacterial infections -Acute necrotizing ulcerative stomatitis, gingivitis, periodontitis -Unexplained anemia -Neutropenia -Chronic thrombocytopenia 	<p style="text-align: center;"><u>Category C</u></p> <ul style="list-style-type: none"> -Bacterial pneumonia, recurrent -Candidiasis of the bronchi, trachea, or lungs -Candidiasis, esophageal -Cervical carcinoma, invasive, confirmed by biopsy -Coccidioidomycosis, disseminated or extrapulmonary -Cryptococcosis, extrapulmonary -Cryptosporidiosis, chronic intestinal (>1 month in duration) -Cytomegalovirus disease (other than liver, spleen, or nodes) -Encephalopathy, HIV-related -Herpes simplex: chronic ulcers (>1 month in duration), or bronchitis, pneumonitis, or esophagitis -Histoplasmosis, disseminated or extrapulmonary -Isosporiasis, chronic intestinal (>1-month in duration) -Kaposi sarcoma -Lymphoma, Burkitt, immunoblastic, or primary central nervous system -<i>Mycobacterium avium</i> complex (MAC) or <i>Mycobacterium kansasii</i>, disseminated or extrapulmonary -<i>Mycobacterium tuberculosis</i>, pulmonary or extrapulmonary -<i>Mycobacterium</i>, other species or unidentified species, disseminated or extrapulmonary -<i>Pneumocystis jiroveci</i> (formerly <i>carinii</i>) pneumonia (PCP) -Progressive multifocal leukoencephalopathy (PML) -<i>Salmonella</i> septicemia, recurrent (nontyphoid) Toxoplasmosis of brain -Wasting syndrome
<p style="text-align: center;"><u>Clinical Stage 4</u></p> <ul style="list-style-type: none"> -HIV wasting syndrome -<i>Pneumocystis</i> pneumonia -Recurrent severe bacterial pneumonia -Chronic herpes simplex infection -Esophageal candidiasis -Extrapulmonary tuberculosis -Kaposi sarcoma -Cytomegalovirus infection -Central nervous system toxoplasmosis -HIV encephalopathy -Cryptococcosis, extrapulmonary (including meningitis) -Disseminated nontuberculosis mycobacteria infection -Progressive multifocal leukoencephalopathy -Candida of the trachea, bronchi, or lungs -Chronic cryptosporidiosis (with diarrhea) -Disseminated mycosis -Recurrent nontyphoidal <i>Salmonella</i> bacteremia -Lymphoma (cerebral or B-cell non-Hodgkin) -Invasive cervical carcinoma -Atypical disseminated leishmaniasis -Symptomatic HIV-associated nephropathy -Symptomatic HIV-associated cardiomyopathy -Reactivation of American trypanosomiasis <p>OR</p> <p>CD4+ T-lymphocyte count of <200 cells/μL</p> <p>OR</p> <p>CD4+ T-lymphocyte percentage of total lymphocytes of <14</p>	

**APPENDIX III: Uptake, Accuracy,
Safety, and Linkage into Care over
Two Years of Promoting Annual
Self-Testing for HIV in Blantyre,
Malawi: A Community-Based
Prospective Study**

Augustine T. Choko, Peter MacPherson, Emily L. Webb, Barbara A. Willey, Helena Feasy, Rodrick Sambakunsi, Aaron Mdolo, Simon D. Makombe, Nicola Desmond, Richard Hayes, **Hendramoorthy Maheswaran**, Elizabeth L. Corbett. **Uptake, Accuracy, Safety, and Linkage into Care over Two Years of Promoting Annual Self-Testing for HIV in Blantyre, Malawi: A Community-Based Prospective Study.** *PLOS Med* 12(9): e1001873. doi:10.1371/journal.pmed.1001873.

RESEARCH ARTICLE

Uptake, Accuracy, Safety, and Linkage into Care over Two Years of Promoting Annual Self-Testing for HIV in Blantyre, Malawi: A Community-Based Prospective Study

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Data Availability Statement: Data are publicly available at [10.17037/DATA.7](https://doi.org/10.17037/DATA.7) through London School of Hygiene & Tropical Medicine Data Compass <http://datacompass.lshtm.ac.uk/>.

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Abstract

Background

Home-based HIV testing and counselling (HTC) achieves high uptake, but is difficult and expensive to implement and sustain. We investigated a novel alternative based on HIV self-testing (HIVST). The aim was to evaluate the uptake of testing, accuracy, linkage into care, and health outcomes when highly convenient and flexible but supported access to HIVST kits was provided to a well-defined and closely monitored population.

Methods and Findings

Following enumeration of 14 neighbourhoods in urban Blantyre, Malawi, trained resident volunteer-counsellors offered oral HIVST kits (OraQuick ADVANCE Rapid HIV-1/2 Antibody Test) to adult (≥ 16 y old) residents ($n = 16,660$) and reported community events, with all deaths investigated by verbal autopsy. Written and demonstrated instructions, pre- and post-test counselling, and facilitated HIV care assessment were provided, with a request to return kits and a self-completed questionnaire. Accuracy, residency, and a study-imposed requirement to limit HIVST to one test per year were monitored by home visits in a systematic quality assurance (QA) sample.

Overall, 14,004 (crude uptake 83.8%, revised to 76.5% to account for population turnover) residents self-tested during months 1–12, with adolescents (16–19 y) most likely to test. 10,614/14,004 (75.8%) participants shared results with volunteer-counsellors. Of 1,257 (11.8%) HIV-positive participants, 26.0% were already on antiretroviral therapy, and 524 (linkage 56.3%) newly accessed care with a median CD4 count of 250 cells/ μ l

Competing Interests: The authors have declared that no competing interests exist.

Abbreviations: aOR, adjusted odds ratio; ART, antiretroviral therapy; HIVST, HIV self-testing; HTC, HIV testing and counselling; IQR, interquartile range; OR, odds ratio; QA, quality assurance; SCQ, self-completed questionnaire.

(interquartile range 159–426). HIVST uptake in months 13–24 was more rapid (70.9% uptake by 6 mo), with fewer (7.3%, 95% CI 6.8%–7.8%) positive participants. Being “forced to test”, usually by a main partner, was reported by 2.9% (95% CI 2.6%–3.2%) of 10,017 questionnaire respondents in months 1–12, but satisfaction with HIVST (94.4%) remained high. No HIVST-related partner violence or suicides were reported. HIVST and repeat HTC results agreed in 1,639/1,649 systematically selected (1 in 20) QA participants (99.4%), giving a sensitivity of 93.6% (95% CI 88.2%–97.0%) and a specificity of 99.9% (95% CI 99.6%–100%). Key limitations included use of aggregate data to report uptake of HIVST and being unable to adjust for population turnover.

Conclusions

Community-based HIVST achieved high coverage in two successive years and was safe, accurate, and acceptable. Proactive HIVST strategies, supported and monitored by communities, could substantially complement existing approaches to providing early HIV diagnosis and periodic repeat testing to adolescents and adults in high-HIV settings.

Introduction

Sub-Saharan Africa is still disproportionately affected by the HIV epidemic, accounting for 71% (24.7 million) of people living with HIV globally; in 2013, 71% of the 2.1 million global new infections, and 73% of the 1.5 million HIV-related deaths, occurred in the region [1]. Despite major investments in HIV testing, treatment, and prevention programmes, only one-quarter of adult Africans have had a recent HIV test, and half of people living with HIV in sub-Saharan Africa do not know they are HIV positive [1–3].

Barriers to HIV testing and counselling (HTC) and initiation of antiretroviral therapy (ART) include overly busy health facilities, concerns about lack of confidentiality and privacy, and high out-of-pocket costs [4–6]. Community-based HTC approaches, including home-based and mobile services, can overcome some of these problems, achieving high population uptake of HTC [7–10]. Compared to facility-based approaches, community-based HTC provides earlier HIV diagnosis and increases uptake of couples testing [4,5]. Nevertheless, evaluation of community-based HTC and HIV services has raised concerns about cost and sustainability [11,12], especially for delivering services to more rural settings [12,13]. For example, despite community-based HTC being national policy in Malawi and Zimbabwe, only 2% of Malawians and 4% of Zimbabweans in 2010 were reached by mobile or door-to-door services [3].

HIV self-testing (HIVST), defined as an individual performing and interpreting his/her own HIV test [14], has the potential to be implemented at a wide scale with a minimal requirement for trained health-workers. As such, HIVST could improve population coverage of regular HTC, recognised as being a critical component of all strategies to further intensify HIV prevention and care in countries with generalised HIV epidemics. We have previously demonstrated very high uptake and accuracy of HIVST in a small feasibility study [7]. However, critical, unanswered questions that need to be addressed before considering large-scale interventions based on HIVST include the following: what levels of HIVST uptake and accuracy can be achieved with population-wide implementation, and do safety concerns, including the potential for coercive testing, suicide, and gender-based violence, preclude implementation [15–17]?

We, therefore, investigated the uptake, accuracy, and outcomes of implementation of community-wide HIVST delivered by trained resident volunteer-counsellors in Blantyre, Malawi [18]. A delivery system based on service provision from the houses of volunteer-counsellors was designed. The aim was to evaluate uptake, accuracy, linkage into care, and health outcomes when highly convenient and flexible but supported access to HIVST kits was provided to a well-defined and closely monitored population. HIVST services were flexibly provided, with facilitated access to HIV care for those willing to share positive results. Participants could opt for support ranging from standard provider-conducted HTC to HIVST at home either in complete privacy or assisted by an attendant volunteer-counsellor.

Methods

Ethical Statement

Ethical approval was obtained from the College of Medicine Ethics Review Committee, University of Malawi; London School of Hygiene & Tropical Medicine; and Liverpool School of Tropical Medicine. All participants opting for HIVST provided written (or witnessed thumbprint) informed consent.

Study Design

This study was a prospective study nested within a cluster-randomised trial (ISRCTN02004005) comparing health outcomes between 14 clusters randomised to HIVST and 14 clusters randomised to routine (facility-based) HTC [18]. The data reported here relate only to the 14 clusters where HIVST was provided. HIVST was provided for a 2-y period in any given cluster, starting between February and May 2012; active surveillance for harms continued for 4–6 mo after the 2-y HIVST period.

Study Setting and Study Population

The study took place in three high-density informal residential settlements in urban Blantyre, as described elsewhere [10,18]. In brief, neighbourhood clusters were defined on the basis of existing community health worker catchment areas and enumerated between April and June 2011. In clusters randomised to the intervention arm, community-based HIVST was available for all adults (≥ 16 y). Services were provided by two resident volunteer-counsellors in each cluster of ~1,200 adults; the volunteer-counsellors were identified using participatory methods [19] and were paid a monthly stipend similar to that of Malawi Ministry of Health community health workers. Volunteer-counsellors received Malawi Ministry of Health HTC training and study-specific HIVST and protocol training. Targets within each cluster were to reach >80% of adult residents each year through promoting HIVST door to door and leafleting. Participants could opt to test at home, with or without the volunteer-counsellor present to provide help as needed.

HIV Self-Testing Kit Provision

Participants (individuals or couples) received pre-test counselling, received instructions on performing HIVST, and were asked to demonstrate understanding using a cotton bud and vial of water in place of the kit itself. An anonymous self-completed questionnaire (SCQ) was provided with an opaque envelope for return of the used kit and SCQ, either to the volunteer-counsellor or into a locked “ballot” box kept at the volunteer-counsellor’s house (S1 Questionnaire). The test kit used was OraQuick ADVANCE Rapid HIV-1/2 Antibody Test (OraSure Technologies). User instructions were modified and included pictures. The ten-item SCQ included questions about the self-read HIVST result, satisfaction indicators, and the results of the individual’s most

recent previous HIV test, if applicable. The question “If you were forced to test, who forced you?” was used to define coercion. Residents were asked to limit HIVST to one test in each 12-mo time period. Post-test counselling was recommended, but not required. All participants received a “self-referral card” allowing them to directly access one of two study clinics, but were encouraged to share results with their resident volunteer-counsellor for standard results-based post-test counselling and referral. A modified counselling protocol (including written information on all local HIV care options) was used for participants unwilling to share their results.

Within seven of the 14 study clusters, a second cluster-randomised controlled trial was conducted that investigated the effect of optional home-based initiation of HIV care (ART eligibility assessment and 2 wk of treatment including ART if indicated) on uptake of ART [10]. This intervention was extended to all 14 HIVST clusters from January 2013 onwards.

At health facilities, a study nurse provided confirmatory HIV testing (Determine HIV-1/2, Alere; and Uni-Gold Recombigen HIV, Trinity Biotech), CD4 count measurement (Cyflow SL-3 platform, Partec), tuberculosis screening (with isoniazid preventive therapy for those eligible [20]), WHO clinical staging, and cotrimoxazole. Participants who met national ART eligibility criteria (CD4 count < 350 cells/ μ l or WHO stage 3 or 4 or breastfeeding or pregnant) were registered for ART.

Ascertainment of Outcomes

Volunteer-counsellors recorded each individual/couple with nature of support provided for the test, age, and sex of the individual(s), and whether they had tested before. Estimates of linkage into care were based on the number of participants who disclosed positive results to counsellors during the first 12 mo compared to the number of participants accessing study clinic confirmatory testing and HIV care over the same time period. Confirmation of participation in the study was based on presentation of the self-referral card.

Recording Social Harms

In each cluster, four community members (key informants) provided weekly reports of all deaths and any known episodes of intimate partner violence. Study nurses conducted verbal autopsies for all reported deaths, including temporal relatedness to HIVST.

Quality Assurance

A systematic sample of HIVST participants was selected for home visit by study nurses, aiming for minimum 5% coverage. Nurses selected from participants tested in the previous week using counsellors' HIVST logs that recorded one participant or couple per row, with 20 rows per page. A random number between 1 and 20 was generated on a weekly basis and provided to nurses on the day of use. Nurses selected the corresponding row number (e.g., each row 11 participant if the number 11 had been supplied that week). If the selected number exceeded the number of participants on any given page, then the nurses continued counting out from row 1 of the same page until that week's number was reached. Checks during the home visit included age, confirmation of residency, whether or not HIVST kits had been used, and self-read result, with offer of confirmatory testing (finger-prick blood parallel testing with Determine HIV-1/2 and Uni-Gold Recombigen HIV).

Statistical Analysis and Sample Size

Stata version 13.0 (StataCorp) and R version 2.15.3 (R Foundation for Statistical Computing) were used for analyses. The sample size for the parent cluster-randomised trial was determined

by the primary outcome (cluster-level tuberculosis case notification rates) and not by HIVST uptake or linkage. Of note, however, primary outcome assumptions were that population uptake of HIVST would be $\geq 70\%$ per year [7,8], with $\geq 80\%$ linkage into HIV care [21] and HIVST accuracy of $\geq 90\%$ [7].

The proportion of residents accepting HIVST was estimated both overall and within sex, age, and neighbourhood strata, using population denominators from the study census (i.e., proportions were calculated using a fixed denominator that was determined before the start of the study, rather than as cumulative incidence, which would have required individual cohort follow-up for all residents) conducted in the year preceding the rollout of the intervention. Since crude uptake in some sex-age-neighbourhood subgroups exceeded the population denominators from the study census, the number of residents accepting HIVST within any single sex-age-neighbourhood subgroup was capped at the census denominator for that subgroup to provide an adjusted uptake.

The first estimate of linkage into care was calculated with the number of participants who presented at a study clinic with a volunteer-counsellor-provided self-referral card as the numerator and the number of participants who disclosed a positive HIV result to the volunteer-counsellor as the denominator. The second estimate was calculated after adjusting for a proportion assumed to be already aware of their positive HIV status and in care.

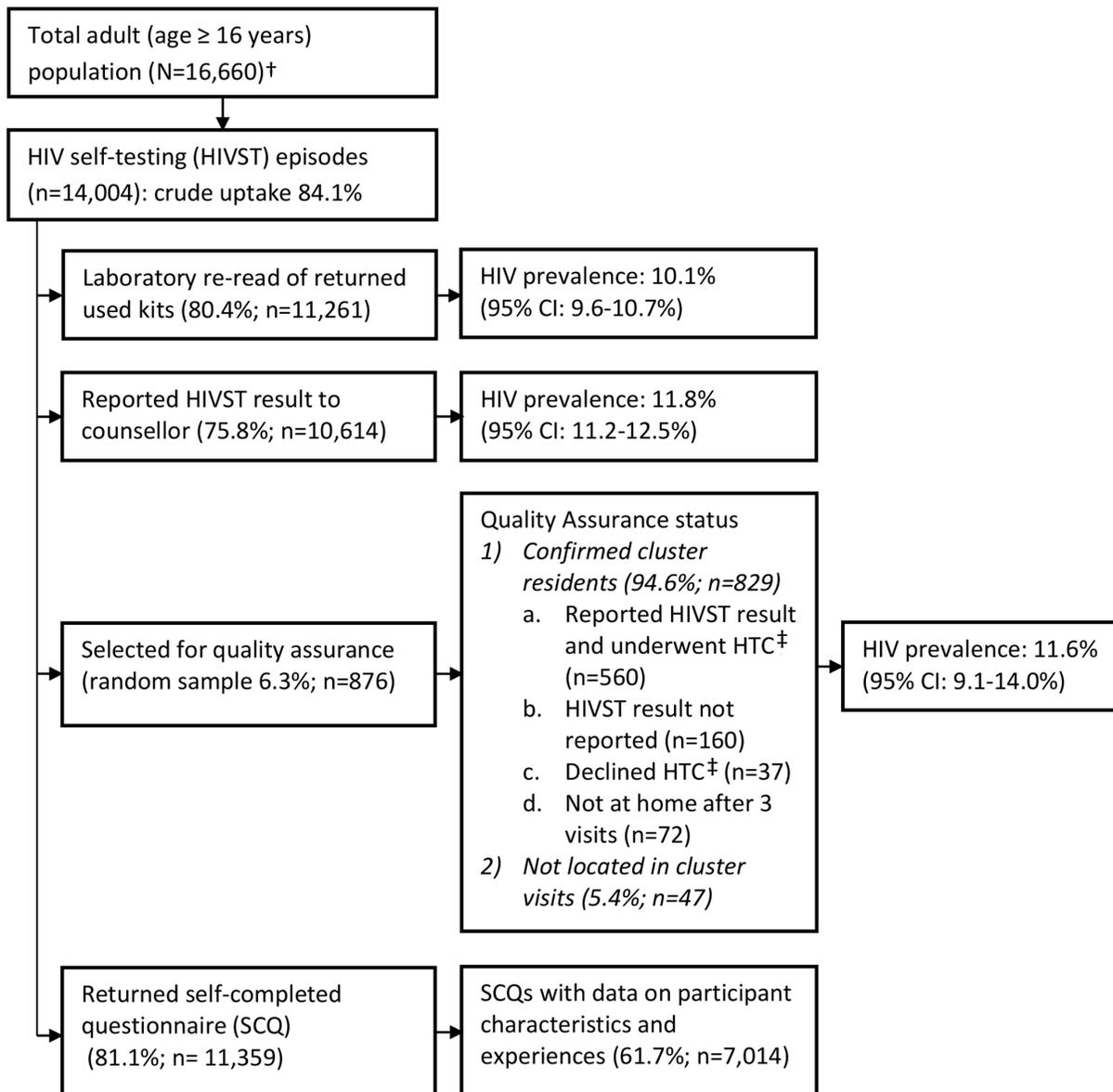
Participant characteristics in months 1–12 and months 13–24 were compared using design-based F-tests calculated by applying the second-order Rao and Scott correction [22,23] to the usual Pearson chi-squared test statistic for two-way tables to allow for the clustered sampling design. The accuracy of self-reported HIVST results in quality assurance (QA) participants was assessed using finger-prick rapid diagnostic test results to calculate sensitivity, specificity, and exact binomial 95% confidence intervals. Univariate and multivariate random effects logistic regression models accounting for clustering at the neighbourhood level were fitted in order to obtain odds ratios (ORs) and 95% CIs for associations between prespecified exposures of interest (age, sex, previous testing, testing alone/with partner, self-read HIVST result) and reported coercion. A substantial proportion of SCQ participants had missing data for at least one of the exposures of interest. Comparison of characteristics of participants with and without complete data showed no significant differences, and, therefore, findings from complete case analysis are presented [24]. Sensitivity analysis was undertaken using multiple imputation methods to handle missing data.

Results

Uptake of HIVST

In 2011, 16,660 adults (16 y or older) were enumerated in the 14 HIVST clusters. During months 1–12 and months 13–24, a total of 14,004 (84.1%) and 13,785 (82.7%) participants accessed the HIVST service, respectively (Figs 1 and 2). Compared to months 1–12, the second year saw higher proportions of men (46.1% versus 43.8%; $p = 0.057$), adolescents (24.7% versus 22.2%; $p < 0.001$), participants with a sexual partner (59.3% versus 37.5%; $p < 0.001$), and participants who had tested for HIV ever (82.2% versus 64.9%, and for testing within the last 12 mo, 61.2% versus 27.3%; $p < 0.001$ for both) (Table 1).

The estimated uptake of HIVST, based on study census denominators, was 84.1% and 82.7% in months 1–12 and months 13–24, respectively. Crude uptake in some age-sex-neighbourhood subgroups (notably among adolescent women [aged 16–19 y]) exceeded population denominators from the census conducted in the year preceding the study (Table 2). Capping uptake in any single age-sex-neighbourhood subgroup at 100% led to revised uptake estimates of 76.5% and 74.4% in months 1–12 and months 13–24, respectively. With both approaches,



† Denominator was not adjusted for migration

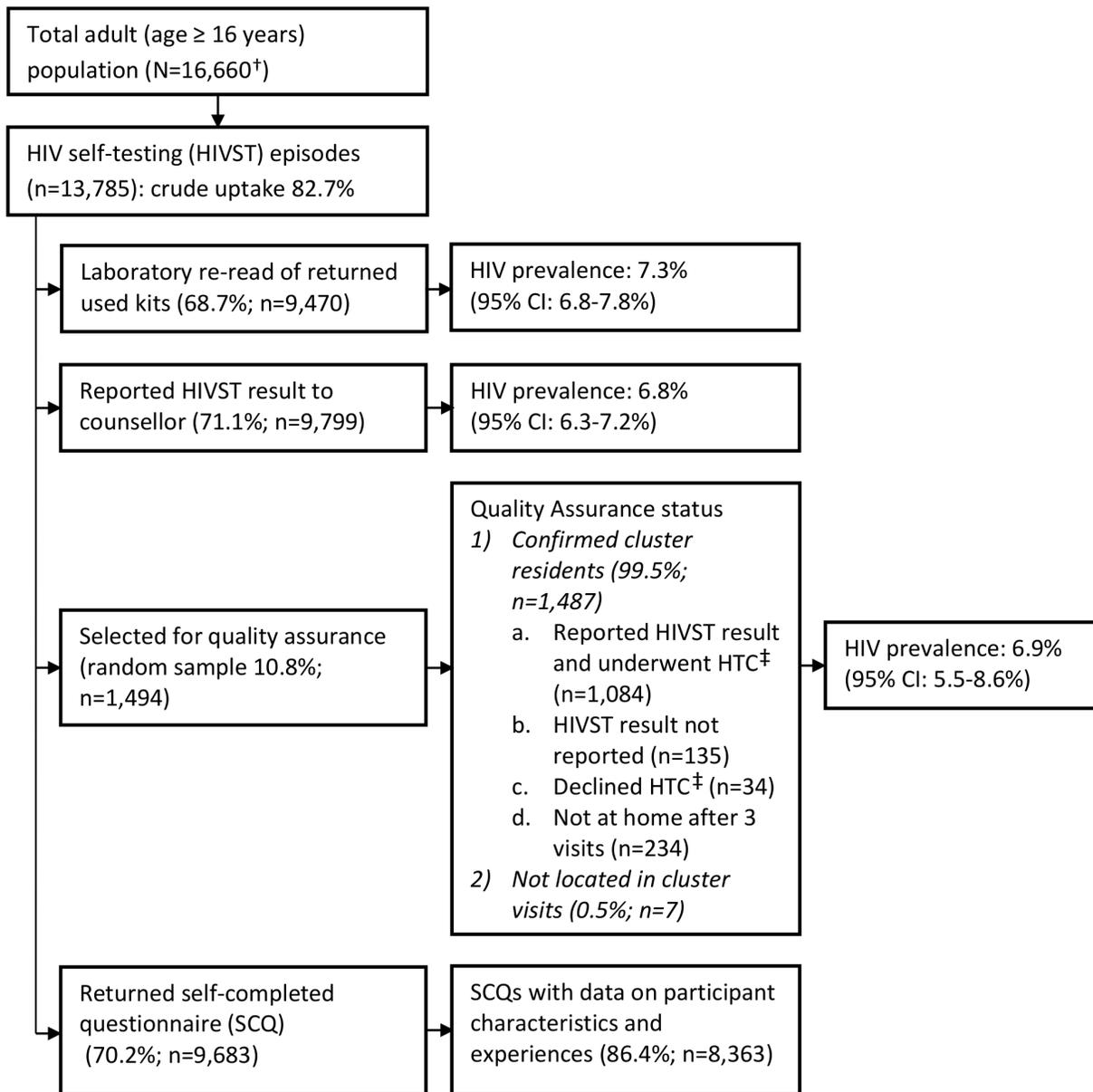
‡ HTC: HIV testing and counselling performed by finger-prick parallel rapid testing by a study nurse.

Fig 1. Flow of study participants in months 1–12 of HIV self-testing.

doi:10.1371/journal.pmed.1001873.g001

there was significantly higher uptake each year amongst women than men, and for progressively younger age groups ($p < 0.001$ for both).

The time course of HIVST uptake within each annual period for which HIVST was restricted to a single test per person (Methods and QA results) is shown by time point, sex, and age group in Fig 3. In comparison to months 1–12, uptake during the second year of availability was more rapid, with a higher proportion accessing services soon after they became available (Fig 3), notably so for adolescents (aged 16–19 y).



† Denominator was not adjusted for migration.

‡ HTC: HIV testing and counselling performed by finger-prick parallel rapid testing by a study nurse.

Fig 2. Flow of study participants in months 13–24 of HIV self-testing.

doi:10.1371/journal.pmed.1001873.g002

HIV Prevalence in HIVST Participants and Linkage into Care

In the first year of HIVST, HIV prevalence in participants sharing results with volunteer-counsellors was 11.8% (95% CI 11.2%–12.5%), similar to the estimate from the rereading of returned kits (10.1%, 95% CI 9.6%–10.7%) (Fig 1). These estimates, however, were substantially higher than the respective figures from months 13–24, which were 6.8% (95% CI 6.3%–7.2%) and 7.3% (95% CI 6.8%–7.8%). HIV prevalence among self-testing participants (shown separately for men and women in Fig 4) was highest in the age group 40–49 y, with a pooled

Table 1. Characteristics of HIV self-testing participants in the first and second years of HIV self-testing availability.

Characteristic	Uptake of HIVST				p-Value ¹
	Month 1–12 (n = 14,004)		Month 13–24 (n = 13,785)		
	n	Percent	n	Percent	
Sex					
Male	6,124	43.8	6,339	46.1	0.057
Female	7,868	56.2	7,415	53.9	
Age group					
<20 y	3,107	22.2	3,399	24.7	<0.001
20–29 y	6,375	45.6	6,381	46.3	
30–39 y	2,995	21.4	2,806	20.4	
40–49 y	897	6.4	730	5.3	
≥50 y	597	4.3	431	3.1	
Able to read and write?					
No	742	5.3	366	2.7	0.002
Yes	13,124	94.7	13,090	97.3	
Ever previously tested for HIV?					
No	4,893	35.1	2,427	17.8	<0.001
Yes	9,040	64.9	11,205	82.2	
Tested for HIV in last 12 mo?					
No	10,034	72.7	5,217	38.8	<0.001
Yes	3,771	27.3	8,227	61.2	
Ever self-tested for HIV before?					
No	13,509	97.9	7,508	55.9	<0.001
Yes	290	2.1	5,931	44.1	
Tuberculosis symptoms?²					
No	13,301	96.8	13,357	98.7	<0.001
Yes	434	3.2	178	1.3	
Who initiated testing?³					
Client	5,405	38.8	3,163	23.1	0.075
Counsellor	8,543	61.2	10,506	76.9	
Have a sexual partner?					
No	6,826	62.5	3,520	40.7	<0.001
Yes	4,098	37.5	5,128	59.3	

¹p-Value from design-based F-test allowing for clustering by neighbourhood of residence.

²Having any of the following: cough of any duration, fever, night sweats, or weight loss.

³The client was considered to have initiated testing if the client visited the community counsellor explicitly to request an HIVST kit; the counsellor was considered to have initiated testing if the community counsellor visited the client at the client's home either by prior arrangement or during door to door rounds.

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prevalence of 22.5% (95% CI 19.4%–25.8%) in months 1–12; the pooled rate in participants aged 16–19 y (2.5%, 95% CI 1.9%–3.2%) was much lower.

In total, 75.8% (95% CI 75.1%–76.5%; 10,614/14,004) of participants who underwent HIVST in months 1–12 reported their result to a volunteer-counsellor, with 1,257 (11.8%, 95% CI 11.2%–12.5%) reporting a positive result. During this same time period, 524 participants presented for HIV care, with all presenting cards identifying them as having been directly

Table 2. Age-sex distribution of study population and study participants with and without adjustment by study census maximum denominators in age-sex-neighbourhood subgroups.

Characteristic	Study Census	Crude Uptake ¹			Revised Uptake ²		
		HIVST Uptake	Percent	p-Value	HIVST Uptake	Percent	p-Value
Months 1–12 of HIVST							
Total	16,660	14,004	84.1	—	12,751	76.5	—
Men							
16–19 y	1,196	1,223	102.3	<0.001	1,068	89.3	<0.001
20–29 y	3,326	2,686	80.8		2,646	79.6	
30–39 y	2,462	1,491	60.6		1,477	60.0	
40–49 y	926	412	44.5		412	44.5	
≥50 y	733	299	40.8		299	40.8	
Women							
16–19 y	1,306	1,884	144.3	<0.001	1,306	100.0	<0.001
20–29 y	3,487	3,682	105.6		3,313	95.0	
30–39 y	1,872	1,502	80.2		1,458	77.9	
40–49 y	627	484	77.2		461	73.5	
≥50 y	510	297	58.2		297	58.2	
Either sex or age missing	215	44	20.5		14	6.5	
Months 13–24 of HIVST							
Total	16,660	13,785	82.7	—	12,396	74.4	—
Men							
16–19 y	1,196	1,382	115.6	<0.001	1,104	92.3	<0.001
20–29 y	3,326	2,892	87.0		2,828	85.0	
30–39 y	2,462	1,448	58.8		1,412	57.4	
40–49 y	926	364	39.3		348	37.6	
≥50 y	733	235	32.1		232	31.7	
Women							
16–19 y	1,306	2,010	153.9	<0.001	1,301	99.6	<0.001
20–29 y	3,487	3,475	99.7		3,270	93.8	
30–39 y	1,872	1,354	72.3		1,331	71.1	
40–49 y	627	363	57.9		353	56.3	
≥50 y	510	195	38.2		190	37.3	
Either sex or age missing	215	67	31.2		27	12.6	

¹For each sex-age group, the number of people in that group who tested through HIVST (years: 2012–2014) is the numerator, and the total number of people in that sex-age group at the time of census (2011) is the denominator. Uptake estimate may exceed 100% due to population turnover.

²For each sex-age group, the numerator is the number of people in that group who tested through HIVST (years: 2012–2014) but now capped at the census denominator for that sex-age group for those age-sex groups where the number of testers exceeded the number of people in that group in the census. The denominator is the total number of people in that sex-age group at the time of census (2011).

³Chi-squared test for HIVST yes/no.

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referred in by a volunteer-counsellor (Fig 5). Thus, our first estimate of linkage is 41.7% (524 of 1,257 self-testing positive). However, in a subset of 3,016 participants in months 1–12, 2,380 (78.9%; 95% CI 77.4%–80.4%) responded to a question about ART. Of these, 219 (9.2%, 95% CI 8.1%–10.4%) were HIV positive, and 57 (26.0%, 95% CI 20.3%–32.4%) of these individuals stated that they were already on ART, consequently increasing our estimate of linkage to 56.3% (524/930). The median CD4 count from 415 participants (72.9% of those attending care) was

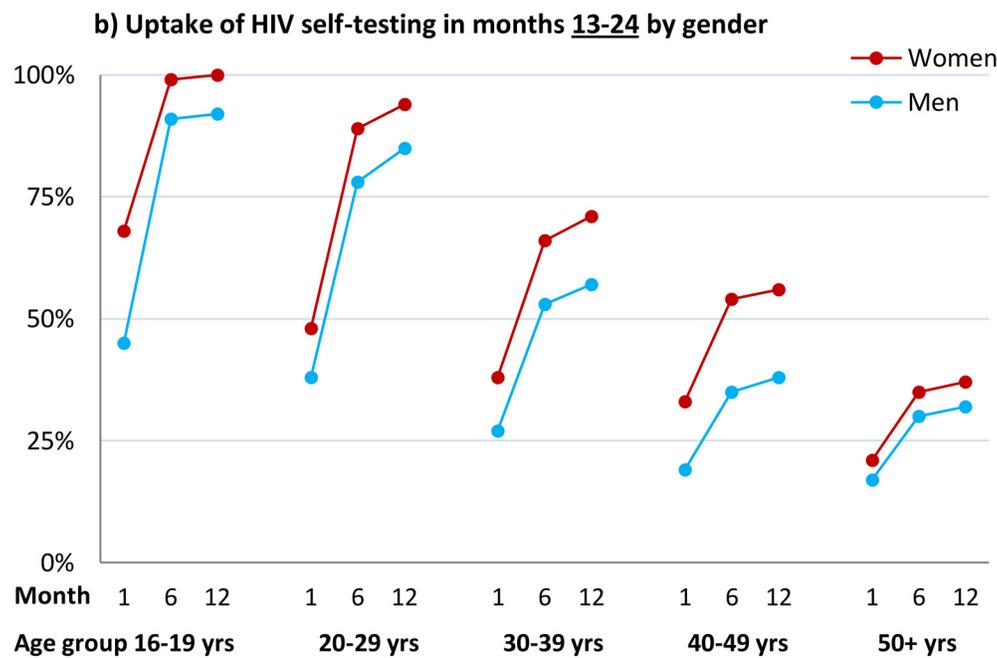
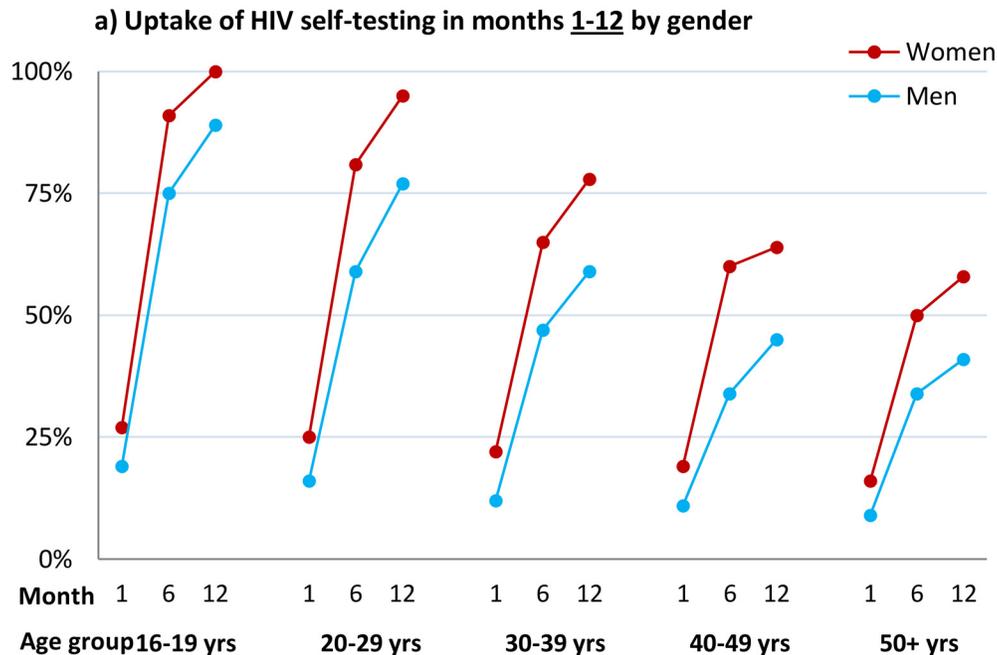


Fig 3. Cumulative uptake of HIV self-testing by sex, age group, and time point. (A) Cumulative uptake of HIVST during the first 12 mo of availability among all HIVST cluster residents by age and time point among men and women. HIVST uptake increased with time, rising to close to 100% by 12 mo in adolescents (age group 16–19 y); uptake for men was lower than for women at every time point. (B) Cumulative uptake of HIVST during months 13–24 of HIVST availability among all cluster residents by age and time point. Uptake defined as an individual having collected an HIVST kit from a community counsellor. Since crude uptake of HIVST exceeded 100% in some age-sex-neighbourhood subgroups, likely explained by migration, revised estimates were calculated where uptake in any single age-sex-neighbourhood subgroup was censored at 100%; study census data were used for denominators.

doi:10.1371/journal.pmed.1001873.g003

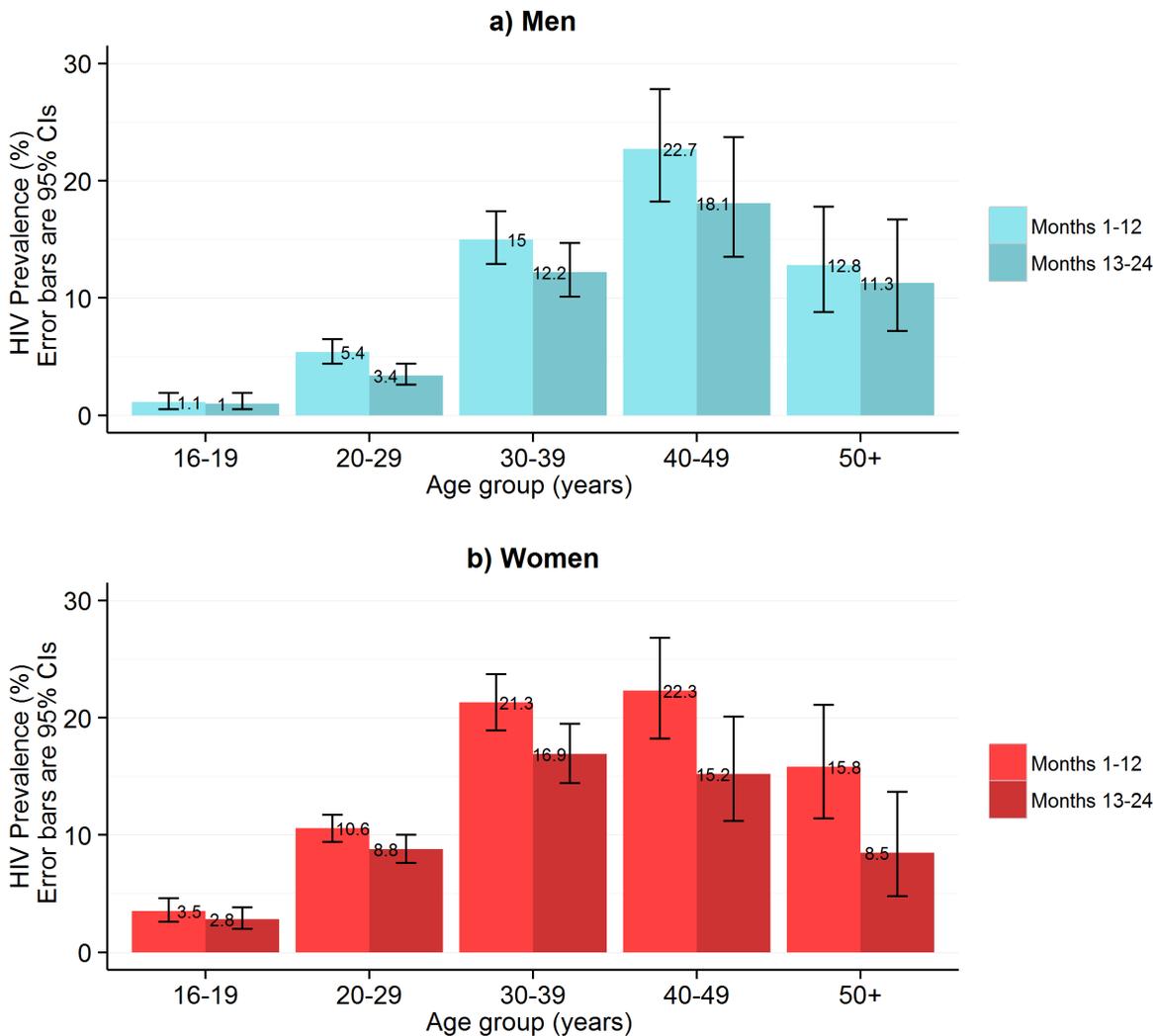


Fig 4. HIV prevalence in self-testing participants who returned used test kits by sex and age group and time of HIV self-testing availability. This figure shows HIV prevalence in HIVST participants for men (A) and women (B), stratified by time of HIVST availability. Bars show HIV prevalence (percent); error bars show 95% confidence intervals. Estimates are based on denominators determined through enumeration. Numerators were based on a reread of used and returned HIVST kits by a laboratory technician within 2 wk of use. Individuals were asked to test only once within each 12-mo time period, and retesting in people already aware of their positive HIV status was discouraged.

doi:10.1371/journal.pmed.1001873.g004

250 cells/ μ l (interquartile range [IQR] 159–426), with 66.3% (275/415) of CD4 counts being below 350 cells/ μ l.

Accuracy

A total of 2,361 (8.5%) of 27,789 HIVST participants were included in QA tracing (shown for separate years in Figs 1 and 2). Only 54 (2.3%) were found not to be cluster residents, while 1,649 (69.8%) agreed to confirmatory HIV testing. Results were positive in 141 (8.6%, 95% CI 7.2%–10.0%). Compared to stated HIVST results, there were 9/1,508 (0.6%) false negatives (including four participants already on ART) and 1/133 false positives, giving agreement of

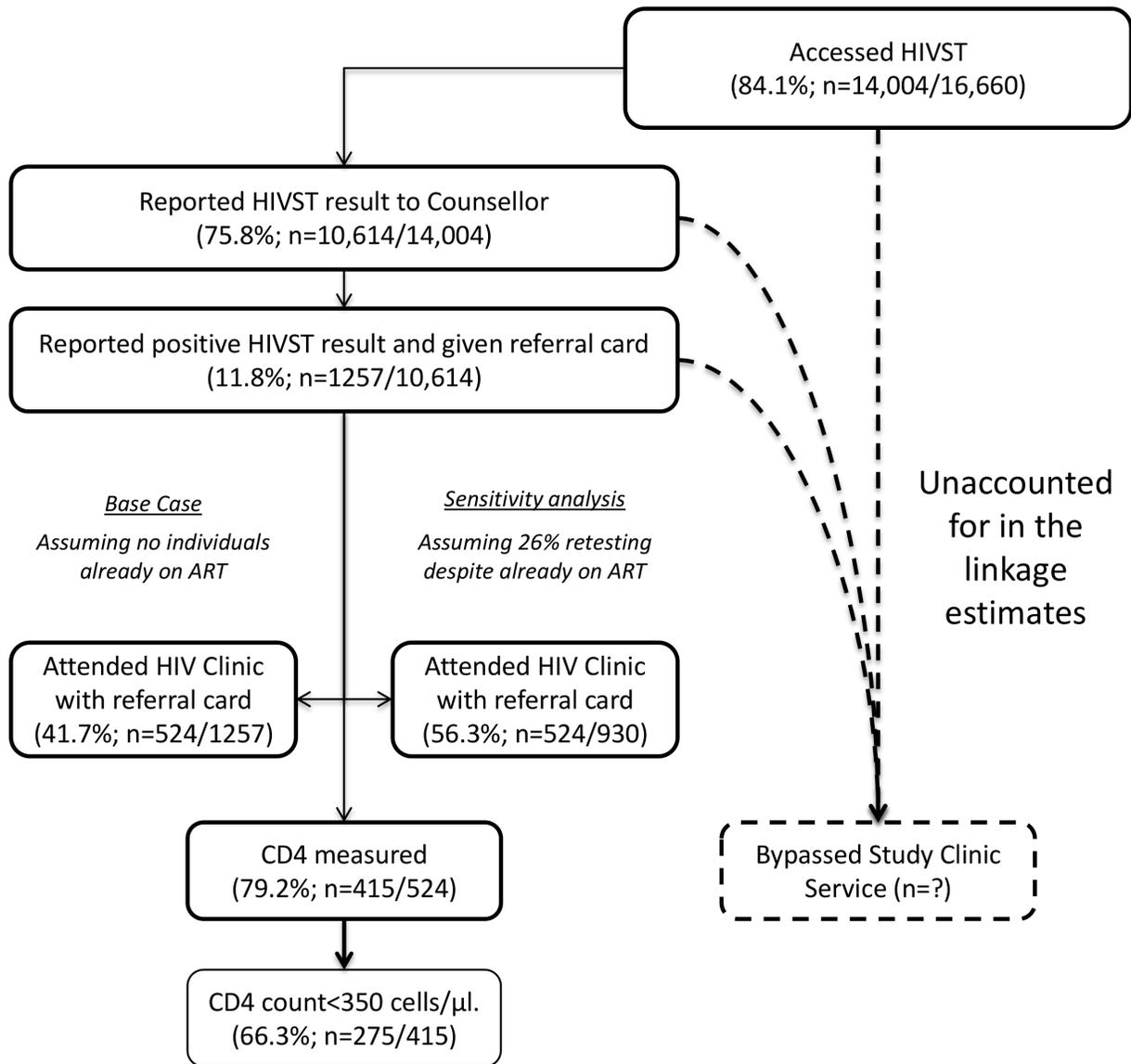


Fig 5. Linkage into HIV care after HIV self-testing (months 1–12).

doi:10.1371/journal.pmed.1001873.g005

1,639/1,649 (99.4%, 95% CI 98.9%–99.7%), sensitivity of 93.6% (95% CI 88.2%–97.0%), and specificity of 99.9% (95% CI 99.6%–100%) (Table 3).

Acceptability of Self-Testing and Social Harms, Including Reported Coercive Testing

During months 1–12, 81.1% (95% CI 80.5%–81.8%; 11,359/14,004) participants returned a SCQ to the counsellor, with 7,014 (61.7%) completing all key fields including self-read HIVST result, coercion, and acceptability indicators (S1 Questionnaire). There was acceptable internal consistency (Cronbach’s alpha = 0.64) for the four variables relating to acceptability: overall satisfaction with HIVST, whether or not they would recommend HIVST to friends and family, how hard it was to self-test, and whether or not they trusted the results of an oral test [25].

Table 3. Summary of quality assurance process and accuracy results.

Self-Reported HIV Self-Test Result	Index Test*		
	Positive	Negative	Total
Positive	132	1	133
Negative	9**	1,507	1,516
Total	141	1,508	1,649

Concordance: 99.4% (95% CI 98.9%–99.7%); sensitivity: 93.6% (95% CI 88.2%–97.0%); specificity: 99.9% (95% CI 99.6%–100.0%).

*Parallel testing with two rapid finger-prick blood tests by a trained nurse.

**Includes four participants later found to be already on ART.

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Acceptability indicators were high in all age group and sex strata, with 94.6% (1,446/1,635) reporting that they were “highly satisfied” with the HIVST process and 97.1% (6,683/6,883) reporting they would “definitely recommend HIVST to their friends and family”. These indicators did not vary significantly by self-reported HIV status, with those testing positive having OR 0.60 (95% CI 0.34–1.05) and OR 0.92 (95% CI 0.56–1.50) relative to HIV-negative participants for being “very satisfied” with the HIVST process and for “definitely” recommending HIVST to friends and family, respectively.

In total, 288/10,017 participants (2.9%, 95% CI 2.6%–3.2%) reported having been coerced into participating in HIVST. Notably, however, satisfaction indicators in the group reporting coercion were high, with 94.4% (252/267) stating that they would recommend HIVST to friends and family, and 92.2% (130/141) reporting that they were highly satisfied with HIVST. In the univariate analysis, men and participants who self-tested with their partner were significantly more likely to report having been coerced into HIVST (Table 4). In multivariate analysis, male sex (adjusted OR [aOR] 1.83, 95% CI 1.38–2.43) and having tested with a partner (aOR 3.86, 95% CI 2.82–5.29) remained significantly associated with reported coercion. There was no significant difference in reporting of coercion by reported HIVST result to volunteer-counsellors (aOR 1.00, 95% CI 0.59–1.71). The findings were comparable when multiple imputation methods were used to handle missing data (S1 Table).

A total of 132 adult deaths were reported through the community liaison system during the first 12 mo of follow-up, including one suicide in an individual who had not self-tested and four murders, none of which had any known or close temporal relationship to self-testing. No intimate partner violence episodes were reported through the community liaison system.

Discussion

The main finding of this study was the high population uptake of HIVST and retesting during 2 y of highly decentralised service provision in an urban community in Malawi. HIVST was safe and accurate, with uptake highest among adolescents, and with acceptable linkage into HIV care services using a delivery model based on trained volunteers. No suicides or other serious unintended consequences related to HIVST were detected by an active community surveillance system, including systematic death reporting and verbal autopsies. Feeling coerced into self-testing (usually by a main partner) was common (2.9% respondents), but was nonetheless associated with a high satisfaction rating for HIVST for all but a small minority of respondents. This model of HIVST is potentially scalable to other low-income settings where annual repeat HIV testing is recommended.

Table 4. Factors associated with reported coercion during months 1–12 of HIV self-testing (n = 7,014).

Characteristic	Number Coerced into HIVST/Total	Percent	OR ¹	95% CI ¹	aOR ¹	95% CI ¹
Women	91/4,138	2.2	1		1	
Men	112/2,868	3.9	1.81	1.36–2.39	1.83	1.38–2.43
Age group						
16–19 y	44/1,470	3.0	1		1	
20–29 y	102/3,276	3.1	1.04	0.73–1.49	1.05	0.73–1.50
30–39 y	47/1,499	3.1	1.05	0.69–1.59	1.01	0.66–1.53
40–49 y	6/446	1.4	0.44	0.19–1.04	0.44	0.18–1.03
≥50 y	4/315	1.3	0.42	0.15–1.17	0.39	0.14–1.10
Ever tested before	159/5,361	3.0	1		1	
Never tested before	44/1,645	2.7	0.90	0.64–1.26	0.86	0.60–1.23
Self-tested alone	136/6,157	2.2	1		1	
Self-tested with partner	67/849	7.9	3.8	2.80–5.13	3.86	2.82–5.29
Self-test self-read result						
Negative	182/6,299	2.9	1.00		1	
Positive	16/649	2.5	0.85	0.51–1.43	1.00	0.59–1.71
Don't know	5/58	8.6	3.2	1.25–8.03	3.17	1.22–8.22
Highly satisfied with HIVST						
Yes	84/1,581	5.3	1.00		ND	ND
No	5/54	9.3	1.82	0.71–4.68	ND	ND
Would recommend HIVST to friends and family						
Yes	188/6,763	2.8	1.00		ND	ND
No	12/120	10.0	3.89	2.10–7.18	ND	ND

¹ORs for age and sex were adjusted for each other only; ORs for all other variables were adjusted for age, sex, and each other.

ND, not done.

doi:10.1371/journal.pmed.1001873.t004

HIV testing needs in Africa have changed dramatically in the last decade due to the massive scale-up of ART services and an increasing focus on early diagnosis and treatment of HIV for prevention [26,27], as well as other biomedical HIV prevention strategies [28,29]. Population surveys and qualitative studies report high readiness to test, but there exist substantial barriers to accessing free clinic-based HIV testing services [30–33].

The high acceptability and ease of distribution of oral test kits makes HIVST of special interest in high-HIV settings, where the aim is to achieve affordable universal coverage and regular repeat testing [34]. Here we report considerable complementarity of this model of HIVST with existing strategies. Although our urban population was already served by free facility-based services, 35% of participants in the first 12 mo had never previously tested, and uptake was high in two important hard-to-reach groups: men and adolescents. Our estimates of adolescent population uptake (~100% for women aged 16–19 y and ~90% for men aged 16–19 y) are in stark contrast with reported adolescent HTC uptake in African DHS surveys [3]. Ideally, HIVST services would capitalise on high acceptability among key populations, facilitating linkage into HIV prevention programmes, such as pre-exposure prophylaxis and voluntary medical male circumcision, as well as ensuring prompt linkage into HIV care [14]. The per-episode costs of providing HIVST compared to the costs of facility-based testing will be reported fully elsewhere.

Our data from the second year of HIVST availability (participants were asked to test only once in each year) show high readiness to retest, as well as reduced numbers of first-time testers and new positive HIV diagnoses, which is consistent with the high coverage reported from the

first year. Importantly, population uptake in the second year was faster, suggesting that under programmatic conditions, experienced volunteer-counsellors could cover larger populations as soon as communities have been familiarised with HIVST concepts.

Optimum systems for linking clients into HIV care/prevention programmes are not well established in Africa [35–38] but are critical to the public health impact and cost-effectiveness of HTC [39]. Here we estimate a timely linkage into confirmatory testing and HIV care following HIVST of 56%, which compares favourably with many other approaches [40] and is well within the expected range for African HTC services [35,36]. This linkage estimate, however, reflects that, in addition to HIVST, participants were asked to attend post-test counselling and were advised to share their HIVST results. Facilitated HIV care assessment and initiation was provided following a successful trial in the first 6 mo of this study [10]. Despite reluctance to be *tested* by a volunteer-counsellor who is a neighbour, willingness to take kits and to *share results* was high. Although at first seemingly paradoxical, other studies have also reported that learning one's HIV status demands a moment of complete privacy, but that being able to turn to someone familiar can then make the next steps of accessing HIV care less daunting [41].

Some of the benefits of community-based HTC are reaching HIV-positive individuals earlier [42], improving survival [43], and reducing costs [44] and onward transmission. A recent meta-analysis has found that when CD4 measurement was offered in tandem with home-based HIV testing, approximately 60% of those who tested HIV positive had CD4 counts greater than 350 cells/ μ l [9]. Here we report a CD4 count profile below this ideal (median 250 cells/ μ l, IQR 159–426) for HIVST participants who subsequently attended care, but still considerably higher than that of HIV care attendees diagnosed from our study clusters following standard non-study HTC (median 154 cells/ μ l, IQR 116–249) [10].

Concerns about the potential impact of user error on diagnostic accuracy from HIVST [45,46] have been widely discussed [14]. Here we report an HIVST accuracy (93.6% sensitivity, 99.9% specificity) very similar to that of unobserved HIVST using the OraQuick ADVANCE Rapid HIV-1/2 Antibody Test in American participants [47]. We have previously reported 97.9% sensitivity and 100% specificity for a small observed/controlled-setting study in Blantyre [7]. In the HIVST model evaluated, users were given a short simple demonstration by trained lay volunteers, and this may have been a key factor in maintaining high accuracy in this relatively low literacy setting. Both accuracy and uptake of services post-testing will need reevaluation if different test kits or less supportive models are considered, for example, over-the-counter or vending machine sales.

Also of note, a much higher than anticipated proportion (26%) of our HIV-positive HIVST participants were on ART already, as were two of our four participants found to have false-negative results. ART is known to reduce sensitivity especially for oral fluid-based rapid diagnostic tests [48]. In Malawi, faith healing, whereby HIV is considered curable through prayer, is widely preached and may prompt ART patients to reconsider their status and need for ART if they get a negative test result via HIVST [49]. Based on our experience, we would recommend careful messaging about retesting while on ART in HIVST package inserts and education campaigns.

Coercion was reported by 3% of our SCQ respondents and was the major social harm, with no suicides or intimate partner violence attributed to HIVST despite active surveillance. Comparable data suggest that feeling coerced affects other modalities of HTC, with an estimated 7% of HTC episodes in Africa occurring without consent [50]. Both pregnant women and their male partners commonly report feeling coerced into testing by health professionals [51]. Among our participants, men and those who tested with their partners were more likely to report coercion. HIVST programmes need to anticipate and guard against coercive and mandatory testing, and to ensure that information about rights is disseminated and that systems for reporting social harms are in place.

Study limitations include uncertainty around our linkage and uptake estimates, and use of aggregate-level data reporting rather than individual cohort follow-up. Population turnover, typically high in urban slums, was not factored into our population denominators, and may in part explain why our crude uptake estimates for adolescent women were >100%. Importantly, our QA programme results ruled out a major contribution to our findings from HIVST offered to non-eligible individuals (non-residents and individuals taking multiple tests). Estimates of linkage into care always have a wide uncertainty (Fig 5), but as disclosure of positive HIVST results was voluntary, even our precise denominators are unknown. Furthermore, we underappreciated the extent of retesting while already on ART, adding to the uncertainty around numbers of newly identified HIV-positive participants. However, these sources of imprecision are unlikely to have affected our overall messages.

In summary, community-level HIVST service provision along with supportive post-test services resulted in high and rapid uptake of accurate HIVST, with very low incidence of major social harms, and acceptable linkage into HIV care. The continued high uptake in the second year suggests that scaling up HIVST could have a sustained impact on the coverage of HIV testing and care in Africa, especially for men and adolescents.

Supporting Information

S1 Checklist. STROBE checklist.
(DOCX)

S1 Questionnaire. Self-completed questionnaire.
(PDF)

S1 Table. Comparison between complete case analysis ($n = 7,014$) presented in Table 4 and analysis based on imputed data ($n = 11,359$).
(DOCX)

Acknowledgments

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Author Contributions

Conceived and designed the experiments: ELC. Performed the experiments: ATC RS AM. Analyzed the data: ATC EW. Contributed reagents/materials/analysis tools: ELC. Wrote the first draft of the manuscript: ATC HM. Contributed to the writing of the manuscript: ATC PM EW BW HF RS AM SM ND RH HM EC. Enrolled patients: RS. Agree with the manuscript's results and conclusions: ATC PM EW BW HF RS AM SM ND RH HM EC. All authors have read, and confirm that they meet, ICMJE criteria for authorship.

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Editors' Summary

Background

Every year, about 2.1 million people (70% of whom live in sub-Saharan Africa) are newly infected with HIV, the virus that causes AIDS, and 1.5 million people (again, mainly in sub-Saharan Africa) die as a result. HIV, which is usually transmitted through unprotected sex with an infected individual, gradually destroys CD4 lymphocytes and other immune system cells, leaving HIV-positive individuals susceptible to other serious infections and to unusual cancers. HIV is diagnosed by looking for antibodies to HIV in blood or saliva. After diagnosis, the progression of HIV infection is monitored by regularly counting the number of CD4 cells in the blood. Initiation of antiretroviral therapy—a combination of drugs that keeps HIV replication in check but that does not cure the infection—is recommended when an individual's CD4 count falls below 500 cells/ μ l or when he or she develops an AIDS-defining condition.

Why Was This Study Done?

HIV-positive individuals need to know their status so that they can take steps to avoid transmitting the virus to other people (for example, by always using a condom during sexual intercourse) and so that they can begin treatment. Treatment helps to keep HIV-positive individuals healthy but also reduces their chances of transmitting the virus to their sexual partners. Unfortunately, many HIV-positive individuals are unaware of their status. The situation is particularly bad in sub-Saharan Africa, where, despite major investments in facility-based and community-based HIV testing and counseling (HTC) programs, only a quarter of adults have had a recent HIV test, and only half of the people living with HIV know they are HIV positive. Barriers to facility-based HTC include concern about lack of confidentiality and fears of stigmatization. Home-based HTC avoids some of these barriers and can achieve high uptake of testing, but doubts have been expressed about the sustainability of this approach to testing. Here, the researchers evaluate an alternative to home-based HTC—HIV self-testing (HIVST)—by undertaking a community-based prospective study of HIVST in Blantyre, Malawi. HIVST involves individuals performing and interpreting their own HIV test and has the potential to be widely implemented with minimal involvement of trained healthcare workers.

What Did the Researchers Do and Find?

Trained resident volunteer-counselors offered one oral HIVST kit (a kit that measures HIV in saliva) per year for a two-year period to 16,660 adult residents in 14 neighborhoods in urban Blantyre. All the participants received instructions on how to use the kits, pre- and post-counseling, and, for participants self-testing HIV positive, a referral card to attend an HIV care clinic. The residents also completed a questionnaire about their experience of HIVST. Three-quarters of the residents self-tested in the first and second year of the study. HIVST uptake was more rapid in the second year than in the first year and was high among men and adolescents, two hard-to-reach populations. Three-quarters of the residents who self-tested during the first year of the study shared their results with a volunteer-counselor. Of the 1,257 participants who discovered they were HIV positive during the first year of the study, more than half accessed HIV care. Importantly, 94.4% of the participants reported that they were happy with HIVST even though 2.9% reported being

forced to take the test, usually by a main partner; no HIVST-related partner violence or suicides were reported by the study's community surveillance system. Finally, HIVST and repeat HTC results agreed in 99.4% of participants selected as a quality assurance sample (one in 20 of the participants).

What Do These Findings Mean?

These findings show that, in urban neighborhoods in Malawi, coverage with community-based HIVST was high (particularly among adolescents and men) in two successive years and that HIVST was safe, accurate, and acceptable. Importantly, HIVST using a delivery model based on trained volunteers led to acceptable linkage into HIV care services, and the approach had a very low incidence of major social harms such as partner violence. Uncertainty about estimates of uptake and linkage to care and other aspects of the study design may limit the accuracy of these results. Nevertheless, these findings suggest that scaling up HIVST could complement existing strategies for providing early HIV diagnosis and periodic repeat testing and could thus have a sustained impact on the coverage of HIV testing and care in Africa and on the control of the HIV/AIDS epidemic.

Additional Information

This list of resources contains links that can be accessed when viewing the PDF on a device or via the online version of the article at <http://dx.doi.org/10.1371/journal.pmed.1001873>.

- Information is available from the US National Institute of Allergy and Infectious Diseases on all aspects of [HIV infection and AIDS](#), including [testing and diagnosis](#)
- [NAM/aidsmap](#) provides basic information about HIV/AIDS, summaries of recent research findings on HIV care and treatment, and [personal stories about living with HIV/AIDS](#)
- Information is available from [Avert](#), an international AIDS charity, on many aspects of HIV/AIDS, including [HIV testing](#), [HIV/AIDS treatment and care](#), and [HIV prevention](#), and on HIV/AIDS in [Malawi](#) and in [sub-Saharan Africa](#); Avert also provides [personal stories about living with HIV/AIDS](#)
- The World Health Organization provides information on all aspects of [HIV/AIDS](#) (in several languages), including its [new consolidated guidelines on HIV testing](#)
- The [UNAIDS Fast-Track Strategy to End the AIDS Epidemic by 2030](#) provides up-to-date information about the AIDS epidemic and efforts to halt it; UNAIDS also provides detailed [region-specific information and policy news](#).

**APPENDIX IV: Effect of Optional
Home Initiation of HIV
Care Following HIV Self-testing on
Antiretroviral Therapy Initiation
Among Adults in Malawi: A
Randomized Clinical Trial**

Peter MacPherson, David G. Lalloo, Emily L. Webb, **Hendramoorthy Maheswaran**, Augustine T. Choko, Simon D. Makombe, Anthony E. Butterworth, Joep J. van Oosterhout, Nicola Desmond, Deus Thindwa, Stephen Bertel Squire, Richard J. Hayes, Elizabeth L. Corbett. **Effect of Optional Home Initiation of HIV Care Following HIV Self-testing on Antiretroviral Therapy Initiation Among Adults in Malawi: A Randomized Clinical Trial.** JAMA. 2014;312(4):372-379. doi:10.1001/jama.2014.6493.

Original Investigation

Effect of Optional Home Initiation of HIV Care Following HIV Self-testing on Antiretroviral Therapy Initiation Among Adults in Malawi

A Randomized Clinical Trial

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 Supplemental content at jama.com

IMPORTANCE Self-testing for HIV infection may contribute to early diagnosis of HIV, but without necessarily increasing antiretroviral therapy (ART) initiation.

OBJECTIVE To investigate whether offering optional home initiation of HIV care after HIV self-testing might increase demand for ART initiation, compared with HIV self-testing accompanied by facility-based services only.

DESIGN, SETTING, AND PARTICIPANTS Cluster randomized trial conducted in Blantyre, Malawi, between January 30 and November 5, 2012, using restricted 1:1 randomization of 14 community health worker catchment areas. Participants were all adult (≥ 16 years) residents ($n = 16\ 660$) who received access to home HIV self-testing through resident volunteers. This was a second-stage randomization of clusters allocated to the HIV self-testing group of a parent trial.

INTERVENTIONS Clusters were randomly allocated to facility-based care or optional home initiation of HIV care (including 2 weeks of ART if eligible) for participants reporting positive HIV self-test results.

MAIN OUTCOMES AND MEASURES The preplanned primary outcome compared between groups the proportion of all adult residents who initiated ART within the first 6 months of HIV self-testing availability. Secondary outcomes were uptake of HIV self-testing, reporting of positive HIV self-test results, and rates of loss from ART at 6 months.

RESULTS A significantly greater proportion of adults in the home group initiated ART (181/8194, 2.2%) compared with the facility group (63/8466, 0.7%; risk ratio [RR], 2.94, 95% CI, 2.10-4.12; $P < .001$). Uptake of HIV self-testing was high in both the home (5287/8194, 64.9%) and facility groups (4433/8466, 52.7%; RR, 1.23; 95% CI, 0.96-1.58; $P = .10$). Significantly more adults reported positive HIV self-test results in the home group (490/8194 [6.0%] vs the facility group, 278/8466 [3.3%]; RR, 1.86; 95% CI, 1.16-2.97; $P = .006$). After 6 months, 52 of 181 ART initiators (28.7%) and 15 of 63 ART initiators (23.8%) in the home and facility groups, respectively, were lost from ART (adjusted incidence rate ratio, 1.18; 95% CI, 0.62-2.25, $P = .57$).

CONCLUSIONS AND RELEVANCE Among Malawian adults offered HIV self-testing, optional home initiation of care compared with standard HIV care resulted in a significant increase in the proportion of adults initiating ART.

TRIAL REGISTRATION clinicaltrials.gov Identifier: NCT01414413

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In 2012, an estimated 35 million individuals were infected with the human immunodeficiency virus (HIV).¹ Antiretroviral therapy (ART) substantially reduces the risk of onward HIV transmission as well as greatly reducing morbidity and mortality,^{2,3} raising hopes that high uptake of annual HIV testing and early initiation of ART could improve HIV prevention as well as care.^{4,5}

Achieving high coverage of HIV testing is a major challenge. Surveys in 15 sub-Saharan African countries between 2009 and 2012 show that only 20.0% of women and 20.5% of men were tested for HIV in the previous year.⁶ Once tested, individuals need to access care and prevention services to maximize the individual and public health benefits of knowledge of HIV status. However, only one-fifth of patients link into care without any periods of loss to follow-up.⁷⁻⁹

Self-testing for HIV infection is a novel approach that is highly acceptable in Malawi and the United States.^{10,11} Self-testing for HIV has been defined as individuals performing and interpreting their HIV test in private,¹² a process that could overcome barriers to conventional facility-based and community-based HIV testing, which lack privacy and convenience.^{13,14} However, no studies in high HIV prevalence settings have investigated linkage into HIV care after HIV self-testing. Home initiation of HIV care has not previously been investigated, although home continuation of ART was noninferior to facility-based services in a Ugandan trial.¹⁵

We therefore tested the hypothesis that offering optional home initiation of HIV care after HIV self-testing might increase population-level uptake of ART and increase willingness to test and to report positive results compared with HIV self-testing accompanied by facility-based services only.

Methods

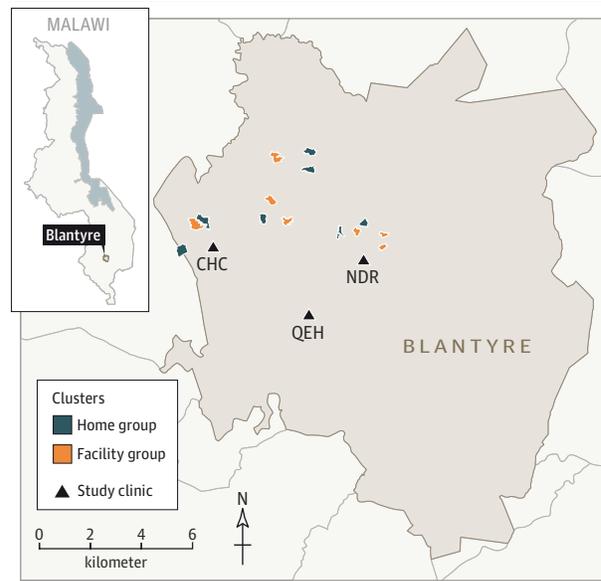
This was a second-stage randomization of clusters allocated to the HIV self-testing group of a parent study, which was a cluster randomized trial comparing health outcomes achieved under HIV self-testing vs standard-of-care HIV testing (with 14 vs 14 clusters in each group of the parent trial).¹⁶ The present study was a cluster randomized trial using the 14 community health worker catchment areas allocated to receive HIV self-testing in the parent trial. These 14 clusters underwent restricted randomization into 2 groups: HIV self-testing followed by optional home initiation of HIV care or HIV self-testing accompanied by facility-based HIV care.

Participants and Study Setting

There are 26 administrative wards in Blantyre, Malawi. Three wards (Ndirande, Likhlabula, and Chilomoni) were selected as the study site. They were all located in the northwest area of the city and comprised high-density urban neighborhoods. Comprehensive HIV care (including ART) was only available at 3 health facilities (Ndirande and Chilomoni Health Centres and Queen Elizabeth Central Hospital).

Between April and June 2011, 14 of a possible 73 community health worker catchment area clusters (5 in Ndirande,

Figure 1. Location of Study Clusters and Allocation



Lake Malawi is shown in light blue. CHC indicates Chilomoni Health Center; NDR, Ndirande Health Center; QEH, Queen Elizabeth Central Hospital.

6 in Likhlabula, and 3 in Chilomoni) (Figure 1) were selected purposely to ensure sufficient distance and separation between cluster boundaries to reduce risk of contamination.¹⁷ Clusters that were delineated by natural boundaries (rivers, roads, forests, etc) were preferentially selected. Boundaries of selected clusters were defined by study research assistants and Ministry of Health community health workers walking the boundary of each community health worker's catchment area recording coordinates with global positioning satellite receivers (eTrex Legend HCx, Garmin International). All households within clusters were enumerated by research assistants recruited from clusters, and a sociodemographic questionnaire was performed with the head of each household, or if unavailable, an adult household representative.

The research ethics committees of the College of Medicine, University of Malawi, Liverpool School of Tropical Medicine, and London School of Hygiene and Tropical Medicine approved the study. All participants provided written informed consent (or a witnessed thumbprint if illiterate) for HIV self-testing and separately for home initiation of care.

Interventions

Two volunteer counselors from each cluster, selected using participatory methods,¹⁸ were trained in HIV testing. Prior to HIV self-testing availability, counselors in all 14 clusters promoted the availability of HIV self-testing by door-to-door visits and leafleting. Between January 30, 2012, and November 5, 2012, oral HIV test kits (OraQuick Advance Rapid HIV-1/2 antibody test, OraSure Technologies) were distributed to adult residents requesting HIV self-testing from the counselors' home (1 kit per resident per year), with pretest information about HIV self-testing, counseling, and demonstration of kit use. Participants were asked to self-test in the privacy of their

own house and to return the used test kit in person to the counselor in a sealed envelope. Participants were not required to report self-test results to the counselor; if they declined to do so, they received generic posttest counseling. Participants who reported self-test results received results-based counseling. Counselors recorded numbers of HIV self-test kits distributed and positive results.

All participants who had positive results on self-testing could self-refer or be referred by counselors to study clinics where study nurses performed confirmatory HIV testing, tuberculosis (TB) screening (and provided isoniazid preventive therapy [IPT] if eligible), World Health Organization (WHO) staging, and CD4 cell counts; provided cotrimoxazole; and made onward referral for ART initiation (routine ART clinics within the same facility) if eligible (CD4 cell count $<350/\mu\text{L}$, WHO stage 3 or 4, pregnant, or breastfeeding).¹⁹

In the 7 clusters allocated to the home group, at the same time during which HIV self-testing was being promoted, counselors additionally promoted (verbally and with leaflets) the availability of home services during the door-to-door visits. The counselors provided a second leaflet and verbal information on home services to participants when attending the counselor's home to request HIV self-testing. Counselors organized home visits by study nurses for participants reporting a positive HIV self-test result and requesting home initiation of care. Nurses visited each participant twice (first visit within 3 days and second visit within 7 days) to carry out confirmatory HIV testing, WHO staging, CD4 cell count (venous blood for laboratory testing), and TB screening (with IPT if eligible) and to provide 2 weeks of ART if the participant was eligible. Participants were provided with completed ART registration cards and a follow-up appointment at their nearest HIV care clinic.

Adult ART initiations during the study period were ascertained by (1) recording home ART initiations and (2) interviewing all adults who initiated ART at any of the 3 clinics serving the study population and using printed satellite maps marked with cluster boundaries and local landmarks, followed if necessary by a home visit, to establish cluster residence.²⁰ Data from clinic registers and treatment cards were extracted for the 6 months following ART initiation in all identified study residents, without reference to group. Self-reported adherence was assessed by questionnaire at 3 points after ART initiation (at 2-4 weeks, 3 months, and 6 months) using the AIDS Clinical Trials Group adherence questionnaire.²¹

Outcomes

The primary outcome compared between groups was the cumulative incidence of ART initiation among all adult cluster residents (regardless of HIV status, ART eligibility, site of HIV testing, or ART initiation) during the first 6 months of HIV self-testing availability. The secondary outcomes compared the cumulative incidence of taking an HIV self-testing kit (regardless of whether used), reporting a positive HIV self-test result to counselors, and loss from ART by 6 months (with participants recorded as still taking ART or transferred out to another clinic classified as retained).

Sample Size

We assumed that adult HIV prevalence was 18.5%,¹⁰ 50% of HIV-positive self-testing adults would report a positive result to counselors, and 5% of the adult population would initiate ART over 6 months in the facility group. A mean cluster population of 1200 adults in 14 clusters provided 80% power at a 5% level of significance to detect a risk ratio (RR) of 1.5 between groups of the adult population who initiated ART, with a coefficient of variation $k = .20$.¹⁷

Randomization and Masking

Clusters were randomized at a public meeting after restricting possible allocations to ensure that for each of the 3 wards, the difference in the number of clusters allocated to each group would be no more than 2 (providing 2100 unique allocation patterns). Community representatives drew colored balls from an opaque bag held above eye level to select the distribution of clusters and group allocation. Counselors and residents were not masked to the intervention, but investigator blinding was maintained until the final analysis.

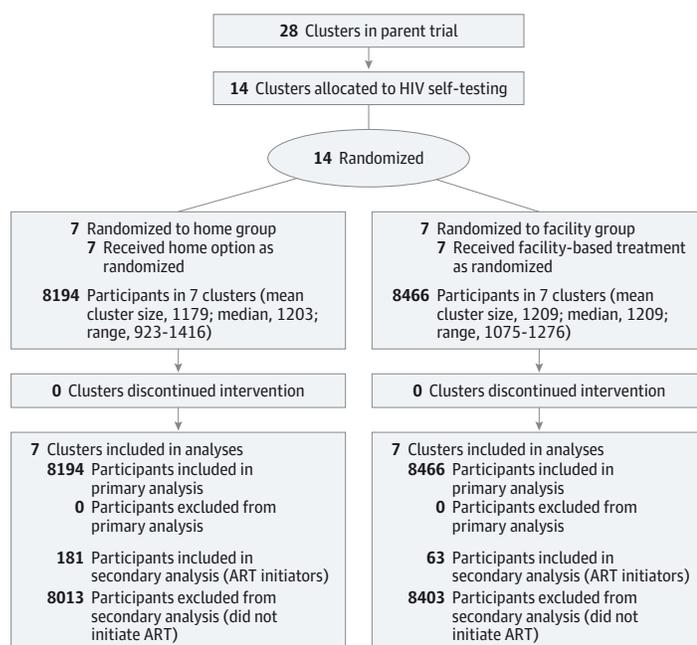
Statistical Methods and Cost Analysis

For the primary and secondary outcomes, analysis was done by intention to treat. CONSORT guidelines were followed in reporting preplanned study outcomes (eMethods 1 in the Supplement).²² The cluster-level proportions of residents who initiated ART, took an HIV self-test kit, and reported a positive HIV self-test result in each intervention group were compared using the *t* test, with the unadjusted RR calculated as the ratio of cluster-averaged means using the method described by Hayes and Moulton.¹⁷ The analysis was adjusted for death reported in households in the year preceding enumeration. Because data on these outcomes were not linked to individuals and were collected and analyzed at the cluster level, there were no missing data to take into account in the analysis.

A separate analysis was used to assess rates of loss from ART with the denominator being adult residents who initiated ART. The ART initiators whose treatment records indicated that they were still taking ART or had transferred to another ART clinic were classified as retained on ART. The ART initiators whose treatment records indicated that they had died or defaulted from ART were classified as lost to ART.²³ No ART initiators had missing data for ART outcome. Cluster-level rates of loss from ART in each group were compared using the *t* test, with the unadjusted rate ratio calculated as the ratio of cluster-averaged means and with subsequent adjustment for sex, age, pregnancy status, CD4 cell count strata, and WHO stage. The 3 of 244 participants (1.2%) for whom WHO stage was missing were not included in this adjusted analysis. Under national treatment guidelines, CD4 cell count was not indicated for pregnant women and individuals in WHO stage 3 or 4 and was not measured prior to ART initiation in facilities. Therefore, for the 69 of 244 individuals (28.3%) without CD4 cell count results, a category for missing was constructed.

Characteristics of ART initiators were compared between groups using χ^2 tests for categorical characteristics and Kruskal-Wallis tests for continuous characteristics. Differ-

Figure 2. Flowchart of HIV Self-testing and ART Initiation in Malawi



ART indicates antiretroviral therapy.

ences in adherence between the 2 groups were compared using χ^2 tests. Tests were 2-sided and a P value of $\leq .05$ was considered significant. Stata version 12.1 (StataCorp) was used for analysis.

A partial cost analysis was undertaken of the home ART initiation service from a programmatic perspective (eMethods 2 in the Supplement).²⁴ The cost estimates do not include the costs of facility-based assessment and initiation or downstream HIV care costs.

Results

The 14 clusters enumerated between April and June 2011 had a combined adult population of 16 660, with 8194 adults resident in 3213 households in the home group and 8466 adults resident in 3397 households in the facility group (Figure 2). Characteristics were well balanced between groups (Table 1), apart from reported household deaths in the previous year (home group: 131/8194, 4.1%; facility group: 81/8466, 2.4%).

Primary Outcome

Between January 30, 2012, and November 5, 2012, 244 cluster resident adults initiated ART during 6 months of HIV self-testing availability. The cumulative incidence of ART initiation was significantly higher in the home group (181/8194, 2.2% of residents) compared with the facility group (63/8466, 0.7% of residents; RR, 2.94; 95% CI, 2.10-4.12; $P < .001$) (Table 2). After adjusting for reported household mortality at baseline, the effect of availability of home care initiation remained statistically significant (adjusted RR, 2.44; 95% CI, 1.61-3.68; $P < .001$).

Of the 181 residents initiating ART in the home group, 116 (64.0%) initiated at home and 65 (36%) initiated at 1 of the 3 health facilities. The difference between groups in ART initiation was maintained throughout the analysis period (Figure 3).

Secondary Outcomes

During the 6 months of availability, a total of 9720 of 16 660 adult residents (58.3%) took an HIV self-test kit. There was no significant difference in uptake between the home (5278/8194, 64.9%) and facility groups (4433/8466, 52.7%; RR, 1.23; 95% CI, 0.96-1.58; $P = .10$). Participants in the home group (490/8194, 6.0%) were significantly more likely to report a positive HIV self-test result than facility group participants (278/8466, 3.3%; RR, 1.86; 95% CI, 1.16-2.97; $P = .006$).

Home ART initiators had significantly higher median CD4 cell counts compared with facility initiators (eTable 1 in the Supplement): median CD4 cell count at ART initiation was highest among home initiators in the home group (219/ μ L, interquartile range [IQR], 135-305) compared with facility initiators in the home group (154/ μ L, IQR, 116-249) and the facility group (187/ μ L, IQR, 100-256; $P = .04$).

Loss From ART Over 6 Months

After 6 months, 52 of 181 participants (28.7%; 30/116 [25.9%] home initiators and 22/65 [33.8%] facility initiators) who initiated ART in the home group and 15 of 63 participants (23.8%) in the facility group were lost from ART. Treatment records showed that 5 of 181 (2.8%) and 1 of 63 (1.6%) ART initiators in the home and facility groups died, respectively. In unadjusted analysis, the rate of loss from ART was higher in ART initiators in the home group (63.4/1000 person-months; 95% CI, 42.7-84.1) than in the facility group (53.5/1000 person-

Table 1. Baseline Characteristics

	Home Group	Facility Group
No. of clusters	7	7
No. of households	3213	3397
No. of adults (aged ≥16 y)	8194	8466
Cluster Characteristics		
Adults per cluster, mean (range), No.	1179 (923-1416)	1209 (1075-1276)
Population density per cluster, persons per m ² , mean (range)	0.016 (0.009-0.030)	0.024 (0.010-0.044)
Household Characteristics		
Adults per household, mean (SD), No.	2.55 (1.26)	2.48 (1.17)
Children per household, mean (SD), No.	1.96 (1.58)	1.93 (1.54)
Household wealth quintile, No. (%) ^a		
1 (poorest)	730 (23.3)	806 (24.3)
2 (poorer than average)	656 (21.0)	703 (21.2)
3 (average)	599 (19.2)	696 (21.0)
4 (wealthier than average)	602 (19.2)	589 (17.8)
5 (least poor)	540 (17.3)	518 (15.6)
Death in household in year preceding enumeration, No. (%)	131 (4.1)	81 (2.4)
Individual Characteristics (Adults Only)		
Age, mean (SD), y	30.4 (11.8)	30.2 (11.4)
Age group, y, No. (%)		
16-19	1312 (16.1)	1227 (14.5)
20-29	3312 (40.5)	3556 (42.1)
30-39	2113 (25.9)	2267 (26.8)
40-49	785 (9.6)	788 (9.3)
50-59	363 (4.4)	355 (4.2)
≥60	285 (3.5)	255 (3.0)
Male, No. (%) ^b	4252 (52.5)	4399 (52.6)
Marital status, No. (%) ^c		
Married or cohabiting	5031 (62.8)	5293 (64.4)
Never married	2441 (30.5)	2403 (29.2)
Widowed, separated, or divorced	535 (6.7)	524 (6.4)
Ever lost a spouse, No. (%) ^d	378 (4.7)	373 (4.5)
Highest level of education, No. (%) ^e		
No schooling	217 (2.7)	237 (2.9)
Primary	3168 (39.7)	3214 (38.7)
Secondary, no MSCE	2389 (30.0)	2863 (34.5)
Secondary with MSCE	1564 (19.6)	1465 (17.6)
Higher	635 (8.0)	520 (6.3)

Abbreviation: MSCE: Malawi secondary certificate of education.

^a Missing values: home group: 86, facility group: 85.

^b Missing values: home group: 7, facility group: 79.

^c Missing values: home group: 163, facility group: 228.

^d Missing values: home group: 180, facility group: 224.

^e Missing values: home group: 197, facility group: 149.

months; 95% CI, 23.7-83.4), although not significant (incidence rate ratio [IRR], 1.18; 95% CI, 0.67-2.10). Adjusting for risk factors had little effect (adjusted IRR, 1.18; 95% CI, 0.62-2.25).

There were 201 ART initiators (82.4% of all ART initiations and 91.0% of initiators who returned for a subsequent clinic appointment) who completed the adherence questionnaire 2 to 4 weeks after ART initiation, 145 (59.4% of all ART initiators and 82.9% of individuals retained in care) who completed the questionnaire at 3 months, and 119 (48.8% of all ART initiators and 67.2% of individuals retained in care) who completed questionnaires at 6 months. Overall, of those with data available, 19 of 164 (11.6%) and 3 of 60 (5.0%) ART initiators in the home and facility groups, respectively, self-reported missing at least 1 dose of ART in the past 4 days at any assessment point ($P = .14$).

Cost Analysis

The total cost of the home-based ART service was US \$20 005.24 (45 809.16 international dollars) (eTable 2 in the Supplement). The average cost per participant assessed was US \$97.11 (222.37 international dollars), and the average cost per participant who initiated ART through the home service was US \$172.46 (394.91 international dollars).

Discussion

The main finding of this cluster randomized trial was that population-level ART initiations were significantly increased (RR, 2.94; 95% CI, 2.10-4.12) by availability of home initiation of care. To our knowledge, this is the first study to investigate the effects of a comprehensive home-based HIV testing, eligibility

Table 2. Primary and Secondary Trial End Points^a

	Home Group		Facility Group		Risk or Rate Ratio (95% CI)	P Value	k ₀
	No./Total No.	% or Rate per 1000 Person-Months (95% CI)	No./Total No.	% or Rate per 1000 Person-Months (95% CI)			
Primary trial outcome:							
ART initiations							
Unadjusted ^b	181/8194 ^c	2.2%	63/8466	0.7%	2.94 (2.10-4.12)	<.001	.15
Adjusted					2.44 (1.61-3.68)	<.001	
Secondary trial outcomes							
HIV self-tests	5287/8194	64.9%	4433/8466	52.7%	1.23 (0.96-1.58)	.10	.23
Reporting of HIV positive self-test results	490/8194	6.0%	278/8466	3.3%	1.86 (1.16-2.97)	.006	.50
Loss from ART if initiated ART							
Unadjusted	52/181	63.4 (42.7-84.1)	15/63	53.5 (23.7-83.4)	1.18 (0.67-2.10)	.52	
Adjusted					1.18 (0.62-2.25)	.57	

Abbreviations: ART, antiretroviral therapy; k₀, intracluster coefficient of variation in facility group; WHO, World Health Organization.

^a For ART initiation, HIV self-tests, and reporting of positive HIV self-test results, denominators are total number of adult residents. For loss from ART, denominator is all adult cluster residents who initiated ART (regardless of site of HIV testing, or site of ART initiation) during first 6 months of HIV self-testing availability. Unadjusted proportions of adult residents initiating ART, taking HIV self-testing kits, and reporting positive HIV self-testing results were compared using the *t* test with the risk ratio calculated as the ratio of cluster-averaged means. Ninety-five percent CIs were calculated based on the *t* distribution and using a Taylor approximation to estimate the standard error of the log risk ratio. The analysis was adjusted for reported household death in the previous year using a logistic regression model to estimate cluster-specific predicted prevalence of the outcome (risk residuals), which were compared using the *t* test with the risk ratio calculated as the ratio of cluster-averaged risk residuals. For this adjusted analysis, 95% CIs and *P* values were calculated from the cluster-specific residuals based on the *t* distribution and using a Taylor approximation to estimate the standard error of the log risk ratio.

Unadjusted rates of loss from ART among ART initiators were compared using the *t* test, with the rate ratio calculated as the ratio of cluster-averaged means. The analysis was adjusted for sex, age, pregnancy status, WHO clinical stage (1/2 or 3/4), and CD4 cell count strata (>350/μL, 201-350/μL, ≤200/μL, or missing [n = 69]) at ART initiation using a Poisson regression model to estimate cluster-specific prevalence of covariates (rate residuals), which were compared using the *t* test with the rate ratio calculated as the ratio of cluster-averaged rate residuals. For this adjusted analysis, 95% CIs and *P* values were calculated from the cluster-specific residuals based on the *t* distribution and using a Taylor approximation to estimate the standard error of the log rate ratio. Three individuals who had missing data for WHO clinical stage were excluded from this adjusted analysis.

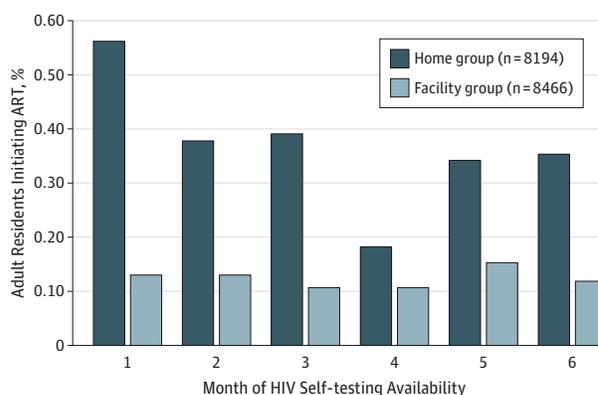
^b Includes all ART initiations among cluster resident adults during the first 6 months of HIV self-testing availability, regardless of site of ART initiation (home or facility).

^c Of the 181 residents initiating ART in the home group, 116 (64.0%) initiated at home and 65 (36%) initiated at 1 of the 3 health facilities.

assessment, and treatment initiation strategy. The uptake of HIV self-testing during the first 6 months of availability was high in both groups (58% overall). At a time when universal test and treat approaches to controlling the HIV epidemic are being considered,⁴ home initiation of HIV care shows high promise as a simple strategy to improve uptake of ART when HIV self-testing is carried out at home.

The absolute difference between groups was 1.5% (2.2% – 0.7%) or, assuming adult HIV prevalence was 18.5% in both groups¹⁰ and 76% of adults eligible for ART under 2010 WHO guidelines were taking ART at baseline,¹ an additional 7.9 per 100 HIV-infected adult residents (181/[8194 × 18.5%] – 63/[8466 × 18.5%]) and 33.0 per 100 ART-eligible HIV-infected adults (181/[8194 × 18.5% × 24%] – (63/[8466 × 18.5% × 24%]) initiated ART when both HIV self-testing and home initiation of HIV care were offered (detailed calculations in eTable 3 in the Supplement). We attribute this increase to removal of existing barriers to initial linkage to ART, including mistrust of routine clinic-based services and the intense pressure of time related to extreme poverty.^{13,25} Reassuringly, offering the option of home initiation of HIV care did not simply shift ART initiations from health facilities to home: the rate of facility ART initiations was maintained between groups, while home initiations provided extra numbers.

Figure 3. Cluster Resident ART Initiations During 6 Months of HIV Self-testing Availability



ART indicates antiretroviral therapy.

Although HIV self-testing has been available for more than 20 years,²⁶ it has only recently been considered for use in national HIV testing programs.²⁷ Following US Food and Drug Administration approval for over-the-counter sale of an oral HIV self-test kit in 2012,²⁸ and 2 pilot studies from Kenya²⁹ and Malawi¹⁰ showing high acceptability and uptake, there has been

renewed interest in HIV self-testing as a strategy for complementing existing HIV testing services.²⁷ Advantages of HIV self-testing include increased convenience and confidentiality compared with facility-based HIV testing.¹⁰

Economic analysis found the cost of home assessment per participant to be US \$97.11 (222.37 international dollars) and the cost per individual initiated with ART to be US \$172.46 (394.91 international dollars). This compares favorably with community-based HIV testing programs (US \$7.77-\$126.48 per individual tested)¹¹ and the annual costs of providing ART in facilities (US \$857.84-\$1165.47).³⁰ Patient costs were not considered in this analysis. However, home initiation of care will likely have savings for individuals who would otherwise incur substantial transport and opportunity costs. The costs of the HIV self-testing service, costs of facility-based initiation of care, and the differences in downstream management costs were not considered. The home-based service identified participants at significantly higher median CD4 cell counts, which will likely affect cost-effectiveness through prolonged survival,³¹ reduced early HIV management costs,³² and increased lifetime HIV treatment costs.

Loss from ART over 6 months was worse in the home group than in the facility group, although the differences were not statistically significant, and overall numbers of initiators were small, limiting power to identify anything other than large differences. Pooled across study groups, 72.5% of ART initiators were still taking ART at 6 months. This is below national HIV program estimates for Malawi (80% retained at 12 months³³), although still within the range seen in other programs.³⁴ The study setting, with recruitment from urban slums, may have led to inclusion of a greater proportion of highly mobile individuals compared with other areas of the country. The trend toward poorer outcomes among ART initiators in the home group means that careful monitoring and treatment support should be provided for home ART initiators in future studies to avoid losing the initial population benefits of home ART initiation.

Perceived lack of confidentiality (which could be more pronounced in smaller or rural communities) has been cited as a potential barrier to uptake when HIV interventions are offered in the home, although in a previous trial of home continuation of ART after facility initiation, dropout due to stigma was extremely uncommon.¹⁵ We overcame these potential dif-

iculties by developing a partnership with the community (through volunteer counselors and community representative groups) and with participants by giving pretest information about the potential advantages and disadvantages of home initiation of HIV care. Regular meetings were held with community stakeholders where concerns could be raised and addressed. No incentives (financial or otherwise) were provided to participants or providers.

Limitations of the study include the need to use all adult cluster residents (not people living with HIV or ART-eligible adults) as our denominator. This reflects the lack of available cluster-level HIV prevalence and CD4 cell count data. However, ART initiation remained statistically significantly increased in the home group after adjusting for household mortality in the previous year, which could have been indicative of differences in HIV prevalence or ART coverage between study groups. To maintain privacy and confidentiality, individual HIV self-testing participants were not followed up as a cohort; reporting results was optional and not required. Therefore, we cannot estimate overall linkage into care after positive HIV self-testing or examine any given step of the HIV care pathway. Total numbers of ART initiations were small, meaning that larger studies are required to fully evaluate the possible trends toward worse retention of ART in the home initiation group. Initiators of ART were followed up for only a short period (6 months) and default from ART was not followed up by active tracing. Clinical outcomes of ART initiators (including causes of death) were not assessed at 6 months. Because HIV self-testing was implemented through neighborhood volunteers living close to participants, home initiation of HIV care was a highly feasible option in this situation and may not apply to other models of HIV self-testing delivery. Other models for encouraging linkage may need to be developed and ideally directly compared for effectiveness.

Conclusions

Among Malawian adults offered HIV self-testing, optional home initiation of care compared with standard HIV care resulted in a significant increase in the proportion of adults initiating ART.

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**APPENDIX V: Literature search
strategy to review cost-
effectiveness studies of HIV
interventions**

Literature search strategy employed:

1. For HIV related terms

MESH headings for HIV related terms were combined with searching terms in title/abstract/keywords. The searches were then combined with 'OR'.

1	HIV/ or Anti-HIV Agents/ or HIV-2/ or HIV-1/ or HIV Infections/
2	Acquired Immunodeficiency Syndrome/
3	Antiretroviral Therapy, Highly Active/
4	(human immunodeficiency virus or human immunodeficiency virus or human immunodeficiency virus or human immune-deficiency virus or human immun*).ab,kw,ti.
5	(acquired immunodeficiency syndrome or acquired immunodeficiency syndrome or acquired immunodeficiency syndrome or acquired immune-deficiency syndrome or acquired human immun*).ab,kw,ti.
6	(HAART or highly active antiretroviral therapy or highly active anti-retroviral therapy or highly active antiretroviral treatment or highly active anti-retroviral treatment or antiretroviral or anti-retroviral).ab,kw,ti.
7	1 or 2 or 3 or 4 or 5 or 6

2. For restricting publication relating to sub-Saharan Africa

MESH headings relating to sub-Saharan Africa were combined with searching for list of countries and regions in sub-Saharan Africa in title/abstract/keywords and country of publication or affiliation. The searches were then combined with 'OR'.

8	(angola or benin or botswana or burkina faso or burundi or cameroon or cape verde or central african republic or chad or comoros or congo or cote d'ivoire or democratic republic of the congo or Djibouti or ethiopia or Eritrea or equatorial guinea or gabon or gambia or ghana or guinea or guinee bissau or guinea-bissau or ivory coast or kenya or Lesotho or Liberia or madagascar or malawi or mali or mozambique or Namibia or niger or nigeria or rwanda or (sao tome and principe) or senegal or sierra leone or somalia or south africa or south sudan or sudan or Swaziland or tanzania or togo or uganda or zaire or zambia or Zimbabwe or sub-Saharan Africa or East Africa or Southern Africa or West Africa).ab,cp,kw,ti.
9	exp "Africa South of the Sahara"/
10	1 or 2

3. For restricting studies relating to economic evaluations

To restrict searches to economic evaluations the University of York Centre for Reviews and Dissemination (CRD) search filter was used. This component was not included when searching the Cochrane Library and the CRD as the databases are restricted to economic evaluation studies. (http://www.york.ac.uk/inst/crd/intertasc/nhs_ee_d_strategies.html).

11	Economics, Pharmaceutical/ or Economics, Behavioral/ or Economics, Medical/ or Economics/ or Economics, Hospital/ or Economics, Dental/ or Economics, Nursing/
12	exp "Costs and Cost Analysis"/
13	(economic\$ or cost or costs or costly or costing or price or prices or pricing or pharmaco-economic\$).ti,ab.
14	(expenditure\$ not energy).ti,ab.
15	value for money.ti,ab.
16	budget\$.ti,ab.
17	or/11-16
18	((energy or oxygen) adj cost).ti,ab.
19	(metabolic adj cost).ti,ab.
20	((energy or oxygen) adj expenditure).ti,ab.
21	or/18-20
22	17 not 21

4. Finalising search

The three broad searches described above were combined with 'AND'. References that are letters, editorials and historical articles were subsequently removed. References of animal only studies were also removed. The final search restricted references to those published in English and to publication date from 1st Jan 2000 onwards.

23	7 and 10 and 22
24	letter.pt.
25	editorial.pt.
26	historical article.pt.
27	Or/24-26
28	23 not 27
29	Animals/
30	Humans/
31	29 not (29 and 30)
32	28 not 31
33	Limit 29 to English language
34	Limit 28 to yr="2000-current"

**Appendix VI: Participant
information leaflet (English version)
– HIV testing and HIV cohort studies**

HTC-101: Participant Information Leaflet (English version)

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Study Title: Cost-effectiveness of Home-based HIV Testing and Counselling in Blantyre, Malawi

Introduction

Good Day, my name is _____, I am working for the Malawi-Liverpool-Wellcome Clinical Research Programme. We are doing research on HIV, which is very common in this country. We are undertaking a study to evaluate the costs and benefits of delivering HIV testing in homes and through health facilities in Blantyre, Malawi. There may be some words that you do not understand. Please ask me to stop as we go through the information and I will take time to explain. A decision of whether or not you want to participate will not affect your right to access these services.

Purpose of this study?

HIV testing allows individuals to learn their HIV status. Those diagnosed as HIV positive can then seek care from health facilities to improve their health. In Malawi, many people do not learn their HIV status early enough. If people who are HIV positive learn their HIV status earlier, they may be less likely to suffer from poor health or die. This will improve their survival and quality of life. It may also save them money, as they do not have to go to the clinic or hospital as often, or take time of work because of poor health. It will also save the Ministry of Health money, which they could spend on other health services.

In Malawi, most people have an HIV test at their local clinic. Recently, a new service has been introduced, where individuals can have a HIV test in their homes. We want to see if providing HIV testing in peoples homes allows them to learn their HIV status earlier, and what the impact of this is on their health. We want to carry out a questionnaire study with people who get an HIV test through their local clinic and in their homes. We want to compare what the impact of using these services is on your quality of life, your costs, and the care you receive after learning your HIV status.

Procedures

Duration: The study takes place over approximately 18 months in total.

What will be asked of you: We will ask individuals aged 16 and over who agree to participate in this study a set of questions aimed at soliciting information on the following: their background, HIV testing services used, HIV test result, costs of attending health facilities, their quality of life, and health services used. We would also like to meet with you again. This will depend on whether you are HIV positive or HIV negative.

HTC-101: Participant Information Leaflet (English version)

If you are HIV negative we would like to meet with you at your local clinic after about 1 year for brief interview. At the follow-up interview we will ask whether you have re-tested for HIV. We will also offer you an HIV test if you wish to be tested.

If you are HIV positive we would like to meet with you each time you attend the HIV clinic for about 1 year. On each visit we will ask a set of set of questions aimed at soliciting information on the following: costs of attending the clinic, your quality of life, the medical care provided at the clinic, and any other medical care you used since the last visit. These interviews will last approximately 15 minutes. At the beginning and the end of the study, we will ask your clinic nurse will take a small amount of blood. This blood will be used to test how well your body is coping with the HIV infection. This is often done as part of routine care in the clinic. If you are HIV positive and you do not return to the clinic for more than 3 months we would like to meet with you for a brief interview. We will also ask that you go to your clinic to see the HIV nurse.

Participation is voluntary: You may withdraw from the study at any time without giving a reason and without any penalty.

Cost, Risks and Discomforts: You will be asked about your HIV status. You may feel uncomfortable to discuss this topic. You do not have to inform us of your HIV status, you may refuse to participate, and may withdraw from the interview at any time. If you withdraw from the interview you will still be able to access HIV services. Taking part in this study will not cost you anything.

Benefits: There will be no direct benefit to you from participation. However, the information you provide may help improve HIV testing services in your community.

Reimbursement: You will be provided with refreshments during the interview. Those who have been specifically asked to attend the clinic for an interview will be reimbursed their travel costs.

Confidentiality: We will not be sharing the identity of those participating in the research with anyone. The information that we collect from this research project will be kept confidential. Information about you that will be collected during the research will not be identified by your name but by a number. Only the researchers will know what your number is and they will lock that information up with a lock and key. The knowledge that we get from doing this research will be shared with you. There will be small meetings in the community and these will be announced. If information from the study is published or presented at scientific or public meetings, your name and other personal information will not be used.

Approval for the study: The College of Medicine Research Ethics Committee, Blantyre, Malawi and the University of Warwick Biomedical Research Ethics Committee, Warwick, UK has approved this study.

Questions: If you have any further questions about the study, you may call Dr Hendramoorthy Maheswaran (Principal Investigator, Tel: XXXXXXXXXX) or COMREC chairperson (Tel: 09999 57805)

**Appendix VII: Participant
information leaflet (Chichewa
version) – HIV testing and HIV
cohort studies**

**Kusalowa Mthumba kwa ntchito yoyeza ndi Kupereka upungu wa HIV
HTC-101: Kalataya uthenga kwa otenga nawo mbari (Chichewa Version)**



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Dzina la kafukufuku: Kusalowa mthumba kwa ntchito yoyeza HIV komanso kupereka upungu pakhomo ku Blantyre, Malawi

Malonje

Mwaswela bwanji, dzina langa ndi _____, ndimagwira ntchito ku **Malawi-Liverpool-Wellcome Trust Clinical Research Programme**. Tikupanga kafukufuku wa HIV, yomwe yafala mu dziko muno. Tikuchita kafukufukuyu pofuna ku unika mitengo ndi phindu lopereka ndondomeko zoyeza HIV m'makomo komanso kudzera ku zipatala za ku Blantyre, Malawi. Pakhoza kupezeka mau ena oti simungathe kuwamvesetsa. Chonde ndifunsemi kuti ndiime kaye pamene tikukamba za uthengawu ndipo ndidzatenga nthawi kufotokozera. Chiganizo chanu pakufuna kutenga mbari mukafukufukuyu kapena ayi sichizakhudza ufulu wanu pofuna kupeza mwayi wofuna kupeza thandizoli.

Cholinga cha kafukufukuyu?

Kuyezetsa HIV kupeleka mwayi kwa anthu kudziwa ngati ali ndi HIV kapena ayi. Onse amene angapezeke ndi HIV, ali ndi mwayi olandira chisamaliro kudzera ku ntchito za umoyo pofuna kukonza thanzi la moyo wawo.. Kuno ku Malawi, anthu ambiri safuna kudziwa mwamsanga ngati ali ndi HIV kapena ayi. Ngati anthu amene ali ndi HIV angathe kudziwa mwamsanga, akhoza kukhala osadwala-dwala komanso atha kupewa imfa . Izi zidzathandizila kuti akhale ndi moyo wautali komanso kutengulira moyo wawo. Zikhozanso kuwathandizila kuti asawononge ndalama, popeza sayenera kupita ku chipatala cha ching'ono kapena chachikulu pafupi-pafupi, kapena kujomba ku ntchito chifukwa chodwalala. Zimenezi zizathandiziranso unduna wa za umoyo kuti usaononge ndalama, zimene zingatthe kugwira ntchito zina za umoyo.

Ku Malawi, anthu ambiri amakayezetsa HIV ku zipatala zazing'ono za mdela lawo. Posachedwapa, thandizo la tsopano lakhazikitsidwa, limene anthu angathe kuyezetsa HIV m'makomo mwawo. Tikufuna kuona ngati ndondomeko yoyeza HIV m'makomo mwa anthu, ikuthandiza anthu kudziwa mwamsanga ngati ali ndi HIV kapena ayi, komanso gwero limene ndondomekoyi liri nalo pa thanzi lawo. Tikufuna tipange dongosolo lo funsa anthu amene ayezetsa HIV ku zipatala zazing'ono-zing'ono za mdela lawo komanso m'makomo mwawo. Tikufuna tisiyanitse gwero limene lingakhalepo pa thanzi lawo chifukwa chogwiritsa ntchito thandizoli, ndalama zimene amagwiritsa ntchito, komanso chisamaliro chimene alandira atadziwa kuti ali ndi HIV.

Ndondomeko

Nthawi yotalika bwanji: kafukufukuyu atenga nthawi yotalika pafupifupi miyezi 18 yonse pamodzi.

Kodi mudzafunsidwa chani: Tidzafunsa anthu amene ali ndi zaka 16 kupita mtsogolo, amene angavomereze kutenga nawo mbari mukafukufukuyu, kudzera mu gulu la mafunso ndi cholinga chofuna kupeza mayankho pa nkhani monga: chiyambi chawo, njira zoyezera HIV zimene agwiritsapo ntchito, zotsatira za kuyezetsa HIV kwao, ndalama zimene amagwiritsa ntchito akamapita ku zipatala, m'mene moyo wawo uliri, komanso thandizo la za umoyo lomwe agwiritsa ntchito. Tidzafuna kukumananso nanu kachiwiri. Izi zidzatengera ngati muli ndi HIV kapena mulibe.

Kusalowa Mthumba kwa ntchito yoyeza ndi Kupereka upungu wa HIV HTC-101: Kalataya uthenga kwa otenga nawo mbari (Chichewa Version)

Ngati mulibe HIV tidzafuna kuti tikumane nanu kudzera ku chipatala cha mdela lanu pakatha chaka chimodzi kuti tidzakufunsi mafunso mwa chidule. Pa nthawiyo tidzafuna kudziwa ngati munayezetsanso HIV komanso tidzakupatsani mwayi oti muyezetse HIV, ngati mungafune kutero.

Ngati muli ndi HIV tidzafuna kukumana nanu nthawi zonse mukapita ku chipatala kokalandira thandizo la HIV kwa chaka chimodzi. Nthawi zonse tikakumana nanu tidzakufunsi mafunso ofuna kupeza mayankho pa nkhani izi: ndalama zimene mwagwiritsa ntchito popita ku chipatala, thanzi la moyo wanu m'mene liriri, mtundu wa chisamaliro chimene mumalandira ku chipatalako, ndi zisamaliro zina zimene munalandirapo kuchokera nthawi imene tinakumana komaliza. Ndongomeko ya mafunsoyo idzatitengera pafupi-fupi mphindi 15. Poyambilira komanso pamapeto a kafukufukuyu, tidzapempha namwino wa kuchipatala chanu kuti akutengeni magazi pang'ono. Magaziwa adzagwiritsidwa ntchito kuyeza m'mene thupi lanu likuthanilana ndi tizilombo ta HIV. Izi zimachitika monga mbali imodzi ya chisamaliro cha masiku onse cha kuchipata. Ngati muli ndi HIV ndipo simunabwelense ku chipatala koposela miyezi 3, tidzafuna kukumana nanu kuti tikufunsi mafunso mwachidule. Tidzakupemphaniso kuti mudzapite ku chipatala chanu kuti mudzakakumane ndi namwino amene amakhudzana ndi ndondomeko za HIV.

Kutenga nawo mbaliku ndi kozipereka: mukhoza kutuluka mukafukufukuyu nthawi ina iriyonse popanda kupereka chifukwa chirichonse komanso popanda kulipira chindapusa china chirichonse.

Mtengo , chiopsyezo ndi Nkhawa: mudzafunsiidwa zokhudzana ndi m'mene mthupi mwanu muliri. Mukhoza kukhala osamasuka kukambirana za nkhanii. simukuyenera kutidziwitsa za m'mene mthupi mwanu muliri, mukhoza kukana kutenga nawo mbari, komanso kutuluka mu kafukufukuyu nthawi ina iriyonse. Ngati mungafune kutuluka mukafukufukuyu mudzakhalabe ndi mwayi opeza chithandizo cha HIV. Simudzalipira chirichonse chifukwa choti mwatenga nawo mbari mukafukufukuyu.

Phindu: sipadzakhala phindu lina lililonse looneka kwa inu, mukalora kutenga nawo mbari, Komabe, mfundo zimene mutapereke, zikhoza kukonza mwatsopano ntchito za ku yezetsa HIV mu dela lanu.

Kubwezedwa ndalama: mudzapatsidwa za kumwa zoziziritsa kukhosi pa nthawi ya mafunsoyo. Anthu amene afunsiidwa kuti apite ku chipatala kuti akafunsiidwe mafunso azabwezedwa ndalama zawo zimene anga gwiritse ntchito pa mayendedwe.

Chinsinsi: sitidzagawana za maina a anthu otenga nawo mbari mukafukufukuyu ndi wina aliyense. Mfundo zomwe zidzapekedwe kuchokera ku kafukufukuyu zidasungidwa mwa chinsinsi. Nkhani yokhudzana ndi inu imene tidzakambirane nthawi imene kafukufukuyu azidzachitika siidzadziwika ndi dzina lanu koma ndi nambala. Ndi anthu ochititsa kafukufukuyu okhawa amene angazadziwe kuti nambala yanu ndi chani, ndipo adzatsekera uthengawo ndi loko komanso kiyi. Tidzagawana nanu nzeru zimene tingapeze. kudzera mukafukufukuyu. Kudzachitika timisonkhano ting'ono-ting'ono m'madalamwanumo potsatira kulengezedwa. Ngati mfundo zochokera mukafukufukuyu ziti zizalembedwe kapena kufalitsidwa m'misonkhano dzina lanu kapena khani ina iriyonse yokamba zainu sizidzagwiritsidwa ntchito.

Chilorezo chobvomereza kuti kafukufukuyu achitikee: komiti yoyang'anira za makafukufuku ya *College of Medicine Research Ethics*, ku Blantyre, Malawi ndi komiti ya university ya Warwick Biomedical Research, Warwick, ku UK yavomereza kafukufukuyu.

Mafunso: Ngati mungakhale ndi mafunso ena okhudzana ndi kafukufukuyu, mukhoza kuyimbira foni Dr Hendramoorthy Maheswaran (mkulu woyendetsa kafukufukuyu pa nambala iyi: 0996151939) kapena wa pampando wa COMREC pa nambala iyi: 09999 57805

Appendix VIII: Consent form
(English version) – HIV testing and
HIV cohort studies

HTC-102: Consent Form (English version)

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Study Title: Cost-effectiveness of Home-based HIV Testing and Counselling in Blantyre, Malawi

- I have been invited to participate in this study comparing the costs and benefits of HIV testing through home and clinic based services
- I have received, read and understood the written information (Participant Information Leaflet) regarding the study
- I understand that it will involve follow-up interviews
- I have been informed that the risks are minimal
- I am aware that there may be no benefit to me personally and that I will not be compensated beyond travel expenses and refreshments.
- I may, at any stage, without prejudice, withdraw my consent and participation in the study.
- I have been provided with the name of a researcher (Dr Hendramoorthy Maheswaran) who can be easily contacted using the number and address I was given for that person.
- I have had sufficient opportunity to ask questions and (of my own free will) declare myself prepared to participate in the study.

Participant's name (print)

Participant's signature

Date

I have accurately read or witnessed the accurate reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Name of staff member (print)
who administered consent

Staff member's signature

Date

IF ILLITERATE, a literate witness must sign.

I have witnessed the accurate reading of the consent form to the participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Witness' name (print)

Witness' signature

Date

Appendix IX: Consent form
(Chichewa version) – HIV testing
and HIV cohort studies

**Kusalowa mthumba kwa ntchito yoyeza ndi Kupereka uphungu wa HIV
HTC-102: Kalata ya chilolezo (Chichewa Version)**



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Study ID Barcode

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**Mutu wa kafukufuku: Kusalowa mthumba kwa ndondomeko yoyezetsa HIV
ndikulandira uphungu pakhomo ku Blantyre, Malawi**

- Ndaitanidwa kudzatenga nawo mbari mukafukufuku ofuna kusiyantsa kuipa ndi ubwino wa pakati poyezetsa HIV ku nyumba ndi ku chipatala
- Ndalandira, ndawerenga ndi kumvesetsa bwino uthenga olembedwawu (Kalatayla uthenga wa otenga nawo mbari) okhudzana ndi kafukufukuyu
- Ndamvesetsa kuti padzakhala ndondomeko yo yankha mafunso motsatana
- Ndadziwitsidwa kuti chiopsyezo kwa ine pakutenga nawo mbali pakafukufukuyu ndi chochepa
- Ndikudziwa kuti palibe phindu lililonse kwa ine, komanso sindidzapatsidwa ndalama ina kupatula ndalama yo yendera ndi zakumwa zoziziritsa ku khosi.
- Ndikhoza, nthawi iriyonse, popanda kusolidwa, kukaniza chilolezo changa komanso kukana kutenga nawo mbari mukafukufukuyu.
- Ndapatsidwa dzina la opangitsa kafukufukuyu (Dr Hendramoorthy Maheswaran) amene angathe kulumikizidwa mosavuta, pogwiritsa ntchito nambala ndi adilesi imene ndinapatsidwa, ya munthuyu.
- Ndakhala ndi mwayi okwanira oti ndifunse mafunso komanso (mwakufuna kwanga) ndikuvomereza kuti ndine okonzeka kutenga nawo mbari mukafukufukuyu.

Dzina la otenga nawo mbari (zilembo zikulizikulu)

Sayini ya otenga nawo mbari

Tsiku

Ndawerenga kapena kuonelera kuwerenga koyonelera kwa kalata ya chilolezo kwa otenga nawo mbari moyonelera, ndipo munthuyu anali ndi mwayi ofunsa mafunso. Ndikuvomereza kuti munthuyu wapereka chilolezo mwaufulu.

Dzina la munthu ogwira ntchito (zilembo za zikulu)
amene anatsogolera ndondomeko ya chilolezo

sayini ya munthu ogwira ntchito

Tsiku

NGATI SATHA KULEMBA NDI KUWERENGA , amene amatha asayinire ngati mboni.

Ndaonelera kuwerenga koyonelera kwa kalataya chilolezo kwa otenga nawo mbari, ndipo munthuyu anali ndi mwayi ofunsa mafunso. Ndikuvomereza kuti munthuyu wapereka chilolezochi mwa ufulu.

Dzina la Mboni (zilembo za zikulu)

sayini ya mboni

Tsiku

Appendix X: HTC-103 Baseline
socio-demographics questionnaire –
HIV testing and HIV cohort studies

P01	HHBAR	Participant Barcode	<div style="border: 1px solid black; padding: 5px; width: fit-content;"> PLACE ID BARCODE HERE </div>	Write Participants Barcode <div style="border: 1px solid black; width: 100px; height: 20px; margin-top: 5px;"></div>
P02	HHID	Interviewer ID	<input type="text"/> <input type="text"/>	P03 CLUSID Cluster ID <input type="text"/> <input type="text"/>
P04	SIT	Place of interview	<input type="checkbox"/> 1. Participant Home <input type="checkbox"/> 2. Chilomoni Clinic	<input type="checkbox"/> 3. Queens Hospital <input type="checkbox"/> 4. Ndirande Clinic
P05	DOI	Date of interview	<input type="text"/>	2 0 1 y y y y
P06	NAM	Physical Address		
P07	NAM2	Draw Map to Home		
		Mapbook Reference:	<input type="text"/> <input type="text"/>	Page <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> Grid
P08	TEL	Telephone number of Participant (1st)	<input type="text"/>	
P09	TEL2	Telephone number of Participant (2nd)	<input type="text"/>	
P10	TEL3	Telephone number of Partner, Spouse, or Family Member	<input type="text"/>	
P11	TEL4	Telephone number of Family Member at participants home village	<input type="text"/>	
P12	DOB	Tsiku lobadwa Date of Birth	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>
			d d	m o n y y y y
P13	AGE	Age	<input type="text"/> <input type="text"/>	Years
P14	SEX	Sex	<input type="checkbox"/> 1. Male <input type="checkbox"/> 2. Female	
P15	PREG	Ngati ndinu mkazi, kodi muli ndi pakati? If female, are you pregnant?	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No <input type="checkbox"/> 99. N/A	
P16	PREGM	Kodi mwakhala ndi pakati kwa miyezi ingati? Months pregnant	<input type="text"/> <input type="text"/>	Write 99 if Not Applicable
P17	MARSTC	Kodi muli pa banja? What is your marital status? (TICK ONE)	<input type="checkbox"/> 1. Married <input type="checkbox"/> 2. Polygamous marriage <input type="checkbox"/> 3. Living together as married <input type="checkbox"/> 4. Never Married <input type="checkbox"/> 5. Separated <input type="checkbox"/> 6. Widower/Widow <input type="checkbox"/> 7. Divorced	

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P18	PARTNER	Ngati simuli pabanja kodi muli ndichibwenzi If NOT MARRIED, do you have a partner at the moment?	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No <input type="checkbox"/> 99. N/A																																						
P19	TOGYRS	Kodi mwakhala limodzi ndi okonedwa anu kwa nthawi yayitali bwanji? How long have you been together with your spouse/partner?	<table border="1" style="display: inline-table; vertical-align: top;"> <tr> <td style="width: 30px; height: 30px;"></td> <td style="width: 30px; height: 30px;"></td> </tr> <tr> <td colspan="2" style="text-align: center;">Years</td> </tr> <tr> <td style="width: 30px; height: 30px;"></td> <td style="width: 30px; height: 30px;"></td> </tr> <tr> <td colspan="2" style="text-align: center;">Months</td> </tr> </table>			Years				Months																															
Years																																									
Months																																									
P20	SCH	Kodi maphuziro anu munafika nawo pati? What is the highest level of formal schooling you have ever attended?	<table border="1" style="display: inline-table; vertical-align: top;"> <tr> <td style="width: 30px; height: 30px;"></td> <td style="width: 30px; height: 30px;"></td> </tr> </table> <table style="font-size: small;"> <tr> <td>PRESCHO = 00</td> <td>FORM 1 = 09</td> <td>UNIVE 1 = 15</td> <td>TRAIN COL</td> </tr> <tr> <td>STAND 1 = 01</td> <td>FORM 2 = 10</td> <td>UNIVE 2 = 16</td> <td>TCYR 1 = 20</td> </tr> <tr> <td>STAND 2 = 02</td> <td>FORM 3 = 11</td> <td>UNIVE 3 = 17</td> <td>TCYR 2 = 21</td> </tr> <tr> <td>STAND 3 = 03</td> <td>FORM 4 = 12</td> <td>UNIVE 4 = 18</td> <td>TCYR 3 = 22</td> </tr> <tr> <td>STAND 4 = 04</td> <td>FORM 5 = 13</td> <td>ABOVE = 19</td> <td>TCYR 4 = 23</td> </tr> <tr> <td>STAND 5 = 05</td> <td>FORM 6 = 14</td> <td></td> <td></td> </tr> <tr> <td>STAND 6 = 06</td> <td></td> <td></td> <td></td> </tr> <tr> <td>STAND 7 = 07</td> <td></td> <td></td> <td></td> </tr> <tr> <td>STAND 8 = 08</td> <td></td> <td></td> <td></td> </tr> </table>			PRESCHO = 00	FORM 1 = 09	UNIVE 1 = 15	TRAIN COL	STAND 1 = 01	FORM 2 = 10	UNIVE 2 = 16	TCYR 1 = 20	STAND 2 = 02	FORM 3 = 11	UNIVE 3 = 17	TCYR 2 = 21	STAND 3 = 03	FORM 4 = 12	UNIVE 4 = 18	TCYR 3 = 22	STAND 4 = 04	FORM 5 = 13	ABOVE = 19	TCYR 4 = 23	STAND 5 = 05	FORM 6 = 14			STAND 6 = 06				STAND 7 = 07				STAND 8 = 08			
PRESCHO = 00	FORM 1 = 09	UNIVE 1 = 15	TRAIN COL																																						
STAND 1 = 01	FORM 2 = 10	UNIVE 2 = 16	TCYR 1 = 20																																						
STAND 2 = 02	FORM 3 = 11	UNIVE 3 = 17	TCYR 2 = 21																																						
STAND 3 = 03	FORM 4 = 12	UNIVE 4 = 18	TCYR 3 = 22																																						
STAND 4 = 04	FORM 5 = 13	ABOVE = 19	TCYR 4 = 23																																						
STAND 5 = 05	FORM 6 = 14																																								
STAND 6 = 06																																									
STAND 7 = 07																																									
STAND 8 = 08																																									
Kodi pakhomo pano muli ndi zinthu izi? Does your household own any of the following (please tick all that apply)?																																									
P21	FRIDG	Fridge? <input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No	P26	WATCH	Watch? <input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No																																				
P22	HHCARM1	Car? <input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No	P27	PHON	Phone? <input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No																																				
P23	BED	Bed? <input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No	P28	KOLO	Koloboyi? <input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No																																				
P24	TELEV	Television? <input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No	P29	RADIO	Radio? <input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No																																				
P25	HHCARM2	Motorcycle? <input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No																																							
P30	LAND	Kodi alipo m'modzi wam'banja limeneli amene ali ndi malo olima? Does any member of your household own any agricultural land?	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No																																						
P31	SHFOOD	M'mwezi wathawu, mwakhalapo ndi mavuto pakapezedwe ka chakudya mowilikiza bwanji? During the past month, how often have you had problems getting the food you need?	<input type="checkbox"/> 1. Never <input type="checkbox"/> 2. Sometimes <input type="checkbox"/> 3. Often <input type="checkbox"/> 4. Always																																						
P32	SKPML	M'sabata ziwiri zapitazi alipo munthu wankulu pakhomo pano amene sanadye kapena kudya mopelewera ndi cholinga choti ana akhale ndi chakudya chokwanira? In the past two weeks, has an adult in your house skipped a meal or ate less in order for there to be enough for the children?	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No																																						
P33	HROOM	Kodi mnyumba mwanu muli zipinda zingati kuphatikiza makitchni? How many rooms, including kitchens, are there in your home?	<table border="1" style="display: inline-table; vertical-align: top;"> <tr> <td style="width: 30px; height: 30px;"></td> <td style="width: 30px; height: 30px;"></td> </tr> </table>																																						
P34	HWAT	Kodi madzi ogwiritsa ntchito pakhomo pano mumatunga kuti? At your home, in which way do you obtain water for domestic use (TICK ONE)? Specify, if other	<input type="checkbox"/> 1. Piped water inside the dwelling <input type="checkbox"/> 2. Piped water inside the yard <input type="checkbox"/> 3. Piped water at kiosk <input type="checkbox"/> 4. Borehole/well <input type="checkbox"/> 5. River/Stream <input type="checkbox"/> 6. Other																																						
P35	HWATD	Kodi komwe mumakatunga madzi mungati ndi kotalika bwanji? At your home, what is the distance to the closest water access point?	<input type="checkbox"/> 1. Less than 200m <input type="checkbox"/> 2. Between 200m & 500m <input type="checkbox"/> 3. Between 500m & 1km <input type="checkbox"/> 4. More than 1km																																						

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P36	HTOL	Kodi pakhomo pano mumagwilitsa ntchito chimbudzi cha mtundu wanji? At your home, what is the MAIN type of toilet facility available for use by your household? (TICK ONE)	<input type="checkbox"/> 1. Flush toilet <input type="checkbox"/> 2. Ventilated pit latrine (VIP) <input type="checkbox"/> 3. Non-Ventilated pit latrine <input type="checkbox"/> 4. None						
P37	HTOLSH	Kodi mumagwiritsa ntchito chimbuzi chimenechi ndi mabanja ena? Do you share this toilet facility with other households?	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No						
P38	HLIT	Kodi pakhomo pano mumagwiritsa ntchito chiyani powunikira? At your home, what is your main source of lighting (TICK ONE)?	<input type="checkbox"/> 1. Collect firewood <input type="checkbox"/> 2. Buy firewood <input type="checkbox"/> 3. Batteries <input type="checkbox"/> 4. Paraffin <input type="checkbox"/> 5. Animal waste <input type="checkbox"/> 6. Electricity <input type="checkbox"/> 7. Candles <input type="checkbox"/> 8. Charcoal <input type="checkbox"/> 9. Crop residue/Grass <input type="checkbox"/> 10. Saw dust						
P39	PINC	Pa masabata anayi apitawa, kodi ndi ndani amene wakhala wozeza ndalama weni weni m'banjali? Over the last 4 weeks, who has been the primary income earner in the household (TICK ONE)? Specify, if other	<input type="checkbox"/> 1. I Have <input type="checkbox"/> 2. Husband/Wife <input type="checkbox"/> 3. Father <input type="checkbox"/> 4. Mother <input type="checkbox"/> 5. Son <input type="checkbox"/> 6. Daughter <input type="checkbox"/> 7. Extended Family <input type="checkbox"/> 8. Other, Specify						
P40	EMPL	Kodi pamasabata anayi apitawa munalembedwapo ntchito yolipidwa? Over the last 4 weeks have you been formally employed (TICK ONE)? Specify, if other	<input type="checkbox"/> 1. Yes, Formal Work <input type="checkbox"/> 2. No, Informal Work <input type="checkbox"/> 3. On Sick Leave <input type="checkbox"/> 4. Retired <input type="checkbox"/> 5. At School, University <input type="checkbox"/> 6. Housework <input type="checkbox"/> 7. Other, Specify						
P41	MASAL	Pa ntchito yanu yeni yeni, kodi ndi chani cheni cheni chimene mumachita kumalo anu antchito? In your MAIN JOB, what is the main activity at the place of work? (TICK ONE)	<input type="checkbox"/> 99. Not Applicable <input type="checkbox"/> 1. Agriculture, Forestry, Fishing <input type="checkbox"/> 2. Mining and Quarrying <input type="checkbox"/> 3. Manufacturing <input type="checkbox"/> 4. Electricity, Water, Other Utilities <input type="checkbox"/> 5. Construction <input type="checkbox"/> 6. Wholesale and Retail Marketing, Hotel/ Restaurants <input type="checkbox"/> 7. Transport and Communication <input type="checkbox"/> 8. Finance and Business <input type="checkbox"/> 9. Social and Community Services <input type="checkbox"/> 10. Other, Specify Specify, if other						
P42	MAHOU	Pa ntchito yanu yeni yeni, kodi ndi maola angati amene mumagwira pa sabata? In your MAIN JOB, how many hours do you work a week?	<table border="1" style="display: inline-table; vertical-align: middle;"> <tr> <td style="width: 30px; height: 30px;"></td> <td style="width: 30px; height: 30px;"></td> <td style="width: 30px; height: 30px;"></td> </tr> </table> Hours						
P43	PINCOM	Kodi mumapeza ndalama zingati kuwerengera zonse PAMODZI pa sabata? (asanachotse msonkho/ kapena china chili chonse) What is your TOTAL estimated income per week from all sources (Before tax/deductions)	MK <table border="1" style="display: inline-table; vertical-align: middle;"> <tr> <td style="width: 30px; height: 30px;"></td> </tr> </table>						

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		<p>Mafunso osatirawa ndi okhuza anthu amene mumakhala nawo m'banja mwanu. Amenewa ndi anthu amene nthawi zambiri mumakhala nawo ndikudyera limodzi zakudya m'banja mwanu.</p> <p>The following questions are about members of your household. These are individuals who normally live and share meals in your household.</p>						
P44	HHNA	<p>Limodzi ndi inuyo, kodi mnyumba mwanu mumakhala anthu aakulu angati (azaka zobadwa khumi zisanu ndi zitatu kapena kuposera pamenepa)?</p> <p>Including yourself, how many adults (aged 18 years and over) live in the household?</p>						
		<table border="1"> <tr> <td></td> <td></td> </tr> </table>						
P45	HHNC	<p>Kodi mnyumbamu mumakhala ana angati (azaka zobadwa zosapitirira zakubadwa khumi zisanu ndi zitatu)?</p> <p>How many children (aged under 18 years of age) live in the household?</p>						
		<table border="1"> <tr> <td></td> <td></td> </tr> </table>						
P46	HOH	<p>Kodi inu ndinu mwini/mkulu wa banja limeneli?</p> <p>Are you the head of the household?</p>						
		<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No						
P47	HOUSINC	<p>Kodi zonse pamodzi pakhomo pano mumapeza ndalama zingati kuchoka kulikonse? (Funsani wotenga nawo mbali kuti aphantikize ndalama zomwe onse pakhomopo amapeza kuphatikizapo iwo eni)</p> <p>What is the combined TOTAL household income per week from all sources? (Ask participant to include the income of all members of the household including themselves)</p> <p>Write '888888' if participant does not know</p>						
		<p>MK</p> <table border="1"> <tr> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> </tr> </table>						

DATA OFFICE USE ONLY

P48 DID Data Officer ID

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P49 DDATE

Date form checked

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**Appendix XI: HTC-104 Post HIV
testing questionnaire: Patient costs
and health-related quality of life –
HIV testing and HIV cohort studies**

Q01	HHBAR	Participant Barcode	<div style="border: 1px solid black; padding: 5px; width: fit-content;"> PLACE ID BARCODE HERE </div>	Write Participant Barcode <div style="border: 1px solid black; display: inline-block; width: 100px; height: 20px;"></div>
Q02	HHID	Interviewer ID	<div style="border: 1px solid black; display: inline-block; width: 40px; height: 20px;"></div>	Q03 CLUSID Cluster ID <div style="border: 1px solid black; display: inline-block; width: 40px; height: 20px;"></div>
Q04	SIT	Place of interview	<input type="checkbox"/> 1. Participant Home <input type="checkbox"/> 3. Queens Clinic <input type="checkbox"/> 2. Chilomoni Clinic <input type="checkbox"/> 4. Ndirande Clinic	
Q05	DOI	Date of interview	<div style="border: 1px solid black; display: inline-block; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; display: inline-block; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; display: inline-block; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; display: inline-block; width: 20px; height: 20px;"></div>	2 0 1 y y y y d d m o n
Q06	DOT	Tsiku limene anayezedwa HIV (Iembani tsiku lalero ngati ayezedwa lero)? Date of HIV Test (Write today's date if tested today)	<div style="border: 1px solid black; display: inline-block; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; display: inline-block; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; display: inline-block; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; display: inline-block; width: 20px; height: 20px;"></div>	2 0 1 y y y y d d m o n
Q07	LOC	Kodi kunali kuti kumene munakayezetsa HIV posachedwapa? Where did you have your recent HIV test?	<input type="checkbox"/> 1. At Home: Oral Self-testing in presence of counsellor <input type="checkbox"/> 2. At Home: Oral Self-testing in Private <input type="checkbox"/> 3. At Home: Finger Prick VCT (not from Hit-TB Study) <input type="checkbox"/> 4. HIV Testing Clinic: Referred by Antenatal clinic (ANC) <input type="checkbox"/> 5. HIV Testing Clinic: Referred by TB clinic <input type="checkbox"/> 6. HIV Testing Clinic: Referred by health professional (not TB, not ANC) <input type="checkbox"/> 7. HIV Testing Clinic: Went solely to learn my HIV status <input type="checkbox"/> 8. Mobile Testing Service <input type="checkbox"/> 9. Private healthcare provider <input type="checkbox"/> 10. Other, Specify Specify, if other <div style="border: 1px solid black; height: 40px; width: 100%;"></div>	
Q08	RES	Zotsatila zoyezetsa HIV HIV test result	<input type="checkbox"/> 1. Positive <input type="checkbox"/> 4. Invalid/indeterminate <input type="checkbox"/> 2. Negative <input type="checkbox"/> 5. Not done <input type="checkbox"/> 3. Not disclosed	
Q09	COU	Kodi munayezetsa limodzi ndi okonedwa anu? Did you test as a Couple? (Couples Testing) <small>Does not necessarily have to be husband/wife</small>	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No	
Q10	COUYR	Ngati ndi choncho, kodi patha zaka zingati chiyezetsereni limodzi ndi okonedwa anu? If yes, years together as a couple?	<input type="checkbox"/> 1. Less than 1yr <input type="checkbox"/> 2. Between 1 and 5yrs <input type="checkbox"/> 3. More than 5yrs <input type="checkbox"/> 4. NOT APPLICABLE	
Q11	COURES	Zotsatira za kuyezetsa HIV kwa munthu amene anayezetsa ngati banja? HIV test result of individual who tested as couple with you?	<input type="checkbox"/> 1. Positive <input type="checkbox"/> 4. Invalid/indeterminate <input type="checkbox"/> 2. Negative <input type="checkbox"/> 5. Not done <input type="checkbox"/> 3. Not disclosed <input type="checkbox"/> 99. NOT APPLICABLE	

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		Mafunso amenewa akukhuza zomwe munakumana nazo poyezetsa HIV chapompano These questions refer to your recent HIV testing experience							
Q12	TRA	<p>Kodi munayenda bwanji kukafika kumalo oyezetsera HIV?</p> <p>How did you get to the HIV testing site?(For home self-testing, how did participant travel to community counsellor to pick up test kit)</p> <p>Specify, if other</p> <div style="border: 1px solid black; height: 40px; width: 100%;"></div>	<p><input type="checkbox"/> 1. Tested in my home</p> <p><input type="checkbox"/> 2. Walked</p> <p><input type="checkbox"/> 3. Public transport</p> <p><input type="checkbox"/> 4. Own transport</p> <p><input type="checkbox"/> 5. Other, Specify</p>						
Q13	TRAT	<p>Kodi munatenga nthawi yayitali bwanji kuti mukafike kumalo oyezetsera HIV? (Pankhani yoziyeza nokha panyumba, muwerengere limodzi ndi nthawi imene anatenga kuti akafike kwa wopereka uphungu wammudzi kuti akatenge chipangizo choziyezera)</p> <p>How long did it take you to get to HIV testing site?(For home self-testing, include time taken to visit counsellor to pick up test kit) One-way travel</p> <p>Write '0' if tested at home</p>	<table border="1"> <tr> <td style="width: 30px; height: 30px;"></td> <td style="width: 30px; height: 30px;"></td> <td>Hours</td> </tr> <tr> <td style="width: 30px; height: 30px;"></td> <td style="width: 30px; height: 30px;"></td> <td>Minutes</td> </tr> </table>			Hours			Minutes
		Hours							
		Minutes							
Q14	WAIT	<p>Kodi munatenga nthawi yayitali bwanji kuti muthandizidwe (pamene munafika kufikira nthawi yimene munathandizidwa)?</p> <p>How long did you spend at the clinic in TOTAL (from arriving to leaving)? For home self-testing, total time spent waiting at counsellors home</p>	<table border="1"> <tr> <td style="width: 30px; height: 30px;"></td> <td style="width: 30px; height: 30px;"></td> <td>Hours</td> </tr> <tr> <td style="width: 30px; height: 30px;"></td> <td style="width: 30px; height: 30px;"></td> <td>Minutes</td> </tr> </table>			Hours			Minutes
		Hours							
		Minutes							
Q15	TRAM	<p>Kodi munagwiritsa ntchito ndalama yina yiriyonse pamayendedwe kuti mukafike kumalo oyezetsera?</p> <p>Did you spend any money on transportation to get there/here? (including for petrol/diesel)</p>	<p><input type="checkbox"/> 1. Yes</p> <p><input type="checkbox"/> 2. No</p>						
Q16	TRAM2	<p>Ngati munagwiritsa ntchito ndalama pamayendedwe, kodi munagwiritsa ntchito ndalama zingati?</p> <p>If you did spend money on transportation, how much did you spend?(Cost for one-way travel)</p> <p>Write '0' if did not spend any money</p>	<p>MK</p> <table border="1"> <tr> <td style="width: 30px; height: 30px;"></td> </tr> </table>						
Q17	WORK	<p>Kodi munayeneka kupempha nthawi yopuma kuntchito kuti mukayezedwe?</p> <p>Did you have to take time off work to get tested?</p>	<p><input type="checkbox"/> 1. Yes</p> <p><input type="checkbox"/> 2. No</p>						
Q18	WORK2	<p>Ngati ndi choncho, kodi munapempha masiku/maola kapena masiku angati kuntchito?</p> <p>IF YES, how many days/hours did you take off?</p> <p>Write '0' if did not take time of work</p> <p>Write '88' if not working</p>	<table border="1"> <tr> <td style="width: 30px; height: 30px;"></td> <td style="width: 30px; height: 30px;"></td> <td>Days</td> </tr> <tr> <td style="width: 30px; height: 30px;"></td> <td style="width: 30px; height: 30px;"></td> <td>Hours</td> </tr> </table>			Days			Hours
		Days							
		Hours							
Q19	FOOD1	<p>Kodi lero munagwiritsa ntchito ndalama yina yiliyonse pa chakudya kapena zakumwa panthawi imene mumadikira kuti muonedwe?</p> <p>Did you spend any money on food/drinks whilst waiting to be seen?</p>	<p><input type="checkbox"/> 1. Yes</p> <p><input type="checkbox"/> 2. No</p>						
Q20	FOOD2	<p>Ngati munagwiritsa ntchito ndalama pa chakudya kapena zakumwa, kodi munagwiritsa ntchito ndalama zingati?</p> <p>If you did spend money on food/drinks, how much did you spend?</p> <p>Write '0' if did not spend any money</p>	<p>MK</p> <table border="1"> <tr> <td style="width: 30px; height: 30px;"></td> </tr> </table>						

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Q21	OTH1	Kodi munagwiritsa ntchito ndalama yina yiriyonse pachinthu chirichonse china chifukwa chopita kuti mukayezetse HIV? Did you spend any money on anything else as a result of going to get the HIV test done?	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No						
Q22	OTH2	Tchulani chinthu chimene munagwiritsirapo ntchito ndalama? Specify what you spent money on?							
Q23	OTH3	Kodi munagwiritsa ntchito ndalama zingati pa chinthu chimenechi? How much did you spend on this? Write '99999' if question not applicable	MK <table border="1"><tr><td></td><td></td><td></td><td></td><td></td></tr></table>						
Q24	FAM	Kodi m'bale wanu kapena mzanu wina aliyense anakuperekezani kuti mukayezetse HIV? Did any family member or friend accompany you to get your HIV test done?	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No						
Q25	FAM1	Ngati ndi choncho, kodi iwowo anapempha masiku/maola kapena matsiku opuma kuntchito angati kuti akuperekezani? If yes, how many days/hours did they take off work to accompany you? Write '0' if did not take time off work Write '99' if question not applicable Write '88' if not working	<table border="1"><tr><td></td><td></td><td>Days</td></tr><tr><td></td><td></td><td>Hours</td></tr></table>			Days			Hours
		Days							
		Hours							
Q26	FAM2	Ngati amagwira ntchito, kodi amapeza ndalama zochuluka bwanji pa tsiku? If they work, how much do they normally earn per day? Write '99999' if question not applicable Write '88888' if participant does not know	MK <table border="1"><tr><td></td><td></td><td></td><td></td><td></td></tr></table>						
Q27	FAM3	Kodi iwowo anagwiritsa ntchito ndalama zingati pamayendedwe kuti akuperekezani inuyo? How much money did they spend on transportation to accompany you? (Cost for one-way travel) Write '0' if did not spend any money Write '99999' if question not applicable	MK <table border="1"><tr><td></td><td></td><td></td><td></td><td></td></tr></table>						
Q28	FAM4	Kodi iwowo anagwiritsa ntchito ndalama zingati pachakudya kapena zakumwa chifukwa choti anakuperekezani inuyo kuti mukayezetse HIV? How much money did they spend on food/drinks whilst waiting with you? Write '0' if did not spend any money Write '99999' if question not applicable	MK <table border="1"><tr><td></td><td></td><td></td><td></td><td></td></tr></table>						
Q29	FAM5	Kodi iwowo anagwiritsa ntchito ndalama yina yiriyonse pachinthu chirichonse china chifukwa choti anakuperekezani inuyo kuti mukayezetse HIV? Did they spend any money on anything else as a result of accompanying you to get the HIV test done?	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No						
Q30	FAM6	Tchulani chinthu chimene iwowo anagwiritsirapo ntchito ndalama Specify what they spent money on							
Q31	FAM7	Kodi zinali ndalama zingati zimene anagwiritsa ntchito pachinthu chimenechi? How much money did they spend on this? Write '0' if did not spend any money Write '99999' if question not applicable	MK <table border="1"><tr><td></td><td></td><td></td><td></td><td></td></tr></table>						

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		Mafunso amenewa akukukhuza ulendo uwuwu These questions refer to this visit
Q32	GEN	<p>Kodi munganene kuti umoyo wanu uli bwanji? <input type="checkbox"/> 1. Bwino kwambiri</p> <p>How would you rate your general health? <input type="checkbox"/> 2. Wabwino</p> <p><input type="checkbox"/> 3. Bwino pang'ono</p> <p><input type="checkbox"/> 4. Si uli bwino</p> <p><input type="checkbox"/> 5. Si uli bwino mpang'ono pomwe</p>
Chongani mu gulu lilironse pansipa, chonde sonyezani mfundo zimene zikufotokoza bwino za umoyo wanu.		
Q33	MOB	<p>Mayendedwe</p> <p><input type="checkbox"/> 1. Ndilibe vuto lina lililonse poyenda</p> <p><input type="checkbox"/> 2. Ndimakhala ndi mavuto ena poyenda</p> <p><input type="checkbox"/> 3. Ndimangobindikira pa kama</p>
Q34	SELF	<p>Kudzisamalira ndekha(mwachitsazo kusamba ndi kudziveka ndekha)</p> <p><input type="checkbox"/> 1. Ndilibe vuto podzisamalira ndekha</p> <p><input type="checkbox"/> 2. Ndimakhala ndi mavuto ena posamba kapena podziveka ndekha</p> <p><input type="checkbox"/> 3. Ndimalephera kusamba kapena kudziveka ndekha</p>
Q35	USUAL	<p>Zochitika za tsiku ndi tsiku (monga kugwira ntchito, kuwerenga,ntchito za pakhomu, za m'banja kapena kuchita zimene zimandisangalatsa)</p> <p><input type="checkbox"/> 1. Ndilibe mavuto ali onse pogwira ntchito zanga za nthawi zonse</p> <p><input type="checkbox"/> 2. Ndili ndi mavuto ena pang'ono pogwira ntchito za nthawi wonse</p> <p><input type="checkbox"/> 3. Ndimalephera kugwira ntchito zanga za nthawi zonse</p>
Q36	PAIN	<p>Ululu/kuphwanya m'thupi kusowetsa mtendere?</p> <p><input type="checkbox"/> 1. Ndilibe ululu kapena sindikumva kuphwanya m'thupi</p> <p><input type="checkbox"/> 2. Ndimakhala ndi ululu kapena kumva kuphwanya m'thupi mwapakatikati</p> <p><input type="checkbox"/> 3. Ndimakhala ndi ululu kapena kumva kuphwanya m'thupi kwambiri</p>
Q37	ANX	<p>Nkhawa/Khumudwa? (Osasangalala)</p> <p><input type="checkbox"/> 1. Sindikuda nkhwawa kapena kukhumudwa</p> <p><input type="checkbox"/> 2. Ndimakhala oda nkhwawa kapena okhumudwa mwapakatikati</p> <p><input type="checkbox"/> 3. Ndimakhala oda nkhwawa kapena okhumudwa kwambiri</p>

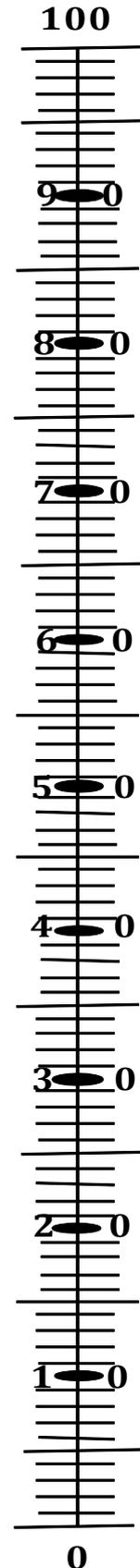
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Kuyerekezedwa kuti umoyo uli bwino kwambiri

Kuti tithandize anthu kunena za umoyo wawo, tajambula mlingo woyesela (chofanana ndi choyesela kuzizila/kutentha kwa m'thupi) womwe umoyo wabwino wayerekezedwa ndi chizindikiro cha 100 ndipo umoyo woipa wayelekezedwa ndi chizindikiro cha 0

Tikufuna mutisonyeze pa mlingowu mmene umoyo ulili lero kuti uli bwino kapena suli bwino mmene inu mukuganizira. Lembani mzere kuchokera pa bokosi pansipa kupita pa mlingo woyesera umene ukufotokoza za ubwino kapena kuipa kwa mmene umoyo wanu ulili lero.

**Mmene
umoyo wanu
ulili lero**



Q38 VAS Write Participants Score Below:

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0
**Kuyerekezedwa kuti
umoyo si uli bwino**

ID

Q39	PAST	<p>Mumiyenzi khumi ndi iwiri yapitayi, ndi kangati mwayezetsapo HIV mpakana kulandira zotsatira za kuyezetsako? (Osaphatikizapo kuyezetsa HIV mwapangitsa posachedwapa)</p> <p>Over the last 12 months, how many times have you had a HIV test where you completed the HIV test?(Not including this most recent HIV test)</p>	<input type="text"/> <input type="text"/>
Q40	FAIL	<p>Mumiyenzi khumi ndi iwiri yapitayi, ndikangati munayesa kuyezetsa HIV koma simunathe kuyezetsa HIV?</p> <p>Over the last 12 months, how many times have you tried to get a HIV test, but did not end up having the HIV test? (Failed Attempt)</p>	<input type="text"/> <input type="text"/>
Q41	FAILT	<p>Pamene munalephera kuyezetsa kotsiriza, ndi chifukwa ninji munalephera kuyezetsa HIV?</p> <p>For that most recent failed attempt, why did you not get the HIV test done?</p> <p>Specify, if other</p> <div style="border: 1px solid black; height: 40px; width: 100%;"></div>	<input type="checkbox"/> 1. I changed my mind <input type="checkbox"/> 2. Clinic/facility closed <input type="checkbox"/> 3. No HIV counsellor <input type="checkbox"/> 4. No HIV testing equipment <input type="checkbox"/> 5. I was told I should wait for the 'Window period" <input type="checkbox"/> 6. NOT APPLICABLE <input type="checkbox"/> 9. Other, Specify
Q42	TB	<p>Kodi munadwalapo chifuwa chachikulu cha TB pamiyezi khumi ndi iwiri yapitayi?</p> <p>Have you had Tuberculosis in the last 12 months?</p>	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No <div style="border: 1px solid black; padding: 5px; text-align: center;"> IF YES, COMPLETE HTC-TB QUESTIONNAIRE </div>
Q43	HOS	<p>Kodi munagonekedwapo mchipatala pamiyezi khumi ndi iwiri yapitayi?</p> <p>Have you been admitted to hospital over the last 12 months?(Excluding for TB, Malaria or Trauma)</p>	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No <div style="border: 1px solid black; padding: 5px; text-align: center;"> IF YES, COMPLETE HTC-HOP QUESTIONNAIRE </div>
Q44	PHC	<p>Kodi munagonekedwapo kuchipatala chaching'ono miyezi isanu ndi umodzi yapitayi pa zifukwa zina (kupatula chifukwa cha TB)?</p> <p>Have you been to the primary health care clinic over the last 6 months (Excluding for TB, Malaria or Trauma)?</p>	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No <div style="border: 1px solid black; padding: 5px; text-align: center;"> IF YES, COMPLETE HTC-PHC QUESTIONNAIRE </div>

DATA OFFICE USE ONLY

Q45 DID Data Officer ID

Q46 DDATE Date form checked

d d m o n y y y y

Appendix XII: Resource use data extraction tool

Cost-HTC: Resource use data extraction tool

The objective of this case report form is to collect information from each of the clinics will be done by interviewing a senior member of staff in the respective clinic, and listing all:

- staff who work in the department, including their position
- consumables, equipment etc used on the ward

The information requested needs to be completed in detail and systematically, obtaining as much information as possible to ensure costs can be applied to each item.

Clinic/Department:	
Interviewer Name:	
Information obtained from (Name, Mobile and Email):	
Date of Interview:	

Page Number	Form to complete
3	Staff and Personnel
6	Consumables (items lasting <1 year)
9	Equipment (items lasting >1 year)
12	Other Recurrent Items
15	Other Capital Items
18	Glossary
20	Additional forms

1. Staff/Personnel

No.	Staff Name/Initial	Description/Position of Staff (e.g. Dr; Nurse; HSW; Pay grade; job title)	% FTE in department	Notes
1				
2				
3				
4				
5				
6				
7				

2. Consumables

No.	Name of Consumable/Item	Detailed Description (e.g. Brand; Make; Model; Number in package etc.)	How much used per MONTH/YEAR	Additional Notes
1				
2				
3				
4				
5				
6				
7				
8				

3. Equipment

No.	Name of Equipment/Item	Detailed Description (e.g. Brand; Make; Model etc.)	% Use by Service Center	Additional Notes
1				
2				
3				
4				
5				
6				

4. Other Recurrent Items (Not included in 'Consumables')

No.	Name of Recurrent Item	Detailed Description (e.g. Brand; Make; Model; Number in package etc.)	How much used per MONTH/YEAR	Additional Notes
1				
2				
3				
4				
5				
6				

5. Other Capital Items

No.	Name of Capital Item	Detailed Description (e.g. Brand; Make; Model etc.)	% Use by Service Center	Additional Notes
1				
2				
3				
4				
5				

Glossary

Staff/Personnel	<ol style="list-style-type: none">1. General Guidance<ol style="list-style-type: none">a. All staffb. For staff who provide services to more than one service center, record proportion of time to this service centerc. Remember to include Senior management staff (e.g. Nurse Manager etc....)d. For unpaid people, record staff position appropriate to the tasks they perform, rather than their experience/ qualifications.e. For students, only include them if they are involved in providing a service to department 2. Bank/Locum Staff<ol style="list-style-type: none">a. Place these costs in “recurrent Items”b. Either consider the total expenditure of locum staff over time period, or note level and average usage
Consumables	<ol style="list-style-type: none">1) Only items with a lifespan of less than one year should be counted as consumables – Longer lasting items should be classified as ‘Equipment’ 2) General guidance<ol style="list-style-type: none">a. Identify all consumables used by the service centre (Medical and non-Medical)b. Quantify how much of item is used in an Average Monthc. Provide sufficient information: Brand/Manufacturer +/- description of item 3) Laboratory<ol style="list-style-type: none">a. Any consumables, such as test reagents, used within the laboratory centre should be identified. If a cost for each type of test is calculated, the consumables specifically used for each different type of test should be identified. 4) Other Service centers<ol style="list-style-type: none">a. Remember to include Furniture, stationery, paper, detergents, cleaning materials.

Equipment	<p>1. General guidance</p> <ul style="list-style-type: none"> a. List all equipment used in service center b. Include both medical and non-medical equipment <ul style="list-style-type: none"> i. Medical equipment includes both diagnostic and therapeutic items ii. Non-medical items include beds and chairs for patients or staff members. c. Record <ul style="list-style-type: none"> i. Manufacturer and model of equipment ii. In case item is not commercially available, record the material, measurements and use of item in detail d. Record number of all pieces in service center e. If item is shared with other service centres: record proportion of use by relevant service center <p>2. Laboratory and Radiology</p> <ul style="list-style-type: none"> a. Any equipment used in performing tests should be listed. b. If a cost for each type of test is being calculated, the amount of time each piece of equipment is used for performing each test also needs to be measured and the total expressed as a proportion of a full day's use. <p>3. Other support centers</p> <ul style="list-style-type: none"> c. Consider all equipment <ul style="list-style-type: none"> i. This may include washing and drying machines for cleaning services ii. Office equipment, such as computers, printers and telephones iii. Storage units, including filing cabinets iv. Relevant security equipment.
Recurrent inputs OR Capital inputs	<ul style="list-style-type: none"> • Estimation should be made whether the input was used within a single year (<i>recurrent input</i>) or during multiple years (<i>capital input</i>). • An example of recurrent input would be an expert consultation led by an external doctor on a single occasion, and capital input might include staff training.

**Appendix XIII: HTC-105 Patient
costs and health-related quality of
life – HIV cohort study**

R01	HHBAR	Participant Barcode	<div style="border: 1px solid black; padding: 5px; width: fit-content;"> PLACE ID BARCODE HERE </div>	Write Participant Barcode <div style="border: 1px solid black; display: inline-block; width: 100px; height: 20px;"></div>
R02	HHID	Interviewer ID	<div style="border: 1px solid black; display: inline-block; width: 40px; height: 20px;"></div>	R03 CLUSID Cluster ID <div style="border: 1px solid black; display: inline-block; width: 40px; height: 20px;"></div>
R04	SIT	Place of interview	<input type="checkbox"/> 1. Participant Home <input type="checkbox"/> 3. Queens ART Clinic <input type="checkbox"/> 2. Chilomoni Clinic <input type="checkbox"/> 4. Ndirande Clinic	
R05	DOI	Date of interview	<div style="display: flex; justify-content: space-around;"> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> </div> d d m o n 2 0 1 y y y y	
R06	HTC104	Did participant complete HTC-104 at same interview?	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No	
R07	FTEL	Telephone number of Participant (1st)	<div style="border: 1px solid black; display: inline-block; width: 100px; height: 20px;"></div>	
R08	FTEL2	Telephone number of Participant (2nd)	<div style="border: 1px solid black; display: inline-block; width: 100px; height: 20px;"></div>	
R09	FTEL3	Telephone number of Partner, Spouse or Family Member	<div style="border: 1px solid black; display: inline-block; width: 100px; height: 20px;"></div>	
Questions to be completed by reviewing HIV patient Cards				
R10	FOLL	What is the reason participant is here at clinic today?	<input type="checkbox"/> 1. Assessment for ART Eligibility <input type="checkbox"/> 2. Collection of CD4 result <input type="checkbox"/> 3. Group Counselling <input type="checkbox"/> 4. Initiation of ART <input type="checkbox"/> 5. Entry into Pre-ART care <input type="checkbox"/> 6. Collection of ART +/- IPT/CPT <input type="checkbox"/> 7. Collection of IPT/CPT (Pre-ART Care) <input type="checkbox"/> 8. Traced after Loss to follow-up <input type="checkbox"/> 9. Other, Specify	
		Specify, if other	<div style="border: 1px solid black; width: 100%; height: 40px;"></div>	
R11	WHO	WHO Clinical stage	<input type="checkbox"/> 1. WHO Stage I <input type="checkbox"/> 3. WHO Stage III <input type="checkbox"/> 2. WHO Stage II <input type="checkbox"/> 4. WHO Stage IV	
R12	WHODAT	Date of when participant had WHO Clinical Stage?	<div style="display: flex; justify-content: space-around;"> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> </div> d d m o n 2 0 1 y y y y	
R13	CD4	Last CD4 count	<div style="border: 1px solid black; display: inline-block; width: 60px; height: 20px;"></div>	
R14	CD4DAT	Date when this CD4 count was done?	<div style="display: flex; justify-content: space-around;"> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> </div> d d m o n 2 0 1 y y y y	

R15	ART	If on ART, which ART regime is participant receiving?	<input type="checkbox"/> 1. Regimen 1a <input type="checkbox"/> 2. Regimen 2a <input type="checkbox"/> 3. Regimen 3a <input type="checkbox"/> 4. Regimen 4a <input type="checkbox"/> 5. Regimen 5a <input type="checkbox"/> 6. Regimen 6a	<input type="checkbox"/> 7. Regimen 7a <input type="checkbox"/> 8. Regimen 8a <input type="checkbox"/> 9. Not Started ARV Drugs <input type="checkbox"/> 10. Defaulted ARV Drugs <input type="checkbox"/> 11. Other, Specify											
		Specify, if other													
R16	ARTSTA	Date ART initiated (Write today's date if initiating today)	<table border="1" style="display: inline-table; vertical-align: middle;"><tr><td style="width: 20px; height: 20px;"></td><td style="width: 20px; height: 20px;"></td></tr></table>			<table border="1" style="display: inline-table; vertical-align: middle;"><tr><td style="width: 20px; height: 20px;"></td><td style="width: 20px; height: 20px;"></td><td style="width: 20px; height: 20px;"></td><td style="width: 20px; height: 20px;"></td></tr></table>					<table border="1" style="display: inline-table; vertical-align: middle;"><tr><td style="width: 20px; height: 20px;"></td><td style="width: 20px; height: 20px;"></td><td style="width: 20px; height: 20px;"></td><td style="width: 20px; height: 20px;"></td></tr></table>				
			d d	m o n	y y y y										
R17	ARTSID	Has the patient experienced any side effects (current)-in the last month? (Tick all that apply)	<input type="checkbox"/> 1. Not on ARV Drugs <input type="checkbox"/> 2. No Side Effects <input type="checkbox"/> 3. Peripheral neuropathy <input type="checkbox"/> 4. Hepatitis <input type="checkbox"/> 5. Skin Rash <input type="checkbox"/> 6. Lipodystrophy <input type="checkbox"/> 7. NOT APPLICABLE <input type="checkbox"/> 8. Other, Specify												
		Specify, if other													
R18	ARTTB	TB Status (Current)	<input type="checkbox"/> 1. TB Not suspected <input type="checkbox"/> 2. TB suspected <input type="checkbox"/> 3. TB confirmed but not yet on treatment <input type="checkbox"/> 4. TB Confirmed and currently taking treatment <input type="checkbox"/> 5. Other, Specify												
		Specify, if other													
R19	ARTPILL	ARVs: Pill count?	<table border="1" style="display: inline-table; vertical-align: middle;"><tr><td style="width: 20px; height: 20px;"></td><td style="width: 20px; height: 20px;"></td><td style="width: 20px; height: 20px;"></td></tr></table>												
R20	ARTPMIS	ARVs: Doses missed	<table border="1" style="display: inline-table; vertical-align: middle;"><tr><td style="width: 20px; height: 20px;"></td><td style="width: 20px; height: 20px;"></td><td style="width: 20px; height: 20px;"></td></tr></table>												
R21	ARTCTX	CPT: Number of tablets given?	<table border="1" style="display: inline-table; vertical-align: middle;"><tr><td style="width: 20px; height: 20px;"></td><td style="width: 20px; height: 20px;"></td><td style="width: 20px; height: 20px;"></td></tr></table>												
R22	ARTFAM	Family Planning: Depot given?	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No												
R23	ARTCON	Number of condoms given?	<table border="1" style="display: inline-table; vertical-align: middle;"><tr><td style="width: 20px; height: 20px;"></td><td style="width: 20px; height: 20px;"></td></tr></table>												
R24	ARTVIR	Viral Load sample taken?	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No												
R25	ARTVIR2	Result of Viral Load?	<table border="1" style="display: inline-table; vertical-align: middle;"><tr><td style="width: 20px; height: 20px;"></td><td style="width: 20px; height: 20px;"></td></tr></table>												

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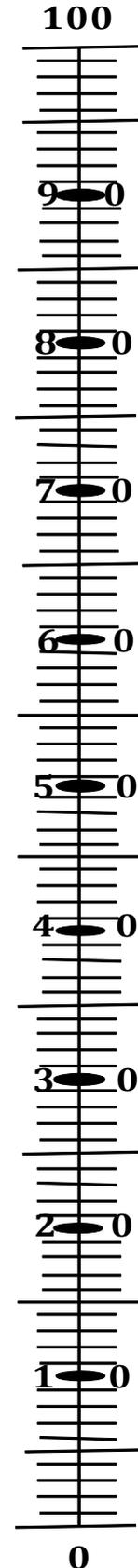
		Mafunso amenewa akukukhuza ulendo uwuwu These questions refer to this visit
R26	GEN	<p>Kodi munganene kuti umoyo wanu uli bwanji? <input type="checkbox"/> 1. Bwino kwambiri</p> <p><input type="checkbox"/> 2. Wabwino</p> <p>How would you rate your general health? <input type="checkbox"/> 3. Bwino pang'ono</p> <p><input type="checkbox"/> 4. Si uli bwino</p> <p><input type="checkbox"/> 5. Si uli bwino mpang'ono pomwe</p>
Chongani mu gulu lililonse pansipa , chonde sonyezani mfundo zimene zikufotokoza bwino za		
R27	MOB	<p>Mayendedwe</p> <p><input type="checkbox"/> 1. Ndilibe vuto lina lililonse poyenda</p> <p><input type="checkbox"/> 2. Ndimakhala ndi mavuto ena poyenda</p> <p><input type="checkbox"/> 3. Ndimangobindikira pa kama</p>
R28	SELF	<p>Kudzisamalira ndekha (mwachitsazo kusamba ndi kudziveka ndekha)</p> <p><input type="checkbox"/> 1. Ndilibe vuto podzisamalira ndekha</p> <p><input type="checkbox"/> 2. Ndimakhala ndi mavuto ena posamba kapena podziveka ndekha</p> <p><input type="checkbox"/> 3. Ndimalephera kusamba kapena kudziveka ndekha</p>
R29	USUAL	<p>Zochitika za tsiku ndi tsiku (monga kugwira ntchito, kuwerenga, ntchito za pakhomu, za m'banja kapena kuchita zimene zimandisangalatsa)</p> <p><input type="checkbox"/> 1. Ndilibe mavuto ali onse pogwira ntchito zanga za nthawi zonse</p> <p><input type="checkbox"/> 2. Ndili ndi mavuto ena pang'ono pogwira ntchito za nthawi wonse</p> <p><input type="checkbox"/> 3. Ndimalephera kugwira ntchito zanga za nthawi zonse</p>
R30	PAIN	<p>Ululu/kuphwanya m'thupi kusowetsa mtendere?</p> <p><input type="checkbox"/> 1. Ndilibe ululu kapena sindikumva kuphwanya m'thupi</p> <p><input type="checkbox"/> 2. Ndimakhala ndi ululu kapena kumva kuphwanya m'thupi mwapakatikati</p> <p><input type="checkbox"/> 3. Ndimakhala ndi ululu kapena kumva kuphwanya m'thupi kwambiri</p>
R31	ANX	<p>Nkhawa/Khumudwa? (Osasangalala)</p> <p><input type="checkbox"/> 1. Sindikuda nkhwawa kapena kukhumudwa</p> <p><input type="checkbox"/> 2. Ndimakhala oda nkhwawa kapena okhumudwa mwapakatikati</p> <p><input type="checkbox"/> 3. Ndimakhala oda nkhwawa kapena okhumudwa kwambiri</p>

Kuyerekezedwa kuti umoyo uli bwino kwambiri

Kuti tithandize anthu kunena za umoyo wawo, tajambula mlingo woyesela (chofanana ndi choyesela kuzizila/kutentha kwa m'thupi) womwe umoyo wabwino wayerekezedwa ndi chizindikiro cha 100 ndipo umoyo woipa wayelekezedwa ndi chizindikiro cha 0.

Tikufuna mutisonyeze pa mlingowu mmene umoyo ulili lero kuti uli bwino kapena suli bwino mmene inu mukuganizira. Lembani mzere kuchokera pa bokosi pansipa kupita pa mlingo woyesera umene ukufotokoza za ubwino kapena kuipa kwa mmene umoyo wanu ulili lero.

**Mmene
umoyo wanu
ulili lero**



R32 VAS Write Participants Score Below:

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**Kuyerekezedwa kuti
umoyo si uli bwino**

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R33	TRA	Kodi munayenda bwanji kuti mufike kuchipatala chaching'ono lero? How did you get to the HIV clinic today? Specify, if other	<input type="checkbox"/> 1. Walked <input type="checkbox"/> 2. Public Transport <input type="checkbox"/> 3. Own Transport <input type="checkbox"/> 4. Other						
R34	TRAT	Kodi munatenga nthawi yayitali bwanji kuti mukafike kuchipatala chaching'ono choyang'ana za HIV lero? How long did it take to get to the HIV clinic today? (One-way travel)	<table border="1"> <tr> <td></td> <td></td> <td>Hours</td> </tr> <tr> <td></td> <td></td> <td>Minutes</td> </tr> </table>			Hours			Minutes
		Hours							
		Minutes							
R35	WAIT	Kodi munatenga nthawi yayitali bwanji kuti muthandizidwe (pamene munafika kufikira nthawi yimene munathandizidwa)? How long did you spend at the clinic in TOTAL (from arriving to leaving)?	<table border="1"> <tr> <td></td> <td></td> <td>Hours</td> </tr> <tr> <td></td> <td></td> <td>Minutes</td> </tr> </table>			Hours			Minutes
		Hours							
		Minutes							
R36	TRAM	Kodi munagwiritsa ntchito ndalama yina yiliyonse pamayendedwe kuti mufike kuno? Did you spend any money on transportation to get here? (including for petrol/diesel)	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No						
R37	TRAM2	Ngati munagwiritsa ntchito ndalama pamayendedwa, kodi munagwiritsa ntchito zingati? If you did spend money on transportation, how much did you spend?(One-way travel) Write '0' if did not spend any money	MK <table border="1"> <tr> <td></td> <td></td> <td></td> <td></td> <td></td> </tr> </table>						
R38	WORK	Kodi munayeneka kutenga nthawi yakuntchito kuti mubwere kuchipatala chaching'ono lero? Did you have to time off work to attend Clinic today?	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No						
R39	WORK2	Ngati ndi choncho, kodi ndi masiku/maola kapena mphindi zingati zantchito zimene munatenga lero? If yes how many days/hours did you take off work today? Write '0' if did not take time off work Write '88' if not working	<table border="1"> <tr> <td></td> <td></td> <td>Days</td> </tr> <tr> <td></td> <td></td> <td>Hours</td> </tr> </table>			Days			Hours
		Days							
		Hours							
R40	FOOD1	Kodi lero munagwiritsa ntchito ndalama yina yiliyonse pa chakudya kapena zakumwa panthawi imene mumadikira kuti muonedwe? Did you spend any money on food/drinks, whilst waiting to be seen today?	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No						
R41	FOOD2	Ngati munagwiritsa ntchito ndalama pa chakudya kapena zakumwa, kodi munagwiritsa ntchito zingati? If you spent money on food/drinks how much did you spend? Write '0' if did not spend any money	MK <table border="1"> <tr> <td></td> <td></td> <td></td> <td></td> <td></td> </tr> </table>						
R42	OTH1	Kodi lero munagwiritsa ntchito ndalama yina yiliyonse pa chinthu china chilichonse chifukwa chobwera kuchipatala chaching'ono lero? Did you spend any money on anything else as a result of attending the clinic today ?	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No						
R43	OTH2	Tchulani chinthu chimene munagwiritsirapo ntchito ndalama Specify what you spent money	<table border="1"> <tr> <td></td> <td></td> <td></td> <td></td> <td></td> </tr> </table>						
R44	OTH3	Kodi munagwiritsa ntchito ndalama zingati pa chinthu chimenechi? How much did you spend on this? Write '0' if did not spend any money Write '99999' if question not applicable	MK <table border="1"> <tr> <td></td> <td></td> <td></td> <td></td> <td></td> </tr> </table>						

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R45	FAM	<p>Kodi m'bale wanu kapena mzanu wina aliyense anakuperekezani pa ulendo wa lero?</p> <p>Did any family member or friend accompany you on today's visit?</p>	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No					
R46	FAM1	<p>Ngati ndi choncho, kodi iwowo anapempha masiku/maola kapena masiku opuma kuntchito angati kuti akuperekezeni inuyo?</p> <p>If yes, how many days/hours did they take off work to accompany you?</p> <p><small>Write '0' if did not take time of work Write '88' if not working Write '99' if question not applicable</small></p>	<table border="1" style="display: inline-table; margin-right: 10px;"> <tr> <td style="width: 20px; height: 20px;"></td> <td style="width: 20px; height: 20px;"></td> </tr> </table> Days <table border="1" style="display: inline-table; margin-right: 10px;"> <tr> <td style="width: 20px; height: 20px;"></td> <td style="width: 20px; height: 20px;"></td> </tr> </table> Hours					
R47	FAM2	<p>Ngati amagwira ntchito, kodi amapeza ndalama zochuluka bwanji pa tsiku?</p> <p>If they work, how much do they normally earn per day?</p> <p><small>Write '88888' if participant does not know Write '99999' if question not applicable</small></p>	MK <table border="1" style="display: inline-table; margin-left: 10px;"> <tr> <td style="width: 20px; height: 20px;"></td> </tr> </table>					
R48	FAM3	<p>Kodi iwowo anagwiritsa ntchito ndalama zingati pamayendedwe kuti akuperekezeni inuyo?</p> <p>How much money did they spend on transportation to accompany you? (One-way travel)</p> <p><small>Write '0' if did not spend any money Write '99999' if question not applicable</small></p>	MK <table border="1" style="display: inline-table; margin-left: 10px;"> <tr> <td style="width: 20px; height: 20px;"></td> </tr> </table>					
R49	FAM4	<p>Kodi iwowo anagwiritsa ntchito ndalama zingati pogula chakudya kapena zakumwa m'mene ankadikira limodzi ndi inuyo?</p> <p>How much money did they spend on food/drinks whilst waiting with you?</p> <p><small>Write '0' if did not spend any money Write '99999' if question not applicable</small></p>	MK <table border="1" style="display: inline-table; margin-left: 10px;"> <tr> <td style="width: 20px; height: 20px;"></td> </tr> </table>					
R50	FAM5	<p>Kodi iwowo anagwiritsa ntchito ndalama ina iriyonse pachinthu chirichonse china m'mene anakuperekezani?</p> <p>Did they spend money on anything else whilst accompanying you?</p>	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No					
R51	FAM6	<p>Tchulani chinthu chimene iwowo anagwiritsirapo ntchito ndalama</p> <p>Specify what they spent money on?</p>	<table border="1" style="width: 100%; height: 80px;"> <tr> <td style="width: 100%; height: 100%;"></td> </tr> </table>					
R52	FAM7	<p>Kodi anagwiritsa ntchito ndalama zingati pachinthu chimenechi?</p> <p>How much money did they spend on this?</p> <p><small>Write '0' if did not spend any money Write '99999' if question not applicable</small></p>	MK <table border="1" style="display: inline-table; margin-left: 10px;"> <tr> <td style="width: 20px; height: 20px;"></td> </tr> </table>					
R53	OFFW	<p>M'mwezi umodzi wapitawu, kodi munapemphapo kuti musapite kuntchito kamba kamatenda?</p> <p>In the last one month, have you taken time off work because of illness?</p>	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No					
R54	OFFW2	<p>Ngati ndi choncho, kodi ndi masiku/maola angati antchito amene munapempha?</p> <p>If yes how many days/hours did you take off work?</p> <p><small>Write '0' if did not take time off work Write '88' if not working</small></p>	<table border="1" style="display: inline-table; margin-right: 10px;"> <tr> <td style="width: 20px; height: 20px;"></td> <td style="width: 20px; height: 20px;"></td> </tr> </table> Days <table border="1" style="display: inline-table; margin-right: 10px;"> <tr> <td style="width: 20px; height: 20px;"></td> <td style="width: 20px; height: 20px;"></td> </tr> </table> Hours					

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R55	OFFW3	<p>Mu mwezi umodzi wapitawu, kodi pali wina aliyense m'banja mwanu kapena mnzanu amene anakusamalirani chifukwa choti munadwala?</p> <p>In the last one month, has a family member or friend had to spend time caring for you because you were ill?</p>	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No						
R56	OFFW4	<p>Ngati zili choncho, mukaphatizika nthawi imene anatero ingakhale yochuluka bwanji?</p> <p>If yes how much time did they spend caring for you in TOTAL</p> <p>Write '0' if did not spend time caring for participant</p>	<table border="1" style="display: inline-table; vertical-align: top;"> <tr> <td style="width: 20px; height: 20px;"></td> <td style="width: 20px; height: 20px;"></td> <td style="padding-left: 5px;">Days</td> </tr> <tr> <td style="width: 20px; height: 20px;"></td> <td style="width: 20px; height: 20px;"></td> <td style="padding-left: 5px;">Hours</td> </tr> </table>			Days			Hours
		Days							
		Hours							
R57	SAWHC	<p>Lero kuchipatala chaching'ono, kodi munaonana ndi wopereka uphungu wa HIV ?</p> <p>At the clinic today, did you see a HIV counsellor?</p>	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No						
R58	SAWNU	<p>Lero kuchipatala chaching'ono, kodi munaonana ndi namwino ?</p> <p>At the clinic today, did you see a Nurse?</p>	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No						
R59	SAWCO	<p>Lero kuchipatala chaching'ono, kodi munaonana ndi Clinical Officer ?</p> <p>At clinic today, did you see a Clinical Officer?</p>	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No						
R60	SAWDR	<p>Lero kuchipatala chaching'ono, kodi munaonana ndi dotolo?</p> <p>At the clinic today, did you see the Doctor?</p>	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No						
R61	TBSP1	<p>Lero kuchipatala chaching'ono, kodi dotolo kapena namwino anakupemphani kuti mukhosomole makhololo kuti awayeze?</p> <p>At the clinic today, did the doctor/nurse ask you to cough up sputum to do some tests?</p>	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No						
R62	TBXR1	<p>Lero kuchipatala chaching'ono, kodi dotolo kapena namwino anakupemphani kuti mujambulidwe pa chidale panu ndi chipangizo chojambulira mthupi?</p> <p>At the clinic today, did the doctor/nurse ask you to go and get an X-Ray of your chest?</p>	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No						
R63	TBBL	<p>Lero kuchipatala chaching'ono, kodi dotolo kapena namwino anatenga magazi kwa inuyo kuti awayeze?</p> <p>At the clinic today, did the doctor/nurse take blood from you to do tests on?</p>	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No						
R64	TBSC	<p>Lero kuchipatala chaching'ono, kodi dotolo kapena namwino anakubayani ndi singano kumsana kwanu kuti atenge madzi oti awayeze?</p> <p>At the clinic today, did the doctor/nurse put a needle into you back to take a sample of liquid?</p>	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No						
R65	TBOTS	<p>Kuchipatala lero, munayezetsa matenda ena ali onse (Chonde fotokozani mwakulemba mubokosimu)</p> <p>At the clinic today, did you have any other tests/investigations done (Please specify each one in a separate box)</p>	<table border="1" style="width: 100%; height: 150px;"> <tr> <td style="height: 50px;"></td> </tr> <tr> <td style="height: 50px;"></td> </tr> <tr> <td style="height: 50px;"></td> </tr> </table>						

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		Tikambiranepo za mankhwala amene anaperekedwa kwa inuyo lero(Kupatula mankhwala ama ARV)? Can we look at the Medications/Drugs that were given to you today (EXCLUDING ARV DRUGS)?	
R66	ADRUG	Name of Drug?	<input type="text"/>
R67	ADRUGD	Dose	<input type="text"/>
R68	ADRUGT	Number of tablets given	<input type="text"/> <input type="text"/>
R69	ADRUG2	Name of Drug?	<input type="text"/>
R70	ADRUGD2	Dose	<input type="text"/>
R71	ADRUGT2	Number of tablets given	<input type="text"/> <input type="text"/>
R72	ADRUG3	Name of Drug?	<input type="text"/>
R73	ADRUGD3	Dose	<input type="text"/>
R74	ADRUGT3	Number of tablets given	<input type="text"/> <input type="text"/>
R75	ADRUG4	Name of Drug?	<input type="text"/>
R76	ADRUGD4	Dose	<input type="text"/>
R77	ADRUGT4	Number of tablets given	<input type="text"/> <input type="text"/>
R78	TB	Kodi munapezekapo ndi chifuwa cha chikulu cha TB m'mwezi umodzi wapitawu? Have you been diagnosed with Tuberculosis in the last 1 month?	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No If YES, COMPLETE HTC-TB QUESTIONNAIRE
R79	HOS	Kodi mwagonekedwapo mchipatala chachikulu m'mwezi umodzi wapitawu? Have you been admitted to hospital over the last 1 month?(Excluding for TB/Malaria/Trauma)	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No If YES, COMPLETE HTC-HOP QUESTIONNAIRE
R80	PHC	Kodi munapitapo kuchipatala chaching'ono miyezi isanu ndi umodzi yapitayi kamba kachifukwa china chilichonse? Have you been to the Primary Health Clinic Over the Last Month? (Excluding for TB/Malaria/Trauma)	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No If YES, COMPLETE HTC-PHC QUESTIONNAIRE

DATA OFFICE USE ONLY

R81 DID Data Officer ID

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R82 DDATE Date form checked

<input type="text"/>							
d	d	m	o	n	y	y	y

**Appendix XIV: Participant
information leaflet (Chichewa
version) - Hospital cohort study**

**Kusalowa Mthumba kwa ntchito yoyeza ndi kupereka uphungu wa HIV
HTC-500X: Tsamba la Uthenga wa otenga nawo mbari (Chichewa version)**



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Dzina la kafukufuku: kusalowa mthumba kwa nchito yoyeza ndi kupereka uphungu wa HIV pa khomo ku Blantyre, Malawi – kuwerengetsera gwero la chisamaliro cha ku chipatala

Chiyambi

Mulibwanji, dzina langa ndi _____, ndikugwira ntchito ndi bungwe la **Malawi-Liverpool-Wellcome Clinical Research Programme**. Tikupanga kafukufuku wa HIV, amene asali wa chilendo mu dziko muno, komanso m'mene tingaperekere thandizo la kuziyeza HIV kwa anthu amene angafune kudziwa za mthupi mwawo ngati ali ndi HIV kapena ayi. Ku mbari ya kafukufuku ameneyu, tikufuna kuona mtengo wa Ndalama komanso zotsatira zimene zimabwera kwa anthu amene alibe kachiroombo ka HIV ndi anthu amene ali ndi kachiroombo HIV amene akufunika kulandira thandizo la mankhwala a chifuwa chachikulu cha TB kapena amene akufunika kugonekedwa ku chipatala kuti athandizidwe pa matenda ena. Pakhoza kukhala mawu ena amene simukutha kumvesetsa. Chonde ndiuzeni kuti ndiime kaye pamene tikukambirana za uthenga umenewu ndipo ndizatenga nthawi kuti ndifotokoze. Chiganizo chakuti mukufuna kutenga nawo mbari kapena ayi, sichizakupangitsani kulephera kupeza thandizo limeneli.

Cholinga cha kafukufukuyu?

Kafukufukuyu ndi mbari imodzi yofufuza za Ndalama zimene zingagwiritsidwe ntchito komanso phindu limene lingakhalepo popereka thandizo lakuziyeza HIV m'makomo komanso kudzera mu zipata zing'ono-zing'ono ku Blantyre, Malawi. Ku Malawi, anthu ambiri samadziwa kuti ali ndi HIV mwamsanga. Komabe, kupereka thandizo la kuziyeza HIV m'makomo mwa anthu kwapezeka kuti ndi chinthu chimene chikuvomerezedwa kwambiri komanso kufikira anthu amene ali ndi HIV mwa m'msanga, komanso asanayambe kudwala matenda ambiri obwera chifukwa cha ka chiombo ka HIV. Ambiri mwa anthu odwala matenda amenewo amafunika kugonekedwa ku chipatala, zimene ziri zinthu zofuna Ndalama zambiri, kwa anthu opereka chisamaliro cha kuchipatala komaso munthu payekha-payekha. Cholinga cha kafukufukuyu ndikuwerengetsera Ndalama zimene zimagwiritsidwa ntchito komanso gwero lake pakukonza mwatsopano moyo wa anthu amene akudwala matenda obwera chifukwa cha kachiroombo ka HIV, amene akufunika kugonekedwa ku chipatala. Uthenga umenewu uzatilora kuti tiwerengetsera mongoganizira Ndalama zimene tingapewe kuononga, pamene tikupereka thandizo lakuziyeza HIV m'makomo, komanso ngati zimenezi zingaonetsere Ndalama zoonjezera pogwira ntchito yopereka thandizo limeneli. Tikufuna kupeza gwero la kugonekedwa ku chipatala kapena kupatsidwa thandizo la mankhwala a TB, pakukhala ndi moyo wathanzi, Ndalama zimene mumaononga pofuna kupeza chisamaliro chakuchipatala komanso Ndalama zimene zimaonongedwa pamene mukupatsidwa thandizo la mankhwala. Tikufuna tipange kafukufuku pogwiritsa ntchito tsamba la ndondomeko ya mafunso ndi anthu amene amagonekedwa ku chipatala kapena ali ndi TB.

Ndondomeko

Nthawi: Kafukufukuyu achitika nthawi imene mwagonekedwa ku chipatala.

**Kusalowa Mthumba kwa ntchito yoyeza ndi kupereka uphungu wa HIV
HTC-500X: Tsamba la Uthenga wa otenga nawo mbari (Chichewa version)**

Kodi muzafunsidwa kuti mutani: Tidzapempha kuti ticheze ndi anthu kuyambira zaka 18 kupita m'mwamba, amene agonekedwapo ku ma wodi akuchipatala chachikulu cha *Queen Elizabeth*, Blantyre komanso amene angavomereze kutenga nawo mbari mu ndondomeko ya mafunso angapo ndicholinga chofuna kupempha uthenga pa nkhani ya zotsatirazi: za moyo wawo, ngati ali ndi HIV kapena ayi, thandizo komanso chisamaliro chimene analandira kuchokera ku chipatala nthawi imene anagonekedwa kuchipatalako, Ndalama zimene anaononga nthawi imene anagonekedwa ku chipatala, komanso gwero lakugonekedwa mu chipatala pofuna kutukula umoyo wawo. Tikufunanso titakumana nanu nthawi yomweyo imenemungagonekedwe kuchipatalako, ndipo sabata linalirilonse kapena kuonjezera apo kufikira mpaka mutatulutsidwa muchipatala. Nthawi ina iriyonse imene tingakuoneni, tidzafuna kukhala nanu kwa mphindi zokwana 15. Tidzaunikanso uthenga wa ku chipatala okhudzana ndi inu pofuna kupeza chifukwa chimene munagonekedwa komanso chisamaliro chakuchipatala chimene munalandira nthawi imene munagonekedwa kuchipatala.

Kutenga nawo mbari ndi ulere: mukhoza kutuluka mu kafukufukuyu nthawi ina iriyonse popanda kupereka chifukwa komanso popanda kuimbidwa mlandu wina uliwonse.

Mtengo wa ndalama, mavuto komanso ululu: muzafunsidwa ngati muli ndi HIV kapena ayi. Mukhoza kukhala omangika pokambirana nkhani imeneyi. Simukuyenera kutidziwitsa ngati muli ndi HIV kapena ayi, mukhoza kukana kutenga nawo mbari, komanso mukhoza kutuluka mu ndondomeko ya mafunso nthawi ina iriyonse. Ngati mungatuluke mukafukufukuyu muzakhalabe ndi kuthekera kopeza thandizo kumalo amene amapereka thandizo la HIV. Simudzalipira kena kalikonse potenga nawo mbari mukafukufukuyu.

Phindu: sipadzakhala phindu looneka ndi maso kwa inu mukatenga nawo mbari. Komabe, uthenga umene mungapereke udzathandiza kukonza mwa tsopano ntchito yoyeza HIV komanso thandizo la mankhwala mu dela lanu.

Kulipiridwa: mudzapatsidwa zokumwa zoziziritsa kukhosi nthawi imene ndondomeko ya mafunso ikuchitika, pofuna kukulipirani chifukwa cha nthawi yanu.

Chinsinsi: Sitidzapereka uthenga okhudzana ndi anthu omwe atatenge nawo mbari mukafukufukuyu kwa wina aliyense. Uthenga umene titatolere mukafukufukuyu udzasungidwa mwa chinsinsi. Uthenga umene utazatoleredwe nthawi imene kafukufukuyu akuchitika siudzadziwika ndi dzina lanu koma ndi nambala. Ndi opangitsa kafukufuku okhawa amene atadzadziwe nambala yanu, ndipo adzatsekera uthenga umenewo ndi loko komanso kiyi. Uthenga umene tingatenge kudzera mu kafukufukuyu uzagawidwa kwa inu. Kudzachitika misonkhano ing'ono-ing'ono mu dela ndipo misonkhano imeneyi idzalengezetsedwa. Ngati uthenga ochokera mukafukufukuyu ungalembedwe mu mabuku kapena kuperekedwa pa misonkhano ya sayansi kapena misonkhano yofikira anthu am'madela onse, dzina lanu komanso uthenga okhudzana ndi inu sizidzagwiritsidwa ntchito.

Chilorezo chakuti kafukufukuyu achitike: komiti yoyang'anila za akafukufuku ya College of Medicine, Blantyre, Malawi komanso komiti ya Univesite ya Warwick Biomedical Research Ethics, Warwick, UK yavomereza kafukufukuyu.

Mafunso: Ngati mungakhale ndi mafunso ena-aliwonse okhudzana ndi kafukufukuyu, mukhoza kumuimbira foni Dr Hendramoorthy Maheswaran (mkulu wa kafukufukuyu, Tel: 0996151939) kapena wapampando wa COMREC (Tel: 0198 9766).

Appendix XV: Consent form
(Chichewa version) - Hospital cohort
study

**Kusalowa Mthumba kwa ntchito yoyeza ndi kupereka uphungu wa HIV
HTC-500: Tsamba la chilorezo (Chichewa version)**



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Nambala ya ID ya kafukufuku

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Dzina la kafukufuku: Kusalowa mthumba kwa nchito yoyeza ndi kupereka uphungu wa HIV pa khomo ku Blantyre, Malawi – kuchulukitsa gwero la chisamaliro cha ku chipatala

- Ndapemphedwa kutenga nawo mbari mu kafukufukuyu, kusiyanita mtengo wa Ndalama komanso gwero la kugonekedwa ku chipatala kapena kufunikira kwa kulandira thandizo la mankhwala a TB pofuna kukhala ndi moyo wa thanzi.
- Ndalandira, kuwerenga komanso kumvesetsa uthenga olembedwa (tsamba la uthenga wa otenga nawo mbari) kukhudzana ndi kafukufukuyu.
- Ndikumvesetsa kuti zimenezi zizakhala ndi kalondo-londo wa ndondomeko ya mafunso
- Ndadziwitsidwa kuti pali mavuto ochepa.
- Ndikudziwa kuti pakhoza kusakhala phindu looneka kwa ine komanso sindidzalipidwa Ndalama yoposela transipoti komanso zoziziritsira kukhosi.
- Nthawi ina iriyonse ndikhoza kuletsa kupereka chilorezo komanso kutenga nawo mbari mukafukufukuyu popanda kuimbidwa mlandu.
- Ndapatsidwa dzina la opangitsa kafukufuku (Dr Hendramoorthy Maheswaran) amene ndingalumikizane naye mosavuta pogwiritsa ntchito nambala komanso adilesi imene ndinapatsidwa ya munthu ameneyu.
- Ndakhala ndi mwayi okwanila ofunsa mafunso komanso (mwakufuna kwa ine ndekha) kulengezetsa kuti ndiri okonzeka kutenga nawo mbari mukafukufukuyu.

Dzina la otenga nawo mbari (sindikizani)	Siginichala ya otenga nawo mbari	Deti
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Ndawerenga molondola kapena kupelekera umboni kuwerenga kolondola kwa tsamba la chilorezo kwa otenga nawo mbari oyenelera, ndipo munthuyo wakhala ndi mwayi ofunsa mafunso. Ndikutsindikiza kuti munthuyo wapereka chilorezo momasuka.

Dzina la membala ogwira ntchito (tsindikizani)	Siginichala ya membala ogwira ntchito amene anatsogolera ntchito yopereka chilorezo	Deti
--	---	------

NGATISAKUTHA KUWERENGA, Operekera umboni amene amatha kuwerenga a siyinire.

Ndaonelera kuwerenga kolondola kwa tsamba la chilorezoli, ndipo munthuyu anali ndi ufulu ofunsa mafunso. Ndikutsimikiza kunena kuti munthuyo wapereka chilorezo momasuka.

Dzina la mboni (tsindikizani)	Siginichala ya mboni	Deti
-------------------------------	----------------------	------

**Appendix XVI: Ward template for
assessing participant's eligibility for
recruitment - Hospital cohort study**

	Date of admission	Name of Patient	Does patient have provisional diagnosis of:	RECRUIT	Bed number
1			-Pneumocystis Carinii Pneumonia -Candidiasis -Cryptococcal Meningitis -Kaposi's Sarcoma	} Yes No	
2			-Pneumocystis Carinii Pneumonia -Candidiasis -Cryptococcal Meningitis -Kaposi's Sarcoma	} Yes No	
3			-Pneumocystis Carinii Pneumonia -Candidiasis -Cryptococcal Meningitis -Kaposi's Sarcoma	} Yes No	
4			-Pneumocystis Carinii Pneumonia -Candidiasis -Cryptococcal Meningitis -Kaposi's Sarcoma	} Yes No	
5			RECRUIT		
6			-Pneumocystis Carinii Pneumonia -Candidiasis -Cryptococcal Meningitis -Kaposi's Sarcoma	} Yes No	
7			-Pneumocystis Carinii Pneumonia -Candidiasis -Cryptococcal Meningitis -Kaposi's Sarcoma	} Yes No	
8			-Pneumocystis Carinii Pneumonia -Candidiasis -Cryptococcal Meningitis -Kaposi's Sarcoma	} Yes No	
9			-Pneumocystis Carinii Pneumonia -Candidiasis -Cryptococcal Meningitis -Kaposi's Sarcoma	} Yes No	
10			RECRUIT		

**Appendix XVII: HTC-DOC Medical
data extraction tool - Hospital
cohort study**

Z01	HHBAR	Participant Barcode	<div style="border: 1px solid black; padding: 5px; width: fit-content;"> PLACE ID BARCODE HERE </div>	Write Participants Barcode <div style="border: 1px solid black; display: inline-block; width: 100px; height: 20px;"></div>
Z02	TBROCC	TB-ROCC Participant ID (write 9999999 if not a TB-ROCC participant)	<div style="border: 1px solid black; display: inline-block; width: 150px; height: 20px;"></div>	
Z03	HHID	Interviewer ID	<div style="border: 1px solid black; display: inline-block; width: 60px; height: 20px;"></div>	
Z04	DOI	Date of completion	<div style="display: flex; justify-content: space-around;"> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> </div> <p style="text-align: center; font-size: small;">d d m o n y y y y</p>	
Z05	DOA	Date of Admission	<div style="display: flex; justify-content: space-around;"> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> </div> <p style="text-align: center; font-size: small;">d d m o n y y y y</p>	
Z06	DIS	What happened to patient? <input type="checkbox"/> 1. Discharged Home <input type="checkbox"/> 2. Transferred to another hospital <input type="checkbox"/> 3. Absonded <input type="checkbox"/> 4. Died	Write date patient died or left QECH <div style="display: flex; justify-content: space-around;"> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> </div> <p style="text-align: center; font-size: small;">d d m o n y y y y</p>	
		If transferred to another hospital, WRITE NAME	<div style="border: 1px solid black; width: 100%; height: 20px;"></div>	
Z07	RES	HIV status of patient?	<input type="checkbox"/> 1. Positive <input type="checkbox"/> 2. Negative <input type="checkbox"/> 3. Not disclosed <input type="checkbox"/> 4. Invalid/indeterminate <input type="checkbox"/> 5. Not done	
Z08	ONART	Is the patient on Anti-Retroviral treatment?	<input type="checkbox"/> 1. HIV negative <input type="checkbox"/> 2. HIV positive and on ART before hospital admission <input type="checkbox"/> 3. HIV positive and started ARV's during this admission <input type="checkbox"/> 4. HIV positive and NOT on ARVs	
Z09	ART	If on ART, which ART regime is participant receiving?	<input type="checkbox"/> 1. Regimen 1a <input type="checkbox"/> 2. Regimen 2a <input type="checkbox"/> 3. Regimen 3a <input type="checkbox"/> 4. Regimen 4a <input type="checkbox"/> 5. Regimen 5a <input type="checkbox"/> 6. Regimen 6a <input type="checkbox"/> 7. Regimen 7a <input type="checkbox"/> 8. Regimen 8a <input type="checkbox"/> 9. Not Applicable	
		If patient started ARVs in hospital, WRITE DATE STARTED	<div style="display: flex; justify-content: space-around;"> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> </div> <p style="text-align: center; font-size: small;">d d m o n y y y y</p>	
Z10	WHO	WHO Clinical stage	<input type="checkbox"/> 1. WHO Stage I <input type="checkbox"/> 2. WHO Stage II <input type="checkbox"/> 3. WHO Stage III <input type="checkbox"/> 4. WHO Stage IV <input type="checkbox"/> 5. Not Recorded	
Z11	CD4	Last CD4 count recorded in patients notes (write '9999' if not applicable or not done)	<div style="border: 1px solid black; display: inline-block; width: 80px; height: 20px;"></div>	
Z12	CD4DAT	Date when this CD4 count was done?	<div style="display: flex; justify-content: space-around;"> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> </div> <p style="text-align: center; font-size: small;">d d m o n y y y y</p>	

Primary Medical Diagnosis

The medical condition of patient that resulted in the hospital admission

Follow guidelines on ICD codebook to complete ICD levels

Z13 PRY1 ICD Level 1

Z14 PRY2 ICD Level 2 ■ WRITE 99 if not applicable

Z15 PRY3 ICD Level 3 ■ ■

Z16 PRY4 ICD Level 4 ■ ■ ■

Z17 PRYX

Alternative Classification of Primary Diagnosis

(Code Primary Diagnosis using table on Right)

Code to Enter	Primary Medical Diagnosis
1	Anaemia
2	Candidiasis of mouth – thrush
3	Candidiasis – excluding thrush
4	Cryptococcal Meningitis
5	Diabetes
6	Gastroenteritis - Acute
7	Gastroenteritis – Chronic
8	Heart Failure
9	Kaposi's Sarcoma
10	Malaria
11	Meningitis (exc TB/Crypto)

Code to Enter	Primary Medical Diagnosis
12	Pneumonia (exc TB/PCP)
13	Pneumocystis Carinii Pneumonia
14	Seizures
15	Sepsis
16	Stroke
17	Tuberculosis
18	Tuberculosis – retreatment
19	Urinary Tract Infection
20	Wasting Syndrome
21	OTHER
22	NOT KNOWN

Co-Morbidities

Any medical condition patient had prior to hospital admission

Z18 CHAR

Does the patient suffer from or recently suffered:

MI	Myocardial Infarction	<input type="checkbox"/> 1. Yes	<input type="checkbox"/> 2. No	
CHF	Congestive Heart Failure	<input type="checkbox"/> 1. Yes	<input type="checkbox"/> 2. No	
PVD	Peripheral Vascular disease	<input type="checkbox"/> 1. Yes	<input type="checkbox"/> 2. No	
CVD	Cerebrovascular Disease	<input type="checkbox"/> 1. Yes	<input type="checkbox"/> 2. No	
DEM	Dementia	<input type="checkbox"/> 1. Yes	<input type="checkbox"/> 2. No	
COPD	COPD	<input type="checkbox"/> 1. Yes	<input type="checkbox"/> 2. No	
CTD	Connective Tissue Disease	<input type="checkbox"/> 1. Yes	<input type="checkbox"/> 2. No	
PUD	Peptic Ulcer Disease	<input type="checkbox"/> 1. Yes	<input type="checkbox"/> 2. No	
ML	Malignant Lymphoma	<input type="checkbox"/> 1. Yes	<input type="checkbox"/> 2. No	
KD	Moderate to Sever Kidney disease	<input type="checkbox"/> 1. Yes	<input type="checkbox"/> 2. No	
HEM	Hemiplegia	<input type="checkbox"/> 1. Yes	<input type="checkbox"/> 2. No	
DM	Diabetes Mellitus	<input type="checkbox"/> 1. Yes - uncomplicated	<input type="checkbox"/> 2. Yes - with end-organ damage	<input type="checkbox"/> 3. No
ST	Solid Tumour	<input type="checkbox"/> 1. Yes - without metastases	<input type="checkbox"/> 2. Yes - with metastases	<input type="checkbox"/> 3. No
LD	Liver disease	<input type="checkbox"/> 1. Yes - mild	<input type="checkbox"/> 2. Yes - moderate to severe	<input type="checkbox"/> 3. No

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Investigations Performed

Any completed Investigation during hospital admission

Z19	INV1	Investigation Code	<input style="width: 20px; height: 20px;" type="text"/> <input style="width: 20px; height: 20px;" type="text"/>	Z22	INV4	Investigation Code	<input style="width: 20px; height: 20px;" type="text"/> <input style="width: 20px; height: 20px;" type="text"/>
	INV1N	Number of times performed	<input style="width: 20px; height: 20px;" type="text"/> <input style="width: 20px; height: 20px;" type="text"/>		INV4N	Number of times performed	<input style="width: 20px; height: 20px;" type="text"/> <input style="width: 20px; height: 20px;" type="text"/>
Z20	INV2	Investigation Code	<input style="width: 20px; height: 20px;" type="text"/> <input style="width: 20px; height: 20px;" type="text"/>	Z23	INV5	Investigation Code	<input style="width: 20px; height: 20px;" type="text"/> <input style="width: 20px; height: 20px;" type="text"/>
	INV2N	Number of times performed	<input style="width: 20px; height: 20px;" type="text"/> <input style="width: 20px; height: 20px;" type="text"/>		INV5N	Number of times performed	<input style="width: 20px; height: 20px;" type="text"/> <input style="width: 20px; height: 20px;" type="text"/>
Z21	INV3	Investigation Code	<input style="width: 20px; height: 20px;" type="text"/> <input style="width: 20px; height: 20px;" type="text"/>	Z24	INV6	Investigation Code	<input style="width: 20px; height: 20px;" type="text"/> <input style="width: 20px; height: 20px;" type="text"/>
	INV3N	Number of times performed	<input style="width: 20px; height: 20px;" type="text"/> <input style="width: 20px; height: 20px;" type="text"/>		INV6N	Number of times performed	<input style="width: 20px; height: 20px;" type="text"/> <input style="width: 20px; height: 20px;" type="text"/>
Z25	INV7	Investigation Code	<input style="width: 20px; height: 20px;" type="text"/> <input style="width: 20px; height: 20px;" type="text"/>	Z25	INV7	Investigation Code	<input style="width: 20px; height: 20px;" type="text"/> <input style="width: 20px; height: 20px;" type="text"/>
	INV7N	Number of times performed	<input style="width: 20px; height: 20px;" type="text"/> <input style="width: 20px; height: 20px;" type="text"/>		INV7N	Number of times performed	<input style="width: 20px; height: 20px;" type="text"/> <input style="width: 20px; height: 20px;" type="text"/>
				Z25		Write Name if not on list	
Z26	INV8	Investigation Code	<input style="width: 20px; height: 20px;" type="text"/> <input style="width: 20px; height: 20px;" type="text"/>	Z26	INV8	Investigation Code	<input style="width: 20px; height: 20px;" type="text"/> <input style="width: 20px; height: 20px;" type="text"/>
	INV8N	Number of times performed	<input style="width: 20px; height: 20px;" type="text"/> <input style="width: 20px; height: 20px;" type="text"/>		INV8N	Number of times performed	<input style="width: 20px; height: 20px;" type="text"/> <input style="width: 20px; height: 20px;" type="text"/>
				Z26		Write Name if not on list	
Z27	INV9	Investigation Code	<input style="width: 20px; height: 20px;" type="text"/> <input style="width: 20px; height: 20px;" type="text"/>	Z27	INV9	Investigation Code	<input style="width: 20px; height: 20px;" type="text"/> <input style="width: 20px; height: 20px;" type="text"/>
	INV9N	Number of times performed	<input style="width: 20px; height: 20px;" type="text"/> <input style="width: 20px; height: 20px;" type="text"/>		INV9N	Number of times performed	<input style="width: 20px; height: 20px;" type="text"/> <input style="width: 20px; height: 20px;" type="text"/>
				Z27		Write Name if not on list	
Z28	INV10	Investigation Code	<input style="width: 20px; height: 20px;" type="text"/> <input style="width: 20px; height: 20px;" type="text"/>	Z28	INV10	Investigation Code	<input style="width: 20px; height: 20px;" type="text"/> <input style="width: 20px; height: 20px;" type="text"/>
	INV10N	Number of times performed	<input style="width: 20px; height: 20px;" type="text"/> <input style="width: 20px; height: 20px;" type="text"/>		INV10N	Number of times performed	<input style="width: 20px; height: 20px;" type="text"/> <input style="width: 20px; height: 20px;" type="text"/>
				Z28		Write Name if not on list	

Investigation Code	Investigation
1	Chest X-Ray
2	Abdominal X-Ray
3	Cervical Spine X-Ray
4	Thoracic Spine X-Ray
5	Lumbar Spine X-Ray
6	Other plain X-Ray
7	Abdominal/Renal Ultrasound
8	Malaria Film
9	Peripheral blood film
10	Group and X match
11	FBC
12	U+E
13	Creatinine
14	LFTs

Investigation Code	Investigation
15	CD4 count
16	HIV Viral Load
17	Hep B sAg
18	Hep C Ab
19	VDRL
20	Urine Dipstix
21	Random / Fasting glucose
22	Malaria RDT
23	Blood Culture
24	Urine microscopy
25	Stool microscopy
26	CSF/LP
27	ECG
28	Echocardiogram

Investigation Code	Investigation
29	MRI Head
30	MRI Spine
31	CT Head
32	CT Thorax
33	CT Abdomen
34	Sputum smear
35	Sputum GXP (Xpert)
36	Sputum culture for TB
37	Lymph node aspirate for Micro (Aafb, cell count)
38	Lymph node aspirate for Cytology
39	Lymph node biopsy for Micro (Aafb)
40	Lymph node biopsy for Histology
41	Diagnostic Pleural tap
42	Diagnostic Ascitic tap
43	Bone Marrow aspirate for Cytology

Medicine Code	Medicine
1	Acetazolamide
2	Acyclovir
3	Albendazole
4	Aminophylline
5	Amitriptyline
6	Amlodipine
7	Amoxicillin
8	Amphotericin
9	Arthemether +Lumefantrine
10	Artesunate
11	Aspirin
12	Atenolol
13	Azithromycin
14	Benzyl penicillin
15	Beclometasone
16	Bisacodyl
17	Bleomycin
18	Captopril
19	Carbamazepine
20	Ceftriaxone
21	Cefuroxime
22	Chloramphenical
23	Chlopromazine
24	Chlorpheniramine
25	Cimetidine
26	Ciprofloxacin
27	Cisplatin
28	Co-trimoxazole
29	Codeine

Medicine Code	Medicine
30	Cyclophosphamide
31	Diazepam
32	Diclofenac
33	Digoxin
34	Doxycycline
35	Enalapril
36	Erythromycin
37	Ferrous sulphate
38	Folic acid
39	Fluconazole
40	Flucloxacillin
41	Furosemide
42	Gentamycin
43	Glibenclamide
44	Griseofulvin
45	Haloperidol
46	Heparin
47	Hydrochlorothiazide
48	Ibuprofen
49	Indomethacine
50	Insulin - Actrapid
51	Insulin - Lente
52	Lumefantrine/Artemether
53	Magnesium Sulphate
54	Methyldopa
55	Metformin
56	Methotrexate
57	Metronidazole
58	Morphine

Medicine Code	Medicine
59	Nystatin
60	Nifedipine
61	Omeprazole
62	Paracetamol
63	Pethidine
64	Phenobarbitone
65	Phenytoin
66	Praziquantel
67	Prednisolone
68	Promethazine
69	Pyridoxine
70	Pyrimethamine with sulfadoxine
71	Quinine Sulphate
72	Ranitidine
73	Salbutamol
74	Sodium Valproate
75	Spirolactone
76	Vincristine
77	Warfarin
78	Normal Saline 0.9% - 1 litre
79	Dextrose 5% - 1 litre
80	Ringers Lactate - 1 litre
81	RHZE
82	RHE
83	RH
84	Streptomycin
85	INH (Isoniazid)

Medications Given To Patient

Z29	ADRUG	Medicine code	<input style="width: 40px; height: 20px;" type="text"/>		
	ADRUGD	Dose	<input style="width: 200px; height: 25px;" type="text"/>	Route Given	<input style="width: 150px; height: 25px;" type="text"/>
	ADRUGT	Total Number of doses given?	<input style="width: 30px; height: 20px;" type="text"/>	<input style="width: 30px; height: 20px;" type="text"/>	<input style="width: 30px; height: 20px;" type="text"/>
Z30	ADRUG2	Medicine code	<input style="width: 40px; height: 20px;" type="text"/>		
	ADRUGD2	Dose	<input style="width: 200px; height: 25px;" type="text"/>	Route Given	<input style="width: 150px; height: 25px;" type="text"/>
	ADRUGT2	Total Number of doses given?	<input style="width: 30px; height: 20px;" type="text"/>	<input style="width: 30px; height: 20px;" type="text"/>	<input style="width: 30px; height: 20px;" type="text"/>
Z31	ADRUG3	Medicine code	<input style="width: 40px; height: 20px;" type="text"/>		
	ADRUGD3	Dose	<input style="width: 200px; height: 25px;" type="text"/>	Route Given	<input style="width: 150px; height: 25px;" type="text"/>
	ADRUGT3	Total Number of doses given?	<input style="width: 30px; height: 20px;" type="text"/>	<input style="width: 30px; height: 20px;" type="text"/>	<input style="width: 30px; height: 20px;" type="text"/>

Z32	ADRUG4	Medicine code	<input type="text"/>	Write Name if not on list	<input type="text"/>
	ADRUGD4	Dose	<input type="text"/>	Route Given	<input type="text"/>
	ADRUGT4	Total Number of doses given?	<input type="text"/>	<input type="text"/>	<input type="text"/>
Z33	ADRUG5	Medicine code	<input type="text"/>	Write Name if not on list	<input type="text"/>
	ADRUGD5	Dose	<input type="text"/>	Route Given	<input type="text"/>
	ADRUGT5	Total Number of doses given?	<input type="text"/>	<input type="text"/>	<input type="text"/>
Z34	ADRUG6	Medicine code	<input type="text"/>	Write Name if not on list	<input type="text"/>
	ADRUGD6	Dose	<input type="text"/>	Route Given	<input type="text"/>
	ADRUGT6	Total Number of doses given?	<input type="text"/>	<input type="text"/>	<input type="text"/>
Z35	ADRUG7	Medicine code	<input type="text"/>	Write Name if not on list	<input type="text"/>
	ADRUGD7	Dose	<input type="text"/>	Route Given	<input type="text"/>
	ADRUGT7	Total Number of doses given?	<input type="text"/>	<input type="text"/>	<input type="text"/>
Z36	ADRUG8	Medicine code	<input type="text"/>	Write Name if not on list	<input type="text"/>
	ADRUGD8	Dose	<input type="text"/>	Route Given	<input type="text"/>
	ADRUGT8	Total Number of doses given?	<input type="text"/>	<input type="text"/>	<input type="text"/>
Z37	ADRUG9	Medicine code	<input type="text"/>	Write Name if not on list	<input type="text"/>
	ADRUGD9	Dose	<input type="text"/>	Route Given	<input type="text"/>
	ADRUGT9	Total Number of doses given?	<input type="text"/>	<input type="text"/>	<input type="text"/>

Procedures Performed

Z38	PRO	Procedure Code	<input type="text"/>	Write Name if not on list	<input type="text"/>
	PRON	Number of times performed	<input type="text"/>		
Z39	PRO2	Procedure Code	<input type="text"/>	Write Name if not on list	<input type="text"/>
	PRO2N	Number of times performed	<input type="text"/>		
Z40	PRO3	Procedure Code	<input type="text"/>	Write Name if not on list	<input type="text"/>
	PRO3N	Number of times performed	<input type="text"/>		
Z41	PRO4	Procedure Code	<input type="text"/>	Write Name if not on list	<input type="text"/>
	PRO4N	Number of times performed	<input type="text"/>		
Z42	PRO5	Procedure Code	<input type="text"/>	Write Name if not on list	<input type="text"/>
	PRO5N	Number of times performed	<input type="text"/>		
Z43	PRO6	Procedure Code	<input type="text"/>	Write Name if not on list	<input type="text"/>
	PRO6N	Number of times performed	<input type="text"/>		

Procedure Code	Procedure
1	Therapeutic Pleural Tap
2	Diagnostic Pleural Tap
3	Therapeutic and Diagnostic Pleural Tap
4	Therapeutic Ascitic Tap
5	Diagnostic Ascitic Tap
6	Therapeutic and Diagnostic Ascitic Tap
7	Therapeutic Pericardial tap
8	Diagnostic Pericardial tap
9	Therapeutic and Diagnostic Pericardial tap

Procedure Code	Procedure
10	Suturing
11	LN aspirate
12	LN biopsy
13	Insertion NG tube
14	Insertion urinary catheter
15	Incision and drainage
16	Blood transfusion – One unit
17	Platelet transfusion – One unit
18	Induced Sputum – inc sputum smear
19	Induced Sputum – inc sputum smear + GXP
20	Induced Sputum – inc GXP (Xpert)

DATA OFFICE USE ONLY

Z43 DID Data Officer ID

Z44 DDATE Date form checked

d d m o n y y y y

**Appendix XVIII: Adapted ICD
codebook used to code primary
medical diagnosis - Hospital cohort
study**

Queen Elizabeth Central Hospital Costing study: Classifying Clinical Conditions

Introduction

A clinical classification software (CCS) was developed by the Agency for Healthcare Research and Quality (AHRQ). The tool provides a method for grouping clinical diagnosis into a manageable number of clinically relevant categories. The classification system allows a meaningful approach to group clinical diagnosis to investigate health service utilisation and costs, and health outcomes. The system collapses clinical diagnosis from the *International Classification of Diseases, 9th Revision, Clinical Modification* (ICD-9-CM), which contains more than 14,000 diagnosis codes, into either a single-level or multi-level classification system. In the single-level classification system, all codes in the ICD-9-CM are aggregated into 285 mutually exclusive categories, most of which are clinically homogeneous. The multi-level clinical classification system is a hierarchical system with four-levels, with the specificity of the clinical categories increasing with the higher levels. At the first of the four levels, the clinical diagnostic category is broad, whilst at the higher levels; the clinical diagnosis becomes more specific.

Methods

The CCS tool provides a simplistic and efficient approach to classifying clinical diagnosis by the medical doctors reviewing the notes of patients recruited into the Cost-HTC Hospital costing study. The classification system has been adapted into a booklet with directions for the medical doctor to follow. The booklet will be used to classify both the primary clinical condition necessitating hospital admission, and all associated clinical diagnosis made prior to admission and during the hospital admission.

Page 1

Figure 1: Overview of how to code clinical diagnosis

Review Medical Notes

Extract primary
clinical diagnosis
made by doctor
managing patient
that resulted in
hospital admission

- 1) Start on Page 2
- 2) Choose appropriate clinical diagnostic category – Level 1
- 3) Write code number into Case Report Form (CRF)
- 4) Follow directions to subsequent pages to classify Level 2 and Level 3 and Level 4 Clinical Diagnosis.
- 5) Stop when directions state so

NB: for several clinical conditions, classification system will not be at three levels.

Page 2

WRITE CODE	Medical Diagnosis – LEVEL 1	Follow-up coding: ->Go to page:
0	No diagnosis Made	STOP
1	Infectious and Parasitic disease	3
2	Neoplasms	6
3	Endocrine, nutritional, and metabolic diseases and immunity disorders	7
4	Diseases of blood and blood-forming organs	9
5	Mental disorders	12
6	Diseases of the nervous system and sense organs	13
7	Diseases of the circulatory system	15
8	Diseases of the respiratory system	17
9	Diseases of the digestive system	20
10	Diseases of the genitourinary system	23
11	Complications of pregnancy, childbirth, and the puerperium	25
12	Diseases of the skin and subcutaneous tissue	26
13	Diseases of the musculoskeletal system	28
14	Congenital anomalies	30
15	Certain conditions originating in the perinatal period	31
16	Injury and poisoning	32
17	Symptoms, signs, and ill-defined conditions AND factors influencing health status	34

Page 3

WRITE CODE	Level 2: Infectious and Parasitic disease	Follow-up coding: ->Go to page:
1.1	Bacterial infection	4
1.2	Mycoses	4
1.3	Viral infection	4
1.4	Other infections; including parasitic	4
1.5	Immunizations and screening for infectious disease	STOP

Page 4

WRITE CODE	Level 3: Infectious and Parasitic disease	Follow-up coding: ->Go to page:
1.1.1	Tuberculosis	5
1.1.2	Septicaemia (except in labour)	5
1.1.3	Sexually transmitted infections (not HIV or hepatitis)	STOP
1.1.4	Other bacterial infections	STOP
1.2.1	Candidiasis of the mouth (thrush)	STOP
1.2.2	Other mycoses	STOP
1.2.3	<i>Candidiasis (excluding thrush)</i>	STOP
1.2.4	<i>Cryptococcal meningitis</i>	STOP
1.3.1	HIV infection	STOP
1.3.2	Hepatitis	STOP
1.3.3	Other viral infections	5
1.4.1	<i>Pneumocystis Carinii Pneumonia</i>	STOP
1.4.2	<i>Malaria</i>	STOP

WRITE CODE	Level 4: Infectious and Parasitic disease	Follow-up coding: ->Go to page:
1.1.1.1	Pulmonary Tuberculosis	STOP
1.1.1.2	Tuberculosis of meninges and central nervous system	STOP
1.1.1.3	Tuberculosis of intestines, peritoneum and mesenteric glands	STOP
1.1.1.4	Tuberculosis of bones and joint	STOP
1.1.1.5	Tuberculosis of genitourinary system	STOP
1.1.1.6	Tuberculosis of other organs	STOP
1.1.1.7	Miliary Tuberculosis	STOP
1.1.2.1	Streptococcal septicaemia	STOP
1.1.2.2	Staphylococcal septicaemia	STOP
1.1.2.3	E. Coli septicaemia	STOP
1.1.2.4	Other gram negative septicaemia	STOP
1.1.2.5	Other specified septicaemia	STOP
1.1.2.6	Unspecified septicaemia	STOP
1.3.3.1	Herpes zoster infection	STOP
1.3.3.2	Herpes simplex infection	STOP
1.3.3.3	Other and unspecified viral infection	STOP
1.4.2.1	Uncomplicated Malaria	STOP
1.4.2.2	Malaria Severe Anaemia	STOP
1.4.2.3	Malaria, Cerebral	STOP
1.4.2.4	Malaria, Acute Renal Failure	STOP
1.4.2.5	Malaria, Severe	STOP
1.4.2.6	Malaria, Other	STOP

Page 6

WRITE CODE	Level 2: Neoplasms	Follow-up coding: ->Go to page:
2.1	Colorectal cancer	STOP
2.2	Other gastrointestinal cancer	STOP
2.3	Cancer of bronchus; lung	STOP
2.4	Cancer of skin	STOP
2.5	Cancer of breast	STOP
2.6	Cancer of uterus and cervix	STOP
2.7	Cancer of ovary and other female genital organs	STOP
2.8	Cancer of male genital organs	STOP
2.9	Cancer of urinary organs	STOP
2.10	Cancer of lymphatic and hematopoietic tissue	STOP
2.11	Cancer; other primary	STOP
2.12	Secondary malignancies	STOP
2.13	Malignant neoplasm without specification of site	STOP
2.14	Neoplasms of unspecified nature or uncertain behavior	STOP
2.15	Maintenance chemotherapy; radiotherapy	STOP
2.16	Benign neoplasms	STOP
2.17	Kaposi's Sarcoma	STOP

Page 7

WRITE CODE	Level 2: Endocrine; nutritional; and metabolic diseases and immunity disorders	Follow-up coding: ->Go to page:
3.1	Thyroid disorders	8
3.2	Diabetes mellitus without complication	STOP
3.3	Diabetes mellitus with complications	8
3.4	Other endocrine disorders	STOP
3.5	Nutritional deficiencies	8
3.6	Disorders of lipid metabolism	STOP
3.7	Gout and other crystal arthropathies	STOP
3.8	Fluid and electrolyte disorders	8
3.9	Cystic fibrosis	STOP
3.10	Immunity disorders	STOP
3.11	Other nutritional; endocrine; and metabolic disorders	8

Page 8

WRITE CODE	Level 3: Endocrine; nutritional; and metabolic diseases and immunity disorders	Follow-up coding: ->Go to page:
3.1.1	Thyrotoxicosis with or without goiter	STOP
3.1.2	Other thyroid disorders	STOP
3.3.1	Diabetes with ketoacidosis or uncontrolled diabetes	STOP
3.3.2	Diabetes with renal manifestations	STOP
3.3.3	Diabetes with ophthalmic manifestations	STOP
3.3.4	Diabetes with neurological manifestations	STOP
3.3.5	Diabetes with circulatory manifestations	STOP
3.3.6	Diabetes with unspecified complications	STOP
3.3.7	Diabetes with other manifestations	STOP
3.5.1	Unspecified protein-calorie malnutrition	STOP
3.5.2	Other malnutrition	STOP
3.8.1	Hyposmolality	STOP
3.8.2	Hypovolemia	STOP
3.8.3	Hyperpotassemia	STOP
3.8.4	Hypopotassemia	STOP
3.8.5	Other fluid and electrolyte disorders	STOP
3.11.1	Disorders of mineral metabolism	STOP
3.11.2	Obesity	STOP
3.11.3	Other and unspecified metabolic; nutritional; and endocrine disorders	STOP

Page 9

WRITE CODE	Level 2: Diseases of the blood and blood- forming organs	Follow-up coding: ->Go to page:
4.1	Anemia	10
4.2	Coagulation and hemorrhagic disorders	10
4.3	Diseases of white blood cells	STOP
4.4	Other hematologic conditions	STOP

WRITE CODE	Level 3: Diseases of the blood and blood-forming organs	Follow-up coding: ->Go to page:
4.1.1	Acute posthemorrhagic anemia	STOP
4.1.2	Sickle cell anemia	STOP
4.1.3	Deficiency and other anemia	11
4.2.1	Coagulation defects	STOP
4.2.2	Thrombocytopenia	STOP
4.2.3	Other coagulation and hemorrhagic disorders	STOP

WRITE CODE	Level 4: Diseases of the blood and blood-forming organs	Follow-up coding: ->Go to page:
4.1.3.1	Iron deficiency anemia	STOP
4.1.3.2	Other deficiency anemia	STOP
4.1.3.3	Aplastic anemia	STOP
4.1.3.4	Chronic blood loss anemia	STOP
4.1.3.5	Acquired hemolytic anemia	STOP
4.1.3.6	Other specified anemia	STOP
4.1.3.7	Anemia; unspecified	STOP

Page 12

WRITE CODE	Level 2: Mental illness	Follow-up coding: ->Go to page:
5.1	Adjustment disorders	STOP
5.2	Anxiety disorders	STOP
5.3	Attention deficit	STOP
5.4	Delirium	STOP
5.5	Developmental disorders	STOP
5.6	Disorders usually diagnosed in infancy	STOP
5.7	Impulse control disorders not elsewhere classified	STOP
5.8	Mood disorders	STOP
5.9	Personality disorders	STOP
5.10	Schizophrenia and other psychotic disorders	STOP
5.11	Alcohol-related disorders	STOP
5.12	Substance-related disorders	STOP
5.13	Suicide and intentional self-inflicted injury	STOP
5.14	Screening and history of mental health and substance abuse codes	STOP
5.15	Miscellaneous mental disorders	STOP

Page 13

WRITE CODE	Level 2: Diseases of the nervous system and sense organs	Follow-up coding: ->Go to page:
6.1	Central nervous system infection	14
6.2	Hereditary and degenerative nervous system conditions	14
6.3	Paralysis	14
6.4	Epilepsy; convulsions	14
6.5	Headache; including migraine	14
6.6	Coma; stupor; and brain damage	STOP
6.7	Eye disorders	14
6.8	Ear conditions	14
6.9	Other nervous system disorders	14

WRITE CODE	Level 3: Diseases of the nervous system and sense organs	Follow-up coding: ->Go to page:
6.1.1	Meningitis (except that caused by TB or STD)	STOP
6.1.2	Encephalitis (except that caused by TB or STD)	STOP
6.1.3	Other CNS infection and poliomyelitis	STOP
6.2.1	Parkinsons disease	STOP
6.2.2	Multiple sclerosis	STOP
6.2.3	Other hereditary and degenerative nervous system conditions	STOP
6.3.1	Hemiplegia	STOP
6.3.2	Other paralysis	STOP
6.4.1	Epilepsy	STOP
6.4.2	Convulsions	STOP
6.5.1	Migraine	STOP
6.5.2	Other headache	STOP
6.7.1	Cataract	STOP
6.7.2	Retinal detachments; defects; vascular occlusion; and retinopathy	STOP
6.7.3	Glaucoma	STOP
6.7.4	Blindness and vision defects	STOP
6.7.5	Inflammation; infection of eye (except that caused by TB or STD)	STOP
6.7.6	Other eye disorders	STOP
6.8.1	Otitis media and related conditions	STOP
6.8.2	Conditions associated with dizziness or vertigo	STOP
6.8.3	Other ear and sense organ disorders	STOP
6.9.1	Disorders of the peripheral nervous system	STOP
6.9.2	Other central nervous system disorders	STOP
6.9.3	Other nervous system symptoms and disorders	STOP

Page 15

WRITE CODE	Level 2: Diseases of the circulatory system	Follow-up coding: ->Go to page:
7.1	Hypertension	16
7.2	Diseases of the heart	16
7.3	Cerebrovascular disease	16
7.4	Diseases of arteries; arterioles; and capillaries	16
7.5	Diseases of veins and lymphatics	16

WRITE CODE	Level 3: Diseases of the circulatory system	Follow-up coding: ->Go to page:
7.1.1	Essential hypertension	STOP
7.1.2	Hypertension with complications and secondary hypertension	STOP
7.2.1	Heart valve disorders	STOP
7.2.2	Peri-; endo-; and myocarditis; cardiomyopathy (except that caused by TB or STD)	STOP
7.2.3	Acute myocardial infarction	STOP
7.2.4	Coronary atherosclerosis and other heart disease	STOP
7.2.5	Nonspecific chest pain	STOP
7.2.6	Pulmonary heart disease	STOP
7.2.7	Other and ill-defined heart disease	STOP
7.2.8	Conduction disorders	STOP
7.2.9	Cardiac dysrhythmias	STOP
7.2.10	Cardiac arrest and ventricular fibrillation	STOP
7.2.11	Congestive heart failure; nonhypertensive	STOP
7.3.1	Acute cerebrovascular disease	STOP
7.3.2	Occlusion or stenosis of precerebral arteries	STOP
7.3.3	Other and ill-defined cerebrovascular disease	STOP
7.3.4	Transient cerebral ischemia	STOP
7.3.5	Late effects of cerebrovascular disease	STOP
7.4.1	Peripheral and visceral atherosclerosis	STOP
7.4.2	Aortic; peripheral; and visceral artery aneurysms	STOP
7.4.3	Aortic and peripheral arterial embolism or thrombosis	STOP
7.4.4	Other circulatory disease	STOP
7.5.1	Phlebitis; thrombophlebitis and thromboembolism	STOP
7.5.2	Varicose veins of lower extremity	STOP
7.5.3	Hemorrhoids	STOP
7.5.4	Other diseases of veins and lymphatics	STOP

Page 17

WRITE CODE	Level 2: Diseases of the respiratory system	Follow-up coding: ->Go to page:
8.1	Respiratory infections	18
8.2	Chronic obstructive pulmonary disease and bronchiectasis	18
8.3	Asthma	18
8.4	Aspiration pneumonitis; food/vomitus	STOP
8.5	Pleurisy; pneumothorax; pulmonary collapse	18
8.6	Respiratory failure; insufficiency; arrest (adult)	18
8.7	Lung disease due to external agents	STOP
8.8	Other lower respiratory disease	18
8.9	Other upper respiratory disease	STOP

Page 18

WRITE CODE	Level 3: Diseases of the respiratory system	Follow-up coding: ->Go to page:
8.1.1	Pneumonia (except that caused by TB or STD)	19
8.1.2	Influenza	STOP
8.1.3	Acute and chronic tonsillitis	STOP
8.1.4	Acute bronchitis	STOP
8.1.5	Other upper respiratory infections	19
8.2.1	Emphysema	STOP
8.2.2	Chronic airway obstruction; not otherwise specified	STOP
8.2.3	Obstructive chronic bronchitis	STOP
8.2.4	Other chronic pulmonary disease	STOP
8.3.1	Chronic obstructive asthma	19
8.3.2	Other and unspecified asthma	19
8.5.1	Pleurisy; pleural effusion	STOP
8.5.2	Pulmonary collapse; interstitial and compensatory emphysema	STOP
8.5.3	Empyema and pneumothorax	STOP
8.6.1	Respiratory failure	STOP
8.6.2	Other respiratory insufficiency	STOP
8.8.1	Postinflammatory pulmonary fibrosis	STOP
8.8.2	Painful respiration	STOP
8.8.3	Other and unspecified lower respiratory disease	STOP

Page 19

WRITE CODE	Level 4: Diseases of the respiratory system	Follow-up coding: ->Go to page:
8.1.1.1	Pneumococcal pneumonia	STOP
8.1.1.2	Other bacterial pneumonia	STOP
8.1.1.3	Pneumonia; organism unspecified	STOP
8.1.1.4	Other pneumonia	STOP
8.1.5.1	Acute upper respiratory infections of multiple or unspecified sites	STOP
8.1.5.2	Chronic sinusitis	STOP
8.1.5.3	Croup	STOP
8.1.5.4	Other and unspecified upper respiratory infections	STOP
8.3.1.1	Chronic obstructive asthma without status asthmaticus or exacerbation	STOP
8.3.1.2	Chronic obstructive asthma with status asthmaticus	STOP
8.3.1.3	Chronic obstructive asthma with acute exacerbation	STOP
8.3.2.1	Other asthma without status asthmaticus or exacerbation	STOP
8.3.2.2	Other asthma with status asthmaticus	STOP
8.3.2.3	Other asthma with acute exacerbation	STOP

WRITE CODE	Level 2: Diseases of the digestive system	Follow-up coding: ->Go to page:
9.1	Intestinal infection	STOP
9.2	Disorders of teeth and jaw	STOP
9.3	Diseases of mouth; excluding dental	STOP
9.4	Upper gastrointestinal disorders	21
9.5	Abdominal hernia	21
9.6	Lower gastrointestinal disorders	21
9.7	Biliary tract disease	21
9.8	Liver disease	21
9.9	Pancreatic disorders (not diabetes)	21
9.10	Gastrointestinal hemorrhage	21
9.11	Noninfectious gastroenteritis	STOP
9.12	Other gastrointestinal disorders	21

WRITE CODE	Level 3: Diseases of the digestive system	Follow-up coding: ->Go to page:
9.4.1	Esophageal disorders	STOP
9.4.2	Gastroduodenal ulcer (except hemorrhage)	STOP
9.4.3	Gastritis and duodenitis	STOP
9.4.4	Other disorders of stomach and duodenum	STOP
9.5.1	Inguinal hernia	STOP
9.5.2	Diaphragmatic hernia	STOP
9.5.3	Other abdominal hernia	STOP
9.6.1	Appendicitis and other appendiceal conditions	STOP
9.6.2	Regional enteritis and ulcerative colitis	STOP
9.6.3	Intestinal obstruction without hernia	STOP
9.6.4	Diverticulosis and diverticulitis	STOP
9.6.5	Anal and rectal conditions	STOP
9.6.6	Peritonitis and intestinal abscess	STOP
9.7.1	Cholelithiasis with acute cholecystitis	STOP
9.7.2	Cholelithiasis with other cholecystitis	STOP
9.7.3	Cholelithiasis without mention of cholecystitis	STOP
9.7.4	Calculus of bile duct	STOP
9.7.5	Cholecystitis without cholelithiasis	STOP
9.7.6	Other biliary tract disease	STOP
9.8.1	Liver disease; alcohol-related	STOP
9.8.2	Other liver diseases	STOP
9.9.1	Acute pancreatitis	STOP
9.9.2	Chronic pancreatitis	STOP
9.9.3	Other pancreatic disorders	STOP
9.10.1	Hemorrhage from gastrointestinal ulcer	STOP
9.10.2	Melena	STOP
9.10.3	Gastroesophageal laceration syndrome	STOP
9.10.4	Other esophageal bleeding	STOP
9.10.5	Hemorrhage of rectum and anus	STOP

Page 22

9.10.6	Hematemesis	STOP
9.10.7	Hemorrhage of gastrointestinal tract	STOP
9.12.1	Constipation	STOP
9.12.2	Dysphagia	STOP
9.12.3	Other and unspecified gastrointestinal disorders	STOP

Page 23

WRITE CODE	Level 2: Diseases of the genitourinary system	Follow-up coding: ->Go to page:
10.1	Diseases of the urinary system	24
10.2	Diseases of male genital organs	24
10.3	Diseases of female genital organs	24

WRITE CODE	Level 3: Diseases of the genitourinary system	Follow-up coding: ->Go to page:
10.1.1	Nephritis; nephrosis; renal sclerosis	STOP
10.1.2	Acute and unspecified renal failure	STOP
10.1.3	Chronic kidney disease	STOP
10.1.4	Urinary tract infections	STOP
10.1.5	Calculus of urinary tract	STOP
10.1.6	Other diseases of kidney and ureters	STOP
10.1.7	Other diseases of bladder and urethra	STOP
10.1.8	Genitourinary symptoms and ill-defined conditions	STOP
10.2.1	Hyperplasia of prostate	STOP
10.2.2	Inflammatory conditions of male genital organs	STOP
10.2.3	Other male genital disorders	STOP
10.3.1	Nonmalignant breast conditions	STOP
10.3.2	Inflammatory diseases of female pelvic organs	STOP
10.3.3	Endometriosis	STOP
10.3.4	Prolapse of female genital organs	STOP
10.3.5	Menstrual disorders	STOP
10.3.6	Ovarian cyst	STOP
10.3.7	Menopausal disorders	STOP
10.3.8	Female infertility	STOP
10.3.9	Other female genital disorders	STOP

Page 25

WRITE CODE	Level 2: Complications of pregnancy; childbirth; and the puerperium	Follow-up coding: ->Go to page:
11.1	Contraceptive and procreative management	STOP
11.2	Abortion-related disorders	STOP
11.3	Complications mainly related to pregnancy	STOP
11.4	Indications for care in pregnancy; labor; and delivery	STOP
11.5	Complications during labor	STOP
11.6	Other complications of birth; puerperium affecting management of mother	STOP
11.7	Normal pregnancy and/or delivery	STOP

Page 26

WRITE CODE	Level 2: Diseases of the skin and subcutaneous tissue	Follow-up coding: ->Go to page:
12.1	Skin and subcutaneous tissue infections	27
12.2	Other inflammatory condition of skin	STOP
12.3	Chronic ulcer of skin	27
12.4	Other skin disorders	STOP

WRITE CODE	Level 3: Diseases of the skin and subcutaneous tissue	Follow-up coding: ->Go to page:
12.1.1	Cellulitis and abscess	STOP
12.1.2	Other skin and subcutaneous infections	STOP
12.3.1	Decubitus ulcer	STOP
12.3.2	Chronic ulcer of leg or foot	STOP
12.3.3	Other chronic skin ulcer	STOP

Page 28

WRITE CODE	Level 2: Diseases of the musculoskeletal system and connective tissue	Follow-up coding: ->Go to page:
13.1	Infective arthritis and osteomyelitis (except that caused by TB or STD)	STOP
13.2	Non-traumatic joint disorders	29
13.3	Spondylosis; intervertebral disc disorders; other back problems	29
13.4	Osteoporosis	STOP
13.5	Pathological fracture	STOP
13.6	Acquired deformities	26
13.7	Systemic lupus erythematosus and connective tissue disorders	STOP
13.8	Other connective tissue disease	STOP
13.9	Other bone disease and musculoskeletal deformities	STOP

WRITE CODE	Level 3: Diseases of the musculoskeletal system and connective tissue	Follow-up coding: ->Go to page:
13.2.1	Rheumatoid arthritis and related disease	STOP
13.2.2	Osteoarthritis	STOP
13.2.3	Other non-traumatic joint disorders	STOP
13.3.1	Spondylosis and allied disorders	STOP
13.3.2	Intervertebral disc disorders	STOP
13.3.3	Other back problems	STOP
13.6.1	Acquired foot deformities	STOP
13.6.2	Other acquired deformities	STOP

WRITE CODE	Level 2: Congenital anomalies	Follow-up coding: ->Go to page:
14.1	Cardiac and circulatory congenital anomalies	STOP
14.2	Digestive congenital anomalies	STOP
14.3	Genitourinary congenital anomalies	STOP
14.4	Nervous system congenital anomalies	STOP
14.5	Other congenital anomalies	STOP

WRITE CODE	Level 2: Certain conditions originating in the perinatal period	Follow-up coding: ->Go to page:
15.1	Liveborn	STOP
15.2	Short gestation; low birth weight; and fetal growth retardation	STOP
15.3	Intrauterine hypoxia and birth asphyxia	STOP
15.4	Respiratory distress syndrome	STOP
15.5	Hemolytic jaundice and perinatal jaundice	STOP
15.6	Birth trauma	STOP
15.7	Other perinatal conditions	STOP

Page 32

WRITE CODE	Level 2: Injury and poisoning	Follow-up coding: ->Go to page:
16.1	Joint disorders and dislocations; trauma-related	STOP
16.2	Fractures	STOP
16.3	Spinal cord injury	STOP
16.4	Intracranial injury	STOP
16.5	Crushing injury or internal injury	STOP
16.6	Open wounds	STOP
16.7	Sprains and strains	STOP
16.8	Superficial injury; contusion	STOP
16.9	Burns	STOP
16.10	Complications	STOP
16.11	Poisoning	STOP
16.12	Other injuries and conditions due to external causes	STOP

WRITE CODE	Level 2: Symptoms; signs; and ill-defined conditions and factors influencing health status	Follow-up coding: ->Go to page:
17.1	Symptoms; signs; and ill-defined conditions	34
17.2	Factors influencing health care	34

WRITE CODE	Level 3: Symptoms; signs; and ill-defined conditions and factors influencing health status	Follow-up coding: ->Go to page:
17.1.1	Syncope	STOP
17.1.2	Fever of unknown origin	STOP
17.1.3	Lymphadenitis	STOP
17.1.4	Gangrene	STOP
17.1.5	Shock	STOP
17.1.6	Nausea and vomiting	STOP
17.1.7	Abdominal pain	STOP
17.1.8	Malaise and fatigue	STOP
17.1.9	Allergic reactions	STOP
17.2.1	Rehabilitation care; fitting of prostheses; and adjustment of devices	STOP
17.2.2	Administrative/social admission	STOP
17.2.3	Medical examination/evaluation	STOP
17.2.4	Other aftercare	STOP
17.2.5	Other screening for suspected conditions (not mental disorders or infectious disease)	STOP

Appendix XIX: HTC ward - Hospital cohort study

Cost-HTC
HTC-WARD: Daily Ward Admissions



B01	HHID	Interviewer ID	<input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/>	B02 WEEKID	Week of study	<input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/>
<p>This form is to record the total number of patients who spent the night on the ward</p>						
B03	DOW	Date of the monday of the week for these records:		<input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/>	<input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/>	<input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/>
		Ward 3A	Ward 3B	Ward 4A		
MON	Monday	<input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/>	<input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/>	<input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/>		
TUES	Tuesday	<input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/>	<input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/>	<input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/>		
WED	Wednesday	<input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/>	<input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/>	<input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/>		
THUR	Thursday	<input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/>	<input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/>	<input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/>		
FRI	Friday	<input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/>	<input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/>	<input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/>		
SAT	Saturday	<input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/>	<input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/>	<input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/>		
SUN	Sunday	<input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/>	<input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/>	<input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/> <input style="width:20px; height:20px;" type="text"/>		

DATA OFFICE USE ONLY

B05 DID Data Officer ID

B06 DDATE Date form checked

d d m o n y y y y

**Appendix XX: HTC 501 Baseline
socio-demographic questionnaire -
Hospital Cohort study**

A01	HHBAR	Participant Barcode	<div style="border: 1px solid black; padding: 5px; width: fit-content;"> PLACE ID BARCODE HERE </div>	Write Participants Barcode <div style="border: 1px solid black; display: inline-block; width: 100px; height: 20px;"></div>
A02	HHID	Interviewer ID	<div style="border: 1px solid black; display: inline-block; width: 40px; height: 20px;"></div>	A03 SIT Place of interview <input type="checkbox"/> 1. Ward 3A <input type="checkbox"/> 3. Ward 4A <input type="checkbox"/> 2. Ward 3B
A04	DOI	Date of interview	<div style="border: 1px solid black; display: inline-block; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; display: inline-block; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; display: inline-block; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; display: inline-block; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; display: inline-block; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; display: inline-block; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; display: inline-block; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; display: inline-block; width: 20px; height: 20px;"></div>	2 0 1 y y y y
A05	DOA	Date of admission	<div style="border: 1px solid black; display: inline-block; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; display: inline-block; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; display: inline-block; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; display: inline-block; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; display: inline-block; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; display: inline-block; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; display: inline-block; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; display: inline-block; width: 20px; height: 20px;"></div>	2 0 1 y y y y
A06	TEL	Telephone number of main contact person during admission	<div style="border: 1px solid black; display: inline-block; width: 100px; height: 20px;"></div>	
A07	DOB	Tsiku lobadwa Date of Birth	<div style="border: 1px solid black; display: inline-block; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; display: inline-block; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; display: inline-block; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; display: inline-block; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; display: inline-block; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; display: inline-block; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; display: inline-block; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; display: inline-block; width: 20px; height: 20px;"></div>	d d m o n y y y y
A08	AGE	Age	<div style="border: 1px solid black; display: inline-block; width: 20px; height: 20px;"></div>	Years
A09	SEX	Sex	<input type="checkbox"/> 1. Male <input type="checkbox"/> 2. Female	
A10	PART	Did the patient consent to participate?	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No <input type="checkbox"/> 3. Absconded <input type="checkbox"/> 4. Discharged <input type="checkbox"/> 5. Died Continue if consent given, otherwise STOP	
A11	PREG	Ngati ndinu mkazi, kodi muli ndi pakati? If female, are you pregnant?	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No <input type="checkbox"/> 99. N/A	
A12	MARSTC	Kodi muli pa banja? What is your marital status? (TICK ONE)	<input type="checkbox"/> 1. Married <input type="checkbox"/> 2. Polygamous marriage <input type="checkbox"/> 3. Living together as married <input type="checkbox"/> 4. Never Married <input type="checkbox"/> 5. Separated <input type="checkbox"/> 6. Widower/Widow <input type="checkbox"/> 7. Divorced	
A13	PARTNER	Ngati simuli pabanja kodi muli ndichibwenzi If NOT MARRIED, do you have a partner at the moment?	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No <input type="checkbox"/> 99. N/A	
A14	TOGYRS	Kodi mwakhala limodzi ndi okonedwa anu kwa nthawi yayitali bwanji? How long have you been together with your spouse/partner?	<div style="border: 1px solid black; display: inline-block; width: 20px; height: 20px;"></div>	Years <div style="border: 1px solid black; display: inline-block; width: 20px; height: 20px;"></div>
A15	SCH	Kodi maphuziro anu munafika nawo pati? What is the highest level of formal schooling you have ever attended?	<div style="border: 1px solid black; display: inline-block; width: 20px; height: 20px;"></div>	PRESCHO = 00 FORM 1 = 09 UNIVE 1 = 15 TRAIN COL STAND 1 = 01 FORM 2 = 10 UNIVE 2 = 16 TCYR 1 = 20 STAND 2 = 02 FORM 3 = 11 UNIVE 3 = 17 TCYR 2 = 21 STAND 3 = 03 FORM 4 = 12 UNIVE 4 = 18 TCYR 3 = 22 STAND 4 = 04 FORM 5 = 13 ABOVE = 19 TCYR 4 = 23 STAND 5 = 05 FORM 6 = 14 STAND 6 = 06 STAND 7 = 07 STAND 8 = 08

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		Kodi pakhomo pano muli ndi zinthu izi? Does your household own any of the following (please tick all that apply)?			
A16	FRIDG	Fridge? <input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No	A21 WATCH Watch? <input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No		
A17	HHCARM1	Car? <input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No	A22 PHON Phone? <input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No		
A18	BED	Bed? <input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No	A23 KOLO Koloboyi? <input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No		
A19	TELEV	Television? <input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No	A24 RADIO Radio? <input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No		
A20	HHCARM2	Motorcycle? <input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No			
A25	LAND	Kodi alipo m'modzi wam'banja limeneli amene ali ndi malo olima? <input type="checkbox"/> 1. Yes Does any member of your household own any agricultural land? <input type="checkbox"/> 2. No			
A26	SHFOOD	M'mwezi wathawu, mwakhalapo ndi mavuto pakapezedwe ka chakudya mowilikiza bwanji? During the past month, how often have you had problems getting the food you need?	<input type="checkbox"/> 1. Never <input type="checkbox"/> 2. Sometimes <input type="checkbox"/> 3. Often <input type="checkbox"/> 4. Always		
A27	SKPML	M'sabata ziwiri zapitazi alipo munthu wankulu pakhomo pano amene sanadye kapena kudya mopelewera ndi cholinga choti ana akhale ndi chakudya chokwanira? In the past two weeks, has an adult in your house skipped a meal or ate less in order for there to be enough for the children?	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No		
A28	HROOM	Kodi mnyumba mwanu muli zipinda zingati kuphatikiza makitchni? How many rooms, including kitchens, are there in your home?	<table border="1" style="width: 60px; height: 30px;"> <tr> <td style="width: 30px;"></td> <td style="width: 30px;"></td> </tr> </table>		
A29	HWAT	Kodi madzi ogwiritsa ntchito pakhomo pano mumatunga kuti? At your home, in which way do you obtain water for domestic use (TICK ONE)? Specify, if other	<input type="checkbox"/> 1. Piped water inside the dwelling <input type="checkbox"/> 2. Piped water inside the yard <input type="checkbox"/> 3. Piped water at kiosk <input type="checkbox"/> 4. Borehole/well <input type="checkbox"/> 5. River/Stream <input type="checkbox"/> 6. Other		
A30	HWATD	Kodi komwe mumakatunga madzi mungati ndi kotalika bwanji? At your home, what is the distance to the closest water access point?	<input type="checkbox"/> 1. Less than 200m <input type="checkbox"/> 2. Between 200m & 500m <input type="checkbox"/> 3. Between 500m & 1km <input type="checkbox"/> 4. More than 1km		
A31	HTOL	Kodi pakhomo pano mumagwilitsa ntchito chimbudzi cha mtundu wanji? At your home, what is the MAIN type of toilet facility available for use by your household? (TICK ONE)	<input type="checkbox"/> 1. Flush toilet <input type="checkbox"/> 2. Ventilated pit latrine (VIP) <input type="checkbox"/> 3. Non-Ventilated pit latrine <input type="checkbox"/> 4. None		
A32	HTOLSH	Kodi mumagwiritsa ntchito chimbuzi chimenechi ndi mabanja ena? Do you share this toilet facility with other households?	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No		
A33	HLIT	Kodi pakhomo pano mumagwiritsa ntchito chiyani powunikira? At your home, what is your main source of lighting (TICK ONE)?	<input type="checkbox"/> 1. Collect firewood <input type="checkbox"/> 6. Electricity <input type="checkbox"/> 2. Buy firewood <input type="checkbox"/> 7. Candles <input type="checkbox"/> 3. Batteries <input type="checkbox"/> 8. Charcoal <input type="checkbox"/> 4. Paraffin <input type="checkbox"/> 9. Crop residue/Grass <input type="checkbox"/> 5. Animal waste <input type="checkbox"/> 10. Saw dust		
A34	PINC	Pa masabata anayi apitawa, kodi ndi ndani amene wakhala wozeza ndalama weni weni m'banjali? Over the last 4 weeks, who has been the primary income earner in the household (TICK ONE)? Specify, if other	<input type="checkbox"/> 1. I Have <input type="checkbox"/> 5. Son <input type="checkbox"/> 2. Husband/Wife <input type="checkbox"/> 6. Daughter <input type="checkbox"/> 3. Father <input type="checkbox"/> 7. Extended Family <input type="checkbox"/> 4. Mother <input type="checkbox"/> 8. Other, Specify		

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A35	EMPL	Kodi pamasabata anayi apitawa munalembedwapo ntchito yolipidwa? Over the last 4 weeks have you been formally employed(TICK ONE)? Specify, if other <div style="border: 1px solid black; height: 20px; width: 100%;"></div>	<input type="checkbox"/> 1. Yes, Formal Work <input type="checkbox"/> 2. No, Informal Work <input type="checkbox"/> 3. On Sick Leave <input type="checkbox"/> 4. Retired <input type="checkbox"/> 5. At School, University <input type="checkbox"/> 6. Housework <input type="checkbox"/> 7. Other, Specify						
A36	MASAL	Pa ntchito yanu yeni yeni, kodi ndi chani cheni cheni chimene mumachita kumalo anu antchito? In your MAIN JOB, what is the main activity at the place of work? (TICK ONE) <input type="checkbox"/> 99. Not Applicable <input type="checkbox"/> 1. Agriculture, Forestry, Fishing <input type="checkbox"/> 2. Mining and Quarrying <input type="checkbox"/> 3. Manufacturing <input type="checkbox"/> 4. Electricity, Water, Other Utilities <input type="checkbox"/> 5. Construction <input type="checkbox"/> 6. Wholesale and Retail Marketing, Hotel/ Restaurants <input type="checkbox"/> 7. Transport and Communication <input type="checkbox"/> 8. Finance and Business <input type="checkbox"/> 9. Social and Community Services <input type="checkbox"/> 10. Other, Specify Specify, if other <div style="border: 1px solid black; height: 20px; width: 100%;"></div>							
A37	MAHOU	Pa ntchito yanu yeni yeni, kodi ndi maola angati amene mumagwira pa sabata? In your MAIN JOB, how many hours do you work a week? Write '999' if not working	<table border="1"> <tr> <td style="width: 20px; height: 20px;"></td> <td style="width: 20px; height: 20px;"></td> <td style="width: 20px; height: 20px;"></td> </tr> </table> Hours						
A38	PINCOM	Kodi mumapeza ndalama zingati kuwerengera zonse PAMODZI pa sabata? (asanachotse msonkho/ kapena china chili chonse) What is your TOTAL estimated income per week from all sources (Before tax/deductions) Write '999999' if not working	MK <table border="1"> <tr> <td style="width: 20px; height: 20px;"></td> </tr> </table>						
<p>Mafunso osatirawa ndi okhuza anthu amene mumakhala nawo m'banja mwanu. Amenewa ndi anthu amene nthawi zambiri mumakhala nawo ndikudyera limodzi zakudya m'banja mwanu.</p> <p>The following questions are about members of your household. These are individuals who normally live and share meals in your household.</p>									
A39	HHNA	Limodzi ndi inuyo, kodi mnyumba mwanu mumakhala anthu aakulu angati (azaka zobadwa khumi zisanu ndi zitatu kapena kuposera pamenepa)? Including yourself, how many adults (aged 18 years and over) live in the household?	<table border="1"> <tr> <td style="width: 20px; height: 20px;"></td> <td style="width: 20px; height: 20px;"></td> </tr> </table>						
A40	HHNC	Kodi mnyumbamu mumakhala ana angati (azaka zobadwa zosapitirira zakubadwa khumi zisanu ndi zitatu)? How many children (aged under 18 years of age) live in the household?	<table border="1"> <tr> <td style="width: 20px; height: 20px;"></td> <td style="width: 20px; height: 20px;"></td> </tr> </table>						
A41	HOH	Kodi inu ndinu mwini/mkulu wa banja limeneli? Are you the head of the household?	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No						
A42	HOUSINC	Kodi zonse pamodzi pakhomu pano mumapeza ndalama zingati kuchoka kulikonse? (Funsani wotenga nawo mbali kuti aphantikize ndalama zomwe onse pakhomopo amapeza kuphatikizapo iwo eni) What is the combined TOTAL household income per week from all sources? (Ask participant to include the income of all members of the household including themselves) Write '888888' if participant does not know	MK <table border="1"> <tr> <td style="width: 20px; height: 20px;"></td> </tr> </table>						

A43	DOT	Tsiku limene anayezedwa HIV (lembali tsiku lalero ngati ayezedwa lero)? Date of HIV Test (Write today's date if tested today)	<table border="1" style="display: inline-table; vertical-align: middle;"><tr><td style="width: 20px; height: 20px;"></td><td style="width: 20px; height: 20px;"></td></tr></table>			<table border="1" style="display: inline-table; vertical-align: middle;"><tr><td style="width: 20px; height: 20px;"></td><td style="width: 20px; height: 20px;"></td><td style="width: 20px; height: 20px;"></td><td style="width: 20px; height: 20px;"></td></tr></table>					<table border="1" style="display: inline-table; vertical-align: middle;"><tr><td style="width: 20px; height: 20px;"></td><td style="width: 20px; height: 20px;"></td></tr></table>						
		d d m o n y y y y															
A44	LOC	Kodi kunali kuti kumene munakayezetsa HIV posachedwapa? Where did you have your recent HIV test?	<input type="checkbox"/> 1. At Home: Oral Self-testing in presence of counsellor <input type="checkbox"/> 2. At Home: Oral Self-testing in Private <input type="checkbox"/> 3. At Home: Finger Prick VCT (not from Hit-TB Study) <input type="checkbox"/> 4. HIV Testing Clinic: Referred by Antenatal clinic (ANC) <input type="checkbox"/> 5. HIV Testing Clinic: Referred by TB clinic <input type="checkbox"/> 6. HIV Testing Clinic: Referred by health professional(not TB, not ANC) <input type="checkbox"/> 7. HIV Testing Clinic: Went solely to learn my HIV status <input type="checkbox"/> 8. Mobile Testing Service <input type="checkbox"/> 9. Private healthcare provider <input type="checkbox"/> 10. Hospital: On this admission <input type="checkbox"/> 11. Hospital: on a previous admission <input type="checkbox"/> 12. NEVER had an HIV test <input type="checkbox"/> 13. Other, specify														
		Specify, if other <table border="1" style="width: 100%; height: 30px;"></table>															
A45	RES	Zotsatila zoyezetsa HIV HIV test result	<input type="checkbox"/> 1. Positive <input type="checkbox"/> 2. Negative <input type="checkbox"/> 3. Not disclosed	<input type="checkbox"/> 4. Invalid/indeterminate <input type="checkbox"/> 5. Not done													
A46	COU	Kodi munayezetsa limodzi ndi okondedwa anu? Did you test as a Couple? (Couples Testing) <small>Does not necessarily have to be husband/wife</small>	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No														
A47	PAST	Mumiyezi khumi ndi iwiri yapitayi, ndi kangati mwayezetsapo HIV mpakana kulandira zotsatira za kuyezetsako? (Osaphatikizapo kuyezetsa HIV mwapangitsa posachedwapa) Over the last 12 months, how many times have you had a HIV test where you completed the HIV test?(Not including this most recent HIV test)	<table border="1" style="display: inline-table; vertical-align: middle;"><tr><td style="width: 20px; height: 20px;"></td><td style="width: 20px; height: 20px;"></td></tr></table>														
A48	FAIL	Mumiyezi khumi ndi iwiri yapitayi, ndikangati munayesa kuyezetsa HIV koma simunathe kuyezetsa HIV? Over the last 12 months, how many times have you tried to get a HIV test, but did not end up having the HIV test? (Failed Attempt)	<table border="1" style="display: inline-table; vertical-align: middle;"><tr><td style="width: 20px; height: 20px;"></td><td style="width: 20px; height: 20px;"></td></tr></table>														
A49	FAILT	Pamene munalephera kuyezetsa kotsiriza, ndi chifukwa ninji munalephera kuyezetsa HIV? For that most recent failed attempt, why did you not get the HIV test done?	<input type="checkbox"/> 1. I changed my mind <input type="checkbox"/> 2. Clinic/facility closed <input type="checkbox"/> 3. No HIV counsellor <input type="checkbox"/> 4. No HIV testing equipment <input type="checkbox"/> 5. I was told I should wait for the 'Window period' <input type="checkbox"/> 6. NOT APPLICABLE <input type="checkbox"/> 9. Other, Specify	Specify, if other <table border="1" style="width: 100%; height: 30px;"></table>													

DATA OFFICE USE ONLY

A50 DID Data Officer ID

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A51 DDATE Date form checked

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**Appendix XXI: HTC 502 Admission
direct non-medical and indirect cost
data collection tool - Hospital
cohort study**

C01	HHBAR	Participant Barcode	<div style="border: 1px solid black; padding: 5px; width: fit-content;"> PLACE ID BARCODE HERE </div>	Write Participant Barcode <div style="border: 1px solid black; width: 100px; height: 20px; margin-top: 5px;"></div>
C02	SPINE	Write Participants SPINE ID	P	<div style="border: 1px solid black; width: 200px; height: 20px; margin-top: 5px;"></div>
C03	TBROCC	TB-ROCC Participant ID (write 9999999 if not a TB-ROCC participant)		<div style="border: 1px solid black; width: 100px; height: 20px; margin-top: 5px;"></div>
C04	HHID	Interviewer ID	<div style="border: 1px solid black; width: 40px; height: 20px; margin-top: 5px;"></div>	C05 SIT Place of interview <input type="checkbox"/> 1.Ward 3A <input type="checkbox"/> 3.Ward 4A <input type="checkbox"/> 2.Ward 3B
C06	DOI	Date of interview	<div style="display: flex; justify-content: space-around; align-items: center;"> <div style="border: 1px solid black; width: 30px; height: 20px; margin: 2px;"></div> <div style="border: 1px solid black; width: 30px; height: 20px; margin: 2px;"></div> <div style="border: 1px solid black; width: 30px; height: 20px; margin: 2px;"></div> <div style="border: 1px solid black; width: 30px; height: 20px; margin: 2px;"></div> </div> <div style="display: flex; justify-content: space-around; margin-top: 5px;"> ddmonyyyy </div>	2 0 1
Mafunso onsewa akukamba za zimene zinachitika tsiku limene munthu anagonekedwa kuchipatala These questions all refer to what happened on the day of admission				
C07	HCHAR	Kodi munayenera kulipila Ndalama inairiyonse/mtengo wa Ndalama ku chipatala nthawi imene munafika kapena munagonekedwa? Did you have to pay for any administrative fees/charges to the hospital when you arrived or when you got admitted?		<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No
C08	HCHARM	Ngati ndi choncho, kodi munalipira mtengo wachipatala wandalama zingati? If yes, how much did you pay in hospital charges? Write '0' if did not pay hospital charges	MK	<div style="border: 1px solid black; width: 100px; height: 20px; margin-top: 5px;"></div>
C09	HCHAR2	Kodi munalipila Ndalama ina iriyonse kuti muyezedwe/ ntchito yofufuza ichtike pa inu, tsiku limene munagonekedwa? Did you have to pay any money to have any tests/investigations done on the day you were admitted? (Either at QECH or privately) (Only include tests/investigations requested by their doctor during admission)		<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No
C10	HCHARM2	Ngati inde, munalipira Ndalama zingati? If yes, how much did you pay? Write '0' if did not pay any charges	MK	<div style="border: 1px solid black; width: 100px; height: 20px; margin-top: 5px;"></div>
C11	TRA	Pa tsiku limene munagonekedwalo, munafikako bwanji ku chipatala chachikulu cha Queen Elizabeth? On the day you were admitted, how did you get to QECH? Specify, if other		<input type="checkbox"/> 1. Ambulance <input type="checkbox"/> 2. Walked <input type="checkbox"/> 3. Public transport <input type="checkbox"/> 4. Own transport <input type="checkbox"/> 5. Other, Specify
C12	TRAM2	Kodi munaononga Ndalama zingati pa transipoti yokafikila ku chipatalako? (Ndalama zogwiritsidwa ntchito popita kapena kubwelera kokha) How much money did you spend on transportation to hospital (Cost of one-way travel)? Write '0' if did not spend money	MK	<div style="border: 1px solid black; width: 100px; height: 20px; margin-top: 5px;"></div>

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C13	FOOD2	<p>Tsike limene munagonekedwa, kodi munagwiritsa ntchito Ndalama zingati kugulira zakudya komanso zokumwa?</p> <p>On the day you were admitted, how much money did you spend on food or drinks Write '0' if did not spend money</p>	MK	<table border="1"> <tr> <td></td> <td></td> <td></td> <td></td> <td></td> </tr> </table>					
<p>Tsiku limene munagonekedwa, munaonongapo Ndalama pa china chirichonse?</p> <p>On the day you were admitted, did you spend money on anything else? (write '0' if did not spend any money on item) (For each item, write total money spent)</p>									
C14	HP	Buku la ku chipatala - Health Passport	MK	<table border="1"> <tr> <td></td> <td></td> <td></td> <td></td> <td></td> </tr> </table>					
C15	AIR	Ma uniti a foni ya m'manja - Airtime for Mobile	MK	<table border="1"> <tr> <td></td> <td></td> <td></td> <td></td> <td></td> </tr> </table>					
C16	BATH	Sopo osambira/ochapira kapena shampu - Bathing/Washing Soap or Shampoo	MK	<table border="1"> <tr> <td></td> <td></td> <td></td> <td></td> <td></td> </tr> </table>					
C17	TOOT	Kologeti ndi/mswachi - Toothpaste and/or Toothbrush	MK	<table border="1"> <tr> <td></td> <td></td> <td></td> <td></td> <td></td> </tr> </table>					
C18	CLOT	Zovala ndi/nsapato - Clothes and/or Shoes	MK	<table border="1"> <tr> <td></td> <td></td> <td></td> <td></td> <td></td> </tr> </table>					
C19	CUP	Makapu ndi/mbale - Cups and/or Plates	MK	<table border="1"> <tr> <td></td> <td></td> <td></td> <td></td> <td></td> </tr> </table>					
C20	BUCK	Ndowa kapena beseni yochapira - Bucket or Basin for washing	MK	<table border="1"> <tr> <td></td> <td></td> <td></td> <td></td> <td></td> </tr> </table>					
C21	TOIL	Tishu - Toliet Paper?	MK	<table border="1"> <tr> <td></td> <td></td> <td></td> <td></td> <td></td> </tr> </table>					
C22	OTH1	<p>Tsiku limene munagonekedwa, munaonongapo Ndalama pa china chirichonse?</p> <p>On the day you were admitted, did you spend money on anything else? (Excluding above list)</p>		<p><input type="checkbox"/> 1. Yes</p> <p><input type="checkbox"/> 2. No</p>					
C23	OTH2	<p>Tchulani chinthu chimene munagwiritsirapo ntchito ndalama?</p> <p>Specify what you spent money on?</p>		<table border="1" style="width: 100%; height: 100%;"> <tr> <td></td> </tr> </table>					
C24	OTH3	<p>Kodi munagwiritsa ntchito ndalama zingati pa chinthu chimenechi?</p> <p>How much did you spend on this? (Write '99999' if question not applicable)</p>	MK	<table border="1"> <tr> <td></td> <td></td> <td></td> <td></td> <td></td> </tr> </table>					
C25	WORK	<p>Kodi munajomba ku ntchito chifukwa chogonekedwa ku chipatala?</p> <p>Did you have to take time of work because of being admitted to hospital?</p>		<p><input type="checkbox"/> 1. Yes</p> <p><input type="checkbox"/> 2. No</p>					

C26	VISIT	Tsiku limene munagonekedwa, ndi achibale angati kapena anzanu angati anabwera ndi inu ku chipatala? On the day you were admitted, how many family members or friends came with you to the hospital?	<input type="text"/> <input type="text"/>
C27	CARE	Angati abale ndi anansi mwatchulawa amene anakudikilirani ku chipatala pa nthawi yomwe munagonekedwa? How many of these family members or friends stayed with you in hospital specifically to look after you during your hospital admission?	<input type="text"/> <input type="text"/>
<p><i>Please explain to patient "the main family member/friend" is the person who stayed with them at hospital to look after them. (Gaurdian)</i></p> <p>Kwa m'bale wanu weni-weni/mzanu, kodi anaononga nadalama zingati tsiku limene munagonekedwa muchipatala:</p> <p>For the main family member/friend, how much did they spend on the day you were admitted on: (Do not include items if mentioned under patient costs) (write '0' if did not spend any money) (write '99999' if question not applicable)</p>			
C28	FAM3	Transipoti - Transportation (one-way travel)?	MK <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>
C29	FAM4	Chakudya ndi/kapena zakumwa - Food and/or Drinks?	MK <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>
C30	FACC	Malo ogona - Accomodation?	MK <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>
C31	FAIR	Ma uniti a foni ya m'manja - Airtime for Mobile?	MK <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>
C32	FBATH	Sopo osambira/ochapira kapena shampu - Bathing/Washing Soap or Shampoo?	MK <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>
C33	FTOOT	Kologeti ndi/mswachi - Toothpaste and/or Toothbrush?	MK <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>
C34	FCLOT	Zovala ndi/nsapato - Clothes and/or Shoes?	MK <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>
C35	FCUP	Makapu ndi/mbale - Cups and/or Plates?	MK <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>
C36	FBUCK	Ndowa kapena beseni yochapira - Bucket or Basin for washing?	MK <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>
C37	FTOIL	Tishu - Toliet Paper?	MK <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>

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C38	FOTH	Patsiku limene munagonekedwa kodi iwowo anagwiritsa ntchito ndalama yina yiriyonse pachinthu chirichonse china chifukwa choti anakuperekezani inuyo? On the day you were admitted, did they spend money on anything else?	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No						
C39	FOTH2	Tchulani chinthu chimene iwowo anagwiritsirapo ntchito ndalama Specify what they spent money on							
C40	FOTH3	Kodi zinali ndalama zingati zimene anagwiritsa ntchito pachinthu chimenechi? How much money did they spend on this? Write '0' if did not spend any money Write '99999' if question not applicable	MK <table border="1"><tr><td></td><td></td><td></td><td></td><td></td></tr></table>						
C41	FWORK	Kodi achibale anu/mzanu anajomba ku ntchito chifukwa choti amakutengerani ku chipatala? Did the family member/friend have to take time off work to come with you to hospital?	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No						
C42	FWORK2	Ngati amagwira ntchito, kodi amapeza ndalama zochuluka bwanji pa tsiku? If they work, how much do they normally earn per day? Write '99999' if question not applicable Write '88888' if participant does not know	MK <table border="1"><tr><td></td><td></td><td></td><td></td><td></td><td></td></tr></table>						
<p>Please ensure you complete HTC-QoL questionnaire with patient</p>									

DATA OFFICE USE ONLY

C43 DID Data Officer ID

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C44 DDATE

Date form checked

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y	y	y	y

**Appendix XXII: HTC 503 Previous
day direct non-medical and indirect
cost data collection tool - Hospital
cohort study**

D01	HHBAR	Participant Barcode	<div style="border: 1px solid black; padding: 5px; width: fit-content;"> PLACE ID BARCODE HERE </div>	Write Participant Barcode <div style="border: 1px solid black; width: 100px; height: 20px; margin-top: 5px;"></div>
D02	SPINE	Write Participants SPINE ID	P	<div style="border: 1px solid black; width: 100%; height: 20px; margin-top: 5px;"></div>
D03	TBROCC	TB-ROCC Participant ID (write 9999999 if not a TB-ROCC participant)		<div style="border: 1px solid black; width: 100%; height: 20px; margin-top: 5px;"></div>
D04	HHID	Interviewer ID	<div style="border: 1px solid black; width: 40px; height: 20px; display: inline-block;"></div>	D05 SIT Place of interview <input type="checkbox"/> 1.Ward 3A <input type="checkbox"/> 3.Ward 4A <input type="checkbox"/> 2.Ward 3B
D06	DOI	Date of interview	<div style="display: flex; justify-content: space-around; align-items: center;"> <div style="border: 1px solid black; width: 20px; height: 20px; display: inline-block;"></div> <div style="border: 1px solid black; width: 20px; height: 20px; display: inline-block;"></div> <div style="border: 1px solid black; width: 20px; height: 20px; display: inline-block;"></div> <div style="border: 1px solid black; width: 20px; height: 20px; display: inline-block;"></div> <div style="border: 1px solid black; width: 20px; height: 20px; display: inline-block;"></div> <div style="border: 1px solid black; width: 20px; height: 20px; display: inline-block;"></div> <div style="border: 1px solid black; width: 20px; height: 20px; display: inline-block;"></div> <div style="border: 1px solid black; width: 20px; height: 20px; display: inline-block;"></div> </div> <p style="text-align: center; font-size: small;">d d m o n y y y y</p>	
D07	WHYS	Reason for interview	<input type="checkbox"/> 1. Routine follow-up <input type="checkbox"/> 2. Transferred to ward <input type="checkbox"/> 3. Being discharged <input type="checkbox"/> 4. Absconded <input type="checkbox"/> 5. Transfer to another hospital <input type="checkbox"/> 6. Died	If absconded, discharged, transferred or died: write date absconded, discharged, transferred or died <div style="display: flex; justify-content: space-around; align-items: center;"> <div style="border: 1px solid black; width: 20px; height: 20px; display: inline-block;"></div> <div style="border: 1px solid black; width: 20px; height: 20px; display: inline-block;"></div> <div style="border: 1px solid black; width: 20px; height: 20px; display: inline-block;"></div> <div style="border: 1px solid black; width: 20px; height: 20px; display: inline-block;"></div> <div style="border: 1px solid black; width: 20px; height: 20px; display: inline-block;"></div> <div style="border: 1px solid black; width: 20px; height: 20px; display: inline-block;"></div> <div style="border: 1px solid black; width: 20px; height: 20px; display: inline-block;"></div> <div style="border: 1px solid black; width: 20px; height: 20px; display: inline-block;"></div> </div> <p style="text-align: center; font-size: small;">d d m o n y y y y</p>
<p>Mafunso onsewa akufotokoza za zimene zinachitika DZULO, pamene munali muli mu chipatala</p> <p>These questions all refer to what happened YESTERDAY, whilst you were in hospital</p>				
D08	HCHAR	Kodi dzulo munalipila Ndalama inairiyonse/mtengo wina uriwonse ku chipatala? Yesterday, did you have to pay for any administrative fees/charges to the hospital?		<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No
D09	HCHARM	Ngati ndi choncho, kodi munalipira mtengo wachipatala wandalama zingati? If yes, how much did you pay in hospital charges? Write '0' if did not pay hospital charges		MK <div style="border: 1px solid black; width: 100%; height: 20px; margin-top: 5px;"></div>
D10	HCHAR2	Kodi DZULO, munalipila Ndalama ina iriyonse kuti muyezedwe china chirichonse/ntchito younika thupi lanu ichtike? YESTERDAY, Did you have to pay any money to have any tests/ investigations done? (Either at QECH or privately) (Only include tests/investigations requested by their doctor)		<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No
D11	HCHARM2	Ngati inde, munalipira Ndalama zingati? If yes, how much did you pay? Write '0' if did not pay any charges		MK <div style="border: 1px solid black; width: 100%; height: 20px; margin-top: 5px;"></div>
D12	FOOD2	Kodi DZULO, munaononga Ndalama zokwana zingati pa zakudya kapena zokumwa? YESTERDAY, how much money did you spend on food or drinks (IN TOTAL) Write '0' if did not spend money		MK <div style="border: 1px solid black; width: 100%; height: 20px; margin-top: 5px;"></div>

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		Kodi DZULO, munaonongapo Ndalama pachina chirichonse choonjezera?						
		YESTERDAY, did you spend money on anything else? (write '0' if did not spend any money on item) (For each item, write total money spent)						
D13	HP	Buku la ku chipatala - Health Passport	MK <table border="1"><tr><td></td><td></td><td></td><td></td><td></td></tr></table>					
D14	AIR	Ma uniti a foni ya m'manja - Airtime for Mobile	MK <table border="1"><tr><td></td><td></td><td></td><td></td><td></td></tr></table>					
D15	BATH	Sopo osambira/ochapira kapena shampu - Bathing/Washing Soap or Shampoo	MK <table border="1"><tr><td></td><td></td><td></td><td></td><td></td></tr></table>					
D16	TOOT	Kologeti ndi/mswachi - Toothpaste and/or Toothbrush	MK <table border="1"><tr><td></td><td></td><td></td><td></td><td></td></tr></table>					
D17	CLOT	Zovala ndi/nsapato - Clothes and/or Shoes	MK <table border="1"><tr><td></td><td></td><td></td><td></td><td></td></tr></table>					
D18	CUP	Makapu ndi/mbale - Cups and/or Plates	MK <table border="1"><tr><td></td><td></td><td></td><td></td><td></td></tr></table>					
D19	BUCK	Ndowa kapena beseni yochapira - Bucket or Basin for washing	MK <table border="1"><tr><td></td><td></td><td></td><td></td><td></td></tr></table>					
D20	TOIL	Tishu - Toliet Paper?	MK <table border="1"><tr><td></td><td></td><td></td><td></td><td></td></tr></table>					
D21	OTH1	Kodi DZULO, munaonongapo Ndalama pachina chirichonse choonjezera? YESTERDAY, did you spend money on anything else?	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No					
D22	OTH2	Tchulani chinthu chimene munagwiritsirapo ntchito Specify what you spent money on?	<table border="1" style="width: 100%; height: 80px;"><tr><td></td></tr></table>					
D23	OTH3	Kodi munagwiritsa ntchito ndalama zingati pa chinthu chimenechi? How much did you spend on this? Write '99999' if question not applicable	MK <table border="1"><tr><td></td><td></td><td></td><td></td><td></td></tr></table>					
D24	WORK	Dzulo, mukanatha kupita ku ntchito mukanapanda kulowa mchipatala kapena kudwala? Yesterday, would you have gone to work if you were not in hospital or ill?	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No					

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D25	VISIT	Dzulo, kodi ndi abale kapena anzanu angati amene anabwera kudzakuonani kapena kukudikirirani mchipatala muno? Yesterday, how family members or friends visited you or stay with you in hospital?							
D26	CARE	Angati abale ndi anansi mwatchulawa amene anakudikilirani ku chipatala pa nthawi yomwe munagonekedwa? How many of these family members or friends stayed with you in hospital specifically to look after you during your hospital admission?							
<p>Please explain to patient "the main family member/friend" is the person who stayed with them at hospital to look after them. (Gaurdian)</p> <p>Kwa m'mbale wanu weni-weni/mzanu, anaononga ndalama zingati nthawi imene anali nanu muchipatala dzulo:</p> <p>For the main family member/friend, how much did they spend yesterday on: (Do not include items mentioned under patient costs) (write '0' if did not spend any money) (write '99999' if question not applicable)</p>									
D27	FAM3	Transipoti - Transportation (one-way travel)	MK						
D28	FAM4	Chakudya ndi/kapena zakumwa - Food and/or Drinks	MK						
D29	FACC	Malo ogona - Accomodation?	MK						
D30	FAIR	Ma uniti a foni ya m'manja - Airtime for Mobile	MK						
D31	FBATH	Sopo osambira/ochapira kapena shampu - Bathing/Washing Soap or Shampoo	MK						
D32	FTOOT	Kologeti ndi/mswachi - Toothpaste and/or Toothbrush	MK						
D33	FCLOT	Zovala ndi/nsapato - Clothes and/or Shoes	MK						
D34	FCUP	Makapu ndi/mbale - Cups and/or Plates	MK						
D35	FBUCK	Ndowa kapena beseni yochapira - Bucket or Basin for washing	MK						
D36	FTOIL	Tishu - Toliet Paper?	MK						

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D37	FOTH	Kodi DZULO, anaononga Ndalama pa chinthu china choonjezera? YESTERDAY, did they spend money on anything else?	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No					
D38	FOTH2	Tchulani chinthu chimene iwowo anagwiritsirapo ntchito ndalama Specify what they spent money on?						
D39	FOTH3	Kodi zinali ndalama zingati zimene anagwiritsa ntchito pachinthu chimenechi? How much money did they spend on this? Write '0' if did not spend any money Write '99999' if question not applicable	MK <table border="1"><tr><td></td><td></td><td></td><td></td><td></td></tr></table>					
D40	FWORK	Kodi anajomba ku ntchito dzulo kuti akhale nanu mchipatala? Did they have to take time off work to spend yesterday with you in hospital?	<input type="checkbox"/> 1. Yes <input type="checkbox"/> 2. No					
D41	FWORK2	Ngati amagwira ntchito, kodi amapeza ndalama zochuluka bwanji pa tsiku? If they work, how much do they normally earn per day? Write '99999' if question not applicable Write '88888' if participant does not know	MK <table border="1"><tr><td></td><td></td><td></td><td></td><td></td></tr></table>					
<p>Please ensure you complete HTC-QoL questionnaire with patient</p>								

DATA OFFICE USE ONLY

D42 DID Data Officer ID

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D43 DDATE

Date form checked

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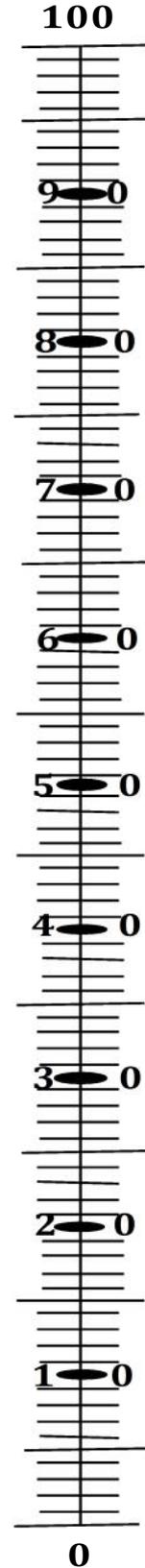
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**Appendix XXIII: HTC QoL health-
related quality of life questionnaire
- Hospital cohort study**

B01	HHBAR	Participant Barcode	<div style="border: 1px solid black; padding: 5px; width: fit-content;"> PLACE ID BARCODE HERE </div>	Write Participant Barcode <div style="border: 1px solid black; display: inline-block; width: 100px; height: 20px;"></div>
B02	HHID	Interviewer ID	<div style="border: 1px solid black; display: inline-block; width: 40px; height: 20px;"></div>	B03 SIT Place of interview <input type="checkbox"/> 1. Ward 3A <input type="checkbox"/> 2. Ward 3B <input type="checkbox"/> 3. Ward 4A
B04	DOI	Date of interview	<div style="display: flex; gap: 10px;"> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> </div> <p style="font-size: small; text-align: center;">d d m o n y y y y</p>	B05 INT Which Interview? <input type="checkbox"/> 1. First Interview <input type="checkbox"/> 2. Follow-up interview
Mafunso amenewa akukukhuza ulendo uwuwu (Highlight questions refer to today)				
B06	GEN	Kodi munganene kuti umoyo wanu uli bwanji? How would you rate your general health?	<input type="checkbox"/> 1. Bwino kwambiri <input type="checkbox"/> 2. Wabwino <input type="checkbox"/> 3. Bwino pang'ono <input type="checkbox"/> 4. Si uli bwino <input type="checkbox"/> 5. Si uli bwino mpang'ono pomwe	
Chongani mu gulu lilironse pansipa, chonde sonyezani mfundo zimene zikufotokoza bwino za umoyo wanu.				
B07	MOB	Mayendedwe	<input type="checkbox"/> 1. Ndilibe vuto lina lililonse poyenda <input type="checkbox"/> 2. Ndimakhala ndi mavuto ena poyenda <input type="checkbox"/> 3. Ndimangobindikira pa kama	
B08	SELF	Kudzisamalira ndekha(mwachitsazo kusamba ndi kudziveka ndekha)	<input type="checkbox"/> 1. Ndilibe vuto podzisamalira ndekha <input type="checkbox"/> 2. Ndimakhala ndi mavuto ena posamba kapena podziveka ndekha <input type="checkbox"/> 3. Ndimalephera kusamba kapena kudziveka ndekha	
B09	USUAL	Zochitika za tsiku ndi tsiku (monga kugwira ntchito, kuwerenga,ntchito za pakhomo, za m'banja kapena kuchita zimene zimandisangalatsa)	<input type="checkbox"/> 1. Ndilibe mavuto ali onse pogwira ntchito zanga za nthawi zonse <input type="checkbox"/> 2. Ndili ndi mavuto ena pang'ono pogwira ntchito za nthawi wonse <input type="checkbox"/> 3. Ndimalephera kugwira ntchito zanga za nthawi zonse	
B10	PAIN	Ululu/kuphwanya m'thupi kusowetsa mtendere?	<input type="checkbox"/> 1. Ndilibe ululu kapena sindikumva kuphwanya m'thupi <input type="checkbox"/> 2. Ndimakhala ndi ululu kapena kumva kuphwanya m'thupi mwapakatikati <input type="checkbox"/> 3. Ndimakhala ndi ululu kapena kumva kuphwanya m'thupi kwambiri	
B11	ANX	Nkhawa/Khumudwa? (Osasangalala)	<input type="checkbox"/> 1. Sindikuda nkhawa kapena kukhumudwa <input type="checkbox"/> 2. Ndimakhala oda nkhawa kapena okhumudwa mwapakatikati <input type="checkbox"/> 3. Ndimakhala oda nkhawa kapena okhumudwa kwambiri	

Kuyerekezedwa kuti umoyo uli bwino kwambiri

Kuti tithandize anthu kunena za umoyo wawo, tajambula mlingo woyesela (chofanana ndi choyesela kuzizila/kutentha kwa m'thupi) womwe umoyo wabwino wayerekezedwa ndi chizindikiro cha 100 ndipo umoyo woipa wayelekezedwa ndi chizindikiro cha 0



Tikufuna mutisonyeze pa mlingowu mmene umoyo ulili lero kuti uli bwino kapena suli bwino mmene inu mukuganizira. Lembani mzere kuchokera pa bokosi pansipa kupita pa mlingo woyesera umene ukufotokoza za ubwino kapena kuipa kwa mmene umoyo wanu ulili lero.

**Mmene
umoyo wanu
ulili lero**

B12 VAS Write Participants Score Below:

**Kuyerekezedwa kuti
umoyo si uli bwino**

DATA OFFICE USE ONLY

B13 DID Data Officer ID

B14 DDATE Date form checked