Adherence to antiretroviral therapy among HIV-infected prisoners: a systematic review and meta-analysis

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ABSTRACT

Data on antiretroviral therapy (ART) adherence among prison inmates are limited and not previously synthesised in a systematic manner. The objective of this study was to provide accurate and up-to-date ART adherence estimates among prison inmates. We searched electronic databases for all studies reporting adherence as a primary or secondary outcome among prison inmates. A random-effects model was used to pool adherence rates; sensitivity, heterogeneity, and publication bias were assessed. Eleven studies involving 2,895 HIV-infected prison inmates were included. The studies were carried out between 1992 and 2011 and reported between 1998 and 2013. A pooled analysis of all studies indicated a pooled estimate of 54.6% (95% confidence interval 48.1 – 60.9%) of prison inmates had adequate (≥95%) ART adherence. The adherence estimates were significantly higher among cross-studies and studies that used self-reported measures. In summary, our findings indicate that optimal adherence remains a challenge among prison inmates. It is crucial to monitor ART adherence and develop appropriate interventions to improve adherence among these population.

Keywords: adherence; prisoners; meta-analysis; antiretroviral therapy

INTRODUCTION

It has been documented that there is a higher burden of HIV infection among incarcerated populations in low-, middle, and high-income countries(Jurgens, Nowak, & Day, 2011) as well as its negative impact on continuity of care; development of trust; and, subsequently, optimal adherence(Seal, 2005). Incarceration provides public health opportunity to provide life-saving antiretroviral therapy (ART) to HIV-infected persons; but multiple barriers to ART access, delivery and adherence persist(R. Y. Chen et al., 2006; Hammett, Kennedy, & Kuck, 2007; Zaller, Thurmond, & Rich, 2007). Even, after release from prisons, non-adherence and loss-to-follow up has been reported as a major issue(Baillargeon et al., 2009). Of paramount importance while in prison is the necessity to maintain patient confidentiality, in order to avoid perceived and experienced stigma(Ines, Moralejo, Marcos, Fuertes, & Luna, 2008; Pontali, 2005; Rosen et al., 2004; Small, Wood, Betteridge, Montaner, & Kerr, 2009) as well as assisting prisoners at delivery to be linked to care in outpatient basis, maintain high level of adherence and re-insertion in the community(Milloy et al., 2011; Springer et al., 2004; Stephenson et al., 2005). There are limited knowledge on the level of achievable ART adherence in prison globally as well as evidence-based interventions. We therefore conducted a systematic review with meta-analysis to fill this research gap, to provide a more accurate and up-to-date ART adherence estimates among prison inmates living with HIV in order to attempt to quantify the burden and inform decision regarding policy responses and public health intervention.

METHODS

Protocol and Registration

The study background, rationale, and methods were specified in advance and documented in a protocol to be published at the international prospective register of systematic reviews (PROSPERO; Number: CRD42016044044)(Uthman, Nduka, & Oladimedji, 2016).

Eligibility Criteria

Type of studies: cross-sectional and cohort studies that reported ART adherence rates as a primary or secondary outcome. No language, publication date or publication status restrictions were imposed. We excluded studies that involved directly observed antiretroviral therapy. Types of participants: HIV-infected prison inmates on ART. Types of outcome measures: adherence rates regardless of measures (such as self-reported, pill count, etc.).

Information Sources and Search Strategy

Two of the authors (OAU & OO) conducted searches on the following electronic databases (from 1980 to January 2016): PubMed, EMBASE, SCI Web of Science, NLM Gateway and Google scholar. We used the following keywords: “prisoners”, “jail”, "adherence", “compliance”, "antiretroviral therapy" “HIV”; “HAART”; “ART” (see **Appendix 1** for the full Medline search strategy). We searched abstract of relevant conference proceedings from 2006 onward (the most recent ones that may not have been indexed in NLM Gateway meeting abstracts). In addition, the bibliographies of relevant review articles and selected articles were examined for pertinent studies.

Study selection

Two authors (OAU and OO) evaluated the eligibility of studies obtained from the literature search using a predefined protocol, and worked independently to scan all abstracts and obtain full text of articles. In cases of discrepancy, agreement was reached by consensus and by discussions with the third reviewer.

Risk of bias assessment

We used the the Risk of Bias Assessment Tool for Nonrandomized Studies (RoBANS)(S. Y. Kim et al., 2013) to appraise the risk of bias for included studies(see **Appendix 2**). This included information on

the selection bias (sample population), selection bias (participation rate), performance bias (outcome assessment), performance bias (analytical methods to control for bias) and other form of bias. The methodological components of the studies were assessed and classified as adequate, inadequate or unclear. Where differences arose, they were resolved by discussions with the third reviewer.

Data abstraction

Two reviewers (OAU and OO) independently extracted and compared the data. For each study that met the selection criteria, details were extracted on study design, study population characteristics, and adherence measures.

Data Analysis

For the meta-analysis, we first stabilized the raw ART adherence proportions from each study using the Freeman-Tukey variant of the arcsine square root transformed proportion(Stuart & Ord, 1994) suitable for pooling. We used a DerSimonian-Laird random effects model(DerSimonian & Laird, 1986) due to anticipated variations in study population, health care delivery systems and epidemic course. To evaluate the stability of the results we applied several sensitivity analyses, including fixed effects analysis and used a one-study removed approach.(Normand, 1999) The purpose of this analysis was to evaluate the influence of individual studies, by estimating pooled estimate in the absence of each study. We assessed heterogeneity among trials by inspecting the forest plots and using the chi-squared test for heterogeneity with a 10% level of statistical significance, and using the I^2 statistic where we interpret a value of 50% as representing moderate heterogeneity.(Higgins & Thompson, 2002; Higgins, Thompson, Deeks, & Altman, 2003) We assessed the possibility of publication bias by evaluating a funnel plot for asymmetry. Because graphical evaluation can be subjective, we also conducted a Egger's regression asymmetry test(Egger, Davey, Schneider, & Minder, 1997) as formal statistical tests for publication bias.

The effect of the following study-level factors on the overall adherence rates was explored using sub-group and meta-regression analyses: type of publication (full-text versus conference abstract), study period (earlier studies conducted before 2000 versus recent studies conducted after 2000), publication year, study design (cross-sectional versus cohort), study's region (North America, Europe & sub-Saharan Africa), study size (small:<150 versus large: 150 plus), adherence threshold (≥95% versus 100%), adherence measures (self-reported versus pharmacy refill). Series of univariable random-effects meta-regression analyses were conducted to investigate the impact of factors on the pooled adherence proportions. Meta-analysis results were reported as combined adherence proportions with 95% confidence intervals (CIs), while meta-regression results are reported as odds ratio with 95% CIs. We assessed the level of agreement between the review authors reviewers using kappa analysis and reported using the Cohen kappa index (Cohen, 1960). All p-values were exact and p-value less the 0.050 was considered statistically significant. Analyses were conducted using Stata version 14 for Windows (Stata Corp, College Station, Texas). This systematic review was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines (http://www.prisma-statement.org).(Liberati et al., 2009; Moher, Liberati, Tetzlaff, & Altman, 2009) The PRISMA checklist is provided in the **Appendix 3**.

RESULTS

Search results and study characteristics

Figure 1 shows the study selection flow diagram. The literature search yielded 739 articles of which 29 duplicate records were removed. An additional 672 articles were screened by their titles and abstracts, leaving 38 full-text articles selected for critical reading (kappa=0.72; good agreement). Twenty-seven did not meet the inclusion criteria as no relevant outcomes were reported (**Appendix 4**). Eleven studies yielding a total of 13 adherence estimates met the inclusion criteria and were included (kappa=1.00;

100% agreement) in the meta-analysis(Catz, Sosman, Scheuerell, & Crumble, 2002; N. E. Chen et al., 2013; Chitsaz et al., 2013; Ines et al., 2008; Mostashari, Riley, Selwyn, & Altice, 1998; Palepu et al., 2004; Paparizos et al., 2013; Perez et al., 2006; Soto Blanco, Perez, De Labry Lima, et al., 2005; Soto Blanco, Perez, & March, 2005; Wakoli, Baliddawa, Kimaiyo, & Braitstein, 2010). The sample was composed of 2895 HIV-infected prisoners on ART. Table 1 presents the characteristics of the included studies. The studies were carried out between 1992 and 2011 and reported between 1998 and 2013. Most were reported as journal articles (n=9, 82%); only two were presented as conference abstracts (18%). When reported the mean age of the participants ranged from 34.0 to 44.7 years and percentage drug users ranged from 32% to 100%. The preponderance of the studies (n=9, 82%) were cross-sectional and two were cohort studies (18%). Most of the studies were conducted in high-income countries (n=10, 91%) and only one study was conducted in low-income country. Studies were carried out in the United States (n=4, 36%), Spain (n=4, 36%), Canada (n=1, 9%), Greece (n=1, 9%), and Kenya (n=1, 9%). Most studies measured adherence using self-reported questionnaires (n=10, 91%) only one study used pharmacy refills. Most of the studies used adherence threshold of 100% (n=8, 73%) and three studies a threshold of ≥95% (n=3, 27%).

Risk of bias of included studies

The summary risk of bias of included studies is shown in **Figure 2**. All studies recruited participants from representative samples, selection bias due to sample population is low in all studies. Selection bias due to participation rate is low in five studies, i.e. participation rate was greater than >70-85% in these five studies and unclear in the remaining six studies. Performance bias due to outcome bias was in all the 11 studies, they all used subjective measures (self-reported questionnaires and pharmacy refill). Performance bias due to confounding was low in five studies that reported adjusted associations, high in two studies and unclear in the remaining four studies. The risk of bias due to other potential bias was low in four studies and unclear in the remaining seven studies.

Overall adherence to ART during and after pregnancy

Proportion of prisoners who achieved adequate adherence levels and 95% CIs from individual studies with a pooled estimate are shown in **Figure 3**. The pooled ART adherence proportions for all studies yielded an estimate of 54.6% (95% CI 48.1 to 60.9%) of patients with adequate ART adherence (≥95%). The I^2 statistics was 90.5%, indicating statistically significant heterogeneity among the studies. The contour-enhanced funnel plot of examination of publication bias is shown in **eFigure 1**. The funnel plot appears symmetric and shows no evidence of publication bias (P = 0.631 for Egger's regression asymmetry test). The results of leave-one-study-out sensitivity analyses showed that no study had undue influence on pooled adherence estimate (**eFigure 2**).

Adherence to ART by different subgroups

The results of subgroup analyses are shown in **Figure 4**. The pooled proportion of prisoners who achieved adequate adherence levels was significantly higher among cross-sectional studies than cohort studies (57.3% versus 38.1%, p-value for interaction = 0.0001); and was significantly higher among studies that used self-reported measures than the study that used pharmacy refill (56.3% versus 32.7%, p-value for interaction = 0.0001). However, there were no statistically significant differential proportion of prisoners that achieved adequate adherence levels by other subgroups: type of publication, study period, publication year, region, study size, and adherence threshold.

Factors modifying adherence estimates as identified by meta-regression analyses

Factors associated with adherence estimates and proportion of explained variability in adherence estimates as identified by univariable meta-regression analyses are shown in **Table 2.** Adherence estimates from cross-sectional studies were 94% statistically significantly higher than those from cohort studies (OR = 1.94, 95% CI 1.43 to 12.62); and adherence estimates from studies that used self-reported measure were 2.4 times as higher as those from pharmacy refill measure (OR = 2.44, 95% CI

1.60 to 3.73). Contrary to expectation, for every 10% increase in percentage of drug-users included in the studies, the adherence estimates increased by 16% (OR = 1.16, 95% CI 1.10 to 1.29) (**eFigure 3**). Percentage of drug-users, study design and adherence measure explain 40.6%, 24.9% and 20.3% in between study variability in adherence rates respectively.

Factors associated with adherence rates as reported in individual studies

Seven studies reported factors associated with adherence estimates among prisoners (**eFigure 3**). The following facilitators of optimal adherence were reported: good patients-physician and peers' relationship, active occupation inside prison, absence of HIV symptoms, good acceptance of treatment, and higher educational attainment. While the following barriers of optimal adherence were reported: depressed mood, no social support, 'bad' quality food/food insecurity, difficulty in taking medications, previous injecting drug use, active medical problems, alcohol use and younger age.

DISCUSSION

Main findings

To our knowledge, this is the first systematic review and meta-analysis to summarize the available data regarding ART adherence among prison inmates and has brought together evidence from 11 studies incorporating 2,895 prison inmates on HIV treatment. We found that the pooled proportion of prison inmates with adequate (≥95%) ART adherence was only about 54.6%, which is still lower compared to other high-risk subgroups, such as HIV-infected drug users (60% [95% CI 52% to 68%], 38 studies)(Malta, Magnanini, Strathdee, & Bastos, 2010), HIV-infected female sex workers (76% [95% CI 68% to 83%], 4 studies)(Mountain et al., 2014), and HIV-infected adolescents (62% [95% CI 57% to 68%], 50 studies)(S. H. Kim, Gerver, Fidler, & Ward, 2014). Interestingly, ART-adherence was twice as high among HIV-infected prisoners in whom adherence was self-reported, compared to those for whom adherence was determined from pharmacy re-fill records. While self-reports are a validated method for

measuring medication adherence(Nguyen, La Caze, & Cottrell, 2014), we cannot rule out the disproportionately larger number of studies using this tool, as opposed to using pharamacy-refill records, which may have biased this result in favour of the former. We also cannot rule out the potential for recall bias when using self-reported measures.

Nonetheless, our findngs may have important public health implications. For instance, that only one out of two HIV-infected prisoners have optimal ART adherence levels, suggests that ART non-adherence constitutes a considerable public health burden, given potential consequences, notably antiretroviral treatment failure and AIDS-specific mortality. Moreover, our meta-analysis was based almost entirely on studies conducted in high-income countries. This potentially suggests that the pooled ART adherence prevalence obtained in our study may be underestimated because prison health services in low- and middle-income countries are less likely to be as comprehensive as prison health services in high-income countries, such that HIV-infected prisoners in the former may be more at risk of ART non-adherence, compared to HIV-infected prisoners in the latter.

Study limitations and strengths

The results of this meta-analysis should be interpreted with caution. We found statistically significant heterogeneity across the studies, thus suggesting that the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance) is important. A considerable proportion of the observed heterogeneity may be explained by differences in adherence thresholds, proportion of participants that were drug users and study design. Nevertheless, even in the presence of high heterogeneity, meta-analysis has been suggested as a preferred option for data synthesis compared to qualitative or narrative interpretation; narrative synthesis can lead to misleading conclusions that should not be generalized beyond the scope of the analysis(Ioannidis, Patsopoulos, & Rothstein, 2008). It is worth noting that the heterogeneity observed in the current study appears to be

the norm rather than the exception in published ART adherence meta-analyses(Falagas, Zarkadoulia, Pliatsika, & Panos, 2008; Peltzer & Pengpid, 2013). Another limitation is bias that can be introduced by the methods used for measuring adherence. Most of the studies included in this meta-analysis used self-reported adherence. Furthermore, this is a conservative bias given that self-report may overestimate adherence, the actual levels of ART adherence may be even lower than what we are reporting. Finally, the meta-regression analysis has several limitations. Meta-regression represents an observational association and suffers from ecological fallacy(Thompson & Higgins, 2002). In addition, meta-regression has low statistical power to detect an association and easily influenced by an outlier(Lambert, Sutton, Abrams, & Jones, 2002).

Despite these limitations, the study strengths are important. We conducted comprehensive searches of databases to ensure that all relevant, published studies were identified. We also conducted meta-regression analyses to investigate whether any particular study-level factor explained the results and could account for the observed variations between studies. In doing so, we have comprehensively and robustly reviewed existing literature in this area, which points to key gaps in the current literature on determinants of ART adherence.

CONCLUSION

Our meta-analysis showed ART adherence among prison inmates is significantly below that recommended for adequate virologic suppression. Only about half of the prisoners achieved optimal adherence (54.6%). Optimal adherence remains a challenge in prisoners and it is crucial to monitor ART adherence, investigate specific risk factors for non-adherence among prisoners and develop appropriate interventions.

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TABLES

Table 1: Characteristics of included studies

Author (year)	Type of publication	Study period	Study design	country	Income category	Male (%)	Mean age	Drug users (%)	Sample size	Adherence measure	Adherence threshold
Catz et al. 2002(Catz et al., 2002)	Conference abstract	Not reported	Cross-sectional	USA	High-income	92	Not reported	Not reported	50	Self-reported	100
Chen et al. 2013(N. E. Chen et al., 2013)	Full-text	2007-2010	Cross-sectional	USA	High-income	66.2	44.7	78.5	653	Self-reported	95
Chitsaz et al. 2013(Chitsaz et al., 2013)	Full-text	2007-2011	Cross-sectional	USA	High-income	72.3	42.8	72.3	1163	Self-reported	95
Ines et al. 2008(Ines et al., 2008)	Full-text	1993-1995	Cross-sectional	Spain	High-income	92	NR	72	50	Self-reported	100
Mostashari et al. 1998(Mostashari et al., 1998)	Full-text	1993-1995	Cross-sectional	USA	High-income	0	35	90	102	Self-reported	100
Palepu et al. 2004(Palepu et al., 2004)	Full-text	1997-2002	Cohort	Canada	High-income	90	34	44.6	101	Pharm Refills	100
Paparizos et al. 2013(Paparizos et al., 2013)	Full-text	2001-2011	Cohort	Greece	High-income	90.3	37.45	32.2	93	Self-reported	95
Perez et al 2006(Perez et al., 2006)	Full-text	2003	Cross-sectional	Spain	High-income	88.7	35.7	Not reported	160	Self-reported	100
Soto Blanco et al 2005 (a)(Soto Blanco, Perez, & March, 2005)	Full-text	2000	Cross-sectional	Spain	High-income	84.7	Not reported	100	177	Self-reported	100
Soto Blanco et al 2005 (b)(Soto Blanco, Perez, De Labry Lima, et al., 2005)	Full-text	2002	Cross-sectional	Spain	High-income	90	35.5	94	281	Self-reported	100
Wakoli et al. 2010(Wakoli et al., 2010)	Conference abstract	Not reported	Cross-sectional	Kenya	Low-income	80	35	Not reported	65	Self-reported	100

Table 2: Factors associated with adherence estimates identified by meta-regression analyses

Factors	OR (95% CI)	p-value	R^2 (%)
Full-text (vs. abstract)	0.63 (0.25 to 1.62)	0.305	1.0
Publication year	0.99 (0.92 to 1.06)	0.779	0.0
Recent (vs. earlier) studies	1.10 (0.90 to 1.35)	0.310	1.7
Cross-sectional (vs cohort) study	1.94 (1.43 to 2.62)	0.000	24.9
American (vs European) study	1.05 (0.51 to 2.17)	0.888	0.0
Male (%)	0.99 (0.98 to 1.01)	0.386	0.0
Mean age (years)	1.03 (0.92 to 1.14)	0.553	0.0
Drug-user (per 10% increase)	1.16 (1.10 to 1.29)	0.000	40.6
Large (vs small) study	1.25 (0.65 to 2.45)	0.461	0.0
100% (vs. 95%) threshold	1.07 (0.54 to 2.12)	0.836	0.0
Self-reported (vs. pharm refill)	2.44 (1.60 to 3.73)	0.000	20.3

FIGURE LEGENDS

Figure 1: Study selection flow diagram

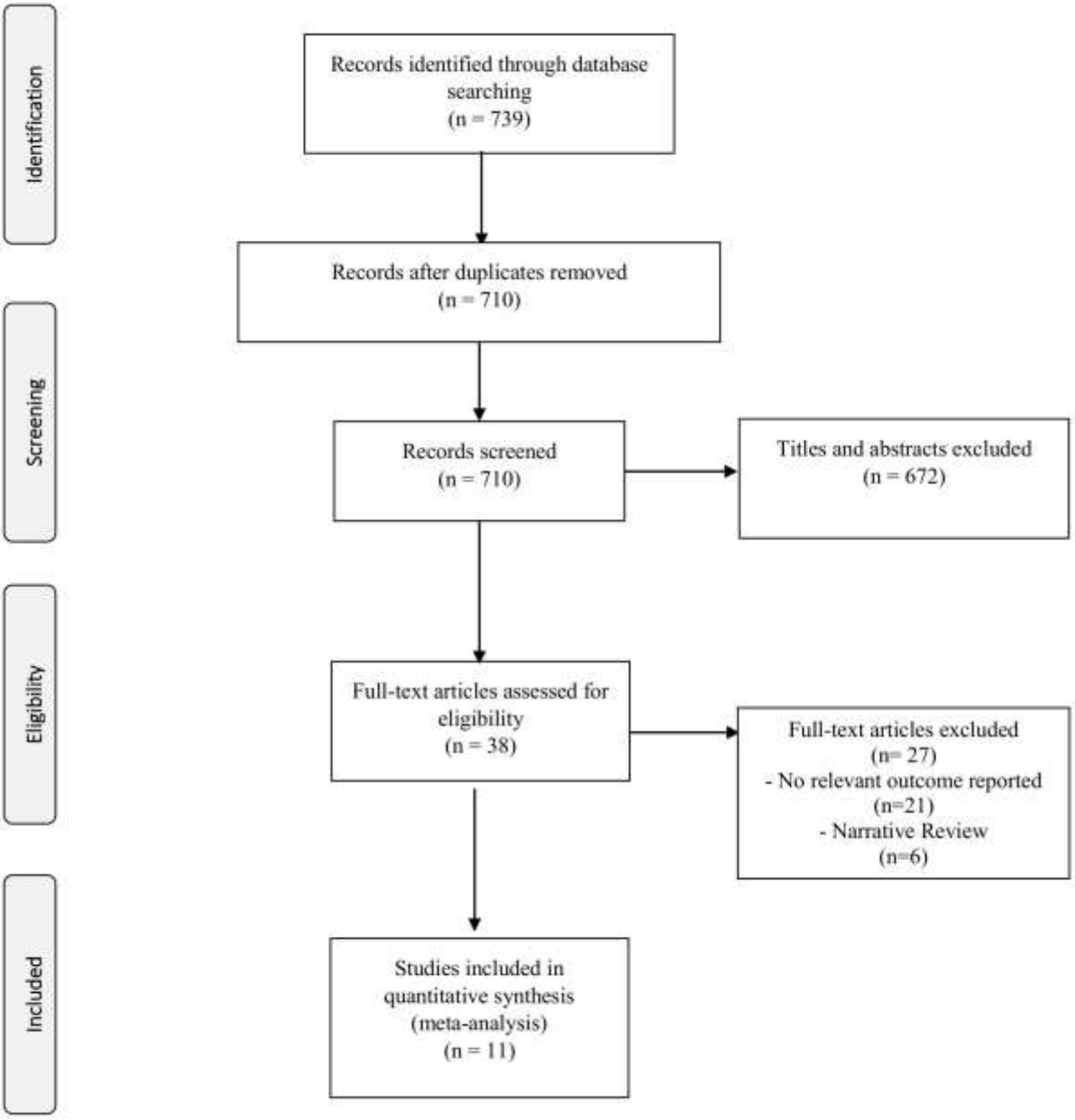


Figure 2: Risk of bias included studies

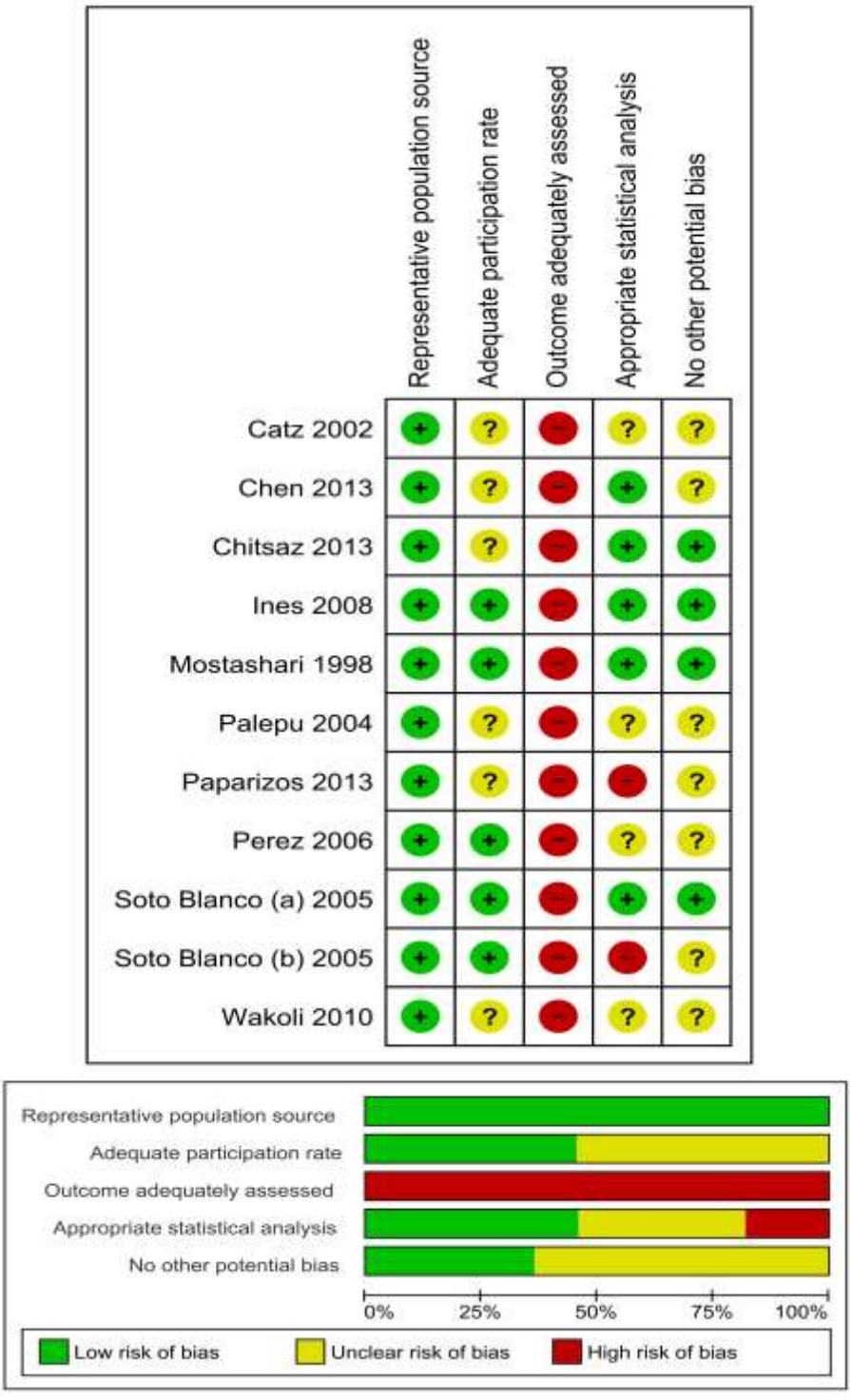


Figure 3: Pooled proportion of prison inmates' adherent to antiretroviral therapy

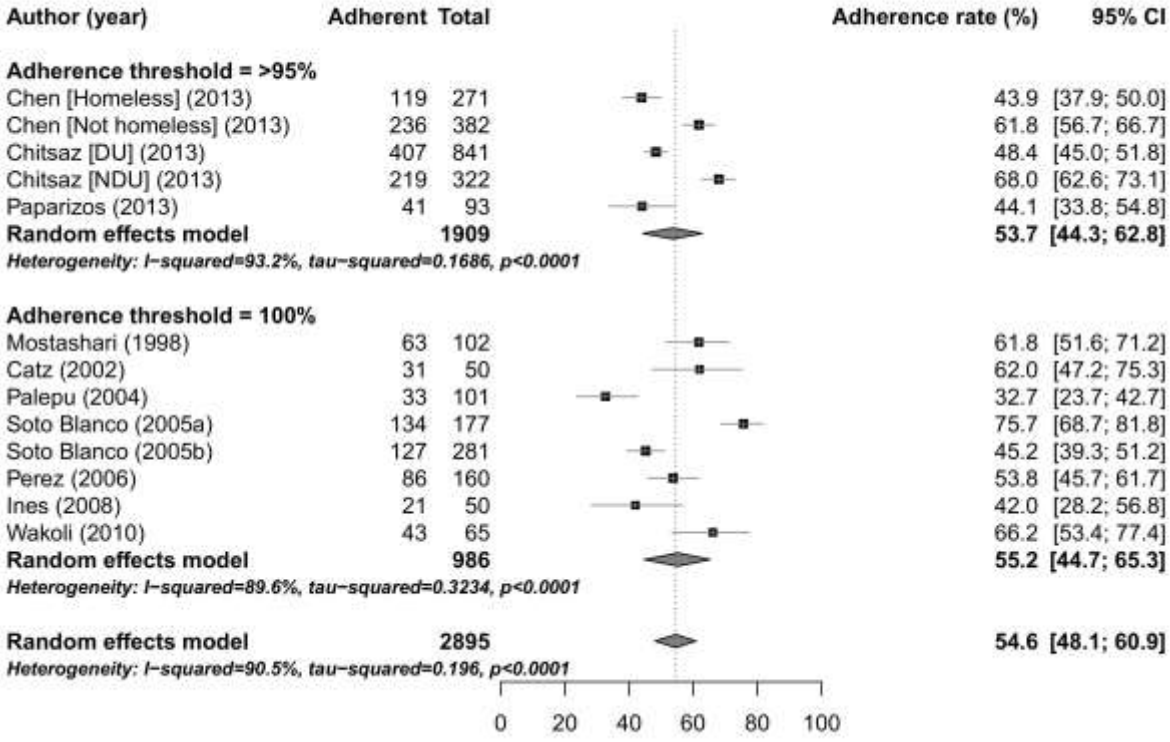
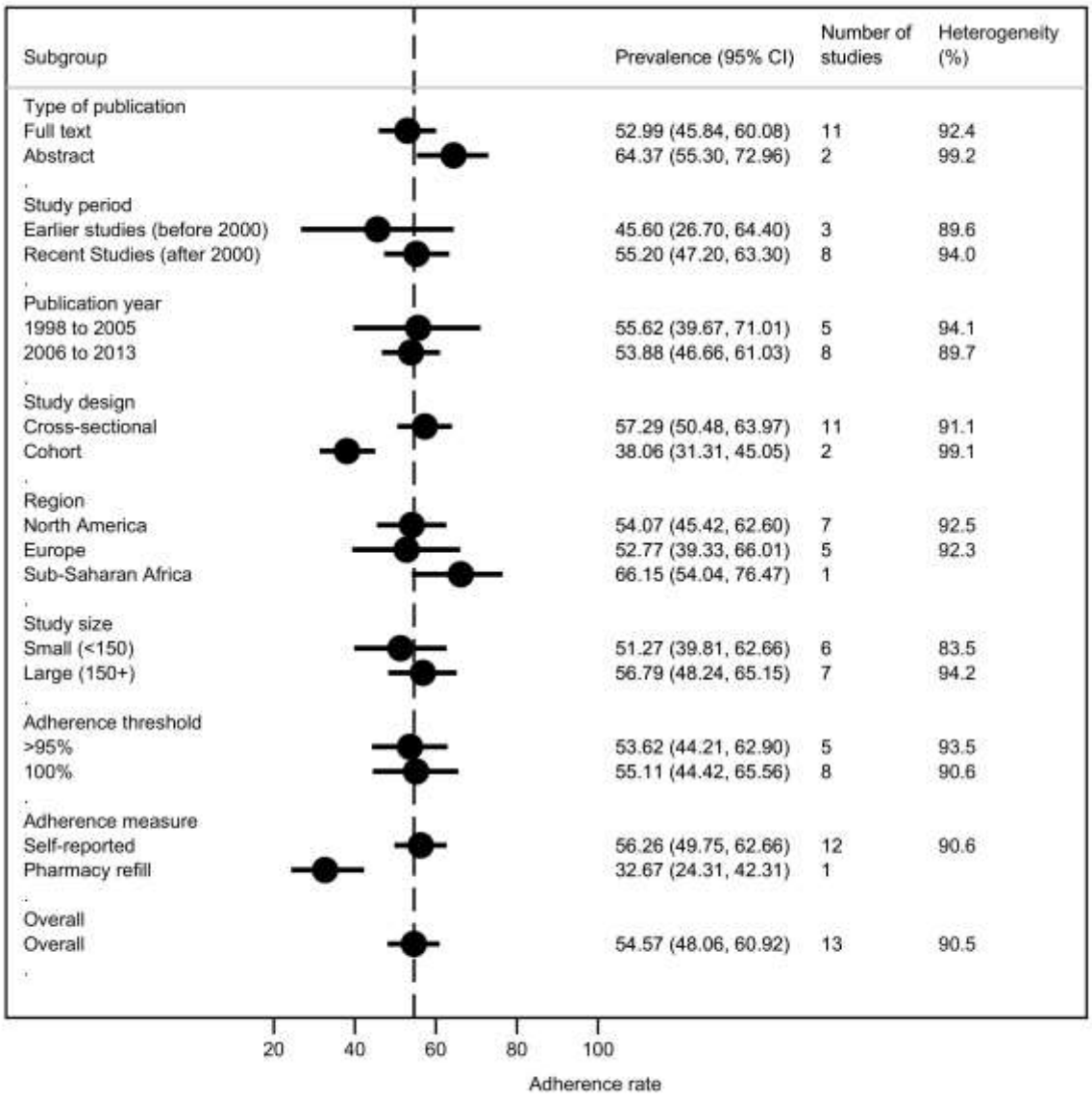


Figure 4: Pooled proportion of prison inmates' adherent to antiretroviral therapy, by different sub-groups



SUPPLEMENTARY DIGITAL CONTENT

Contents

APPENDICIES

Appendix 1: Medline search strategy

1	adherence.mp.
2	nonadherence.mp.
3	compliance.mp.
4	noncompliance.mp.
5	non-compliance.mp.
6	"pill count?".mp.
7	MEMS.mp.
8	"medication event monitoring system".mp.
9	"pharm* refil*".mp.
10	exp Medication Adherence/
11	or/1-10
12	"*prison*".mp.
13	prisoner?.mp.
14	imprison.mp.
15	incarcerat*.mp.
16	"*offend*".mp.
17	"remand*".mp.
18	"*detain*".mp.
19	"*criminal*".mp.
20	"*convict*".mp.
21	"*felon*".mp.
22	pre-trial.mp.
23	under-trial.mp.
24	"jail".mp.
25	"gaol".mp.
26	"detention".mp.
27	"correction*".mp.
28	"sentence*".mp.
29	"probation*".mp.
30	"parole*".mp.
31	re-entry.mp.
32	reentry.mp.
33	"post-release".mp.
34	"transition*".mp.
35	"supervis*".mp.
36	inmate?.mp.
37	in-mate?.mp.
38	"correctional facility".mp.
39	exp prisoner/
40	exp prison/
41	exp criminal/
42	exp detention/
43	exp jail/
44	exp parole/
45	exp offender/
46	or/12-45

47	(hiv or hiv or hiv-1 or hiv-2).mp.
48	human immunodeficiency virus.mp.
49	human immunedeficiency virus.mp.
50	human immune-deficiency virus.mp.
51	hiv infections.mp.
52	aids.ti,ab.
53	acquired immune-deficiency syndrome.mp.
54	acquired immunedeficiency syndrome.mp.
55	acquired immunodeficiency syndrome.mp.
56	acquired immuno-deficiency syndrome.mp.
57	(HAART or highly active anti?retroviral therapy or highly active anti retroviral therapy).mp.
58	Antiretroviral Therapy.mp.
59	retroviral*.mp.
60	Antiviral Agents.mp.
61	human immunodeficiency.mp.
62	antiretroviral*.mp.
63	exp hiv infections/
64	exp human immunodeficiency virus/
65	exp acquired immune-deficiency syndrome/
66	exp acquired immunodeficiency syndrome/
67	exp acquired immuno-deficiency syndrome/
68	exp hiv/
69	exp hiv-1/
70	exp hiv-2/
71	exp HIV SERONEGATIVITY/
72	exp HIV SEROPOSITIVITY/
73	exp HIV SEROPREVALENCE/
74	exp HIV ANTIBODIES/
75	exp ANTIRETROVIRAL THERAPY, HIGHLY ACTIVE/
76	exp Antiretroviral Therapy/
77	or/47-76
78	11 and 46 and 77

Appendix 2: Risk of bias assessment

Bias type	**Adequate**	**Inadequate**	**Unclear**
Selection (sample population)	Rationale for cases (prisoners) selection explained	Sample selection ambiguous and sample unlikely to be representative	Insufficient information
Selection (participation rate)	High participation rate (>70-85%)	Low participation rate (<70%)	Insufficient information
Performance bias (outcome assessment)	Objective measures of adherence	Self-reported measure of adherence	Insufficient information
Performance bias (analytical methods to control for bias)	Analysis appropriate for type of sample (unadjusted, univariable analyses etc.)	Analysis does not account for common adjustment (adjusted, multivariable analyses)	Insufficient information
Other form of bias	There is no evidence of bias from other sources.	There is potential bias present from other sources	Insufficient information

Appendix 3: PRISMA checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	NA
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	3
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	4
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	4
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	5-6

Section/topic	#	Checklist item	Reported on page #
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	5-6
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	4
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	5-6
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	6
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	6-7
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	7
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	7
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	7-8
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	7
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	8-9
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	9
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	10-11
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	11
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	11

Appendix 4: Excluded studies

Study	Reason
Anonymous[1]	No relevant outcome reported
Babudieri 2000[2]	No relevant outcome reported
Babudieri 2005[3]	No relevant outcome reported
Baillargeon 2000[4]	No relevant outcome reported
Baillargeon 2009[5]	No relevant outcome reported
Beckwith 2010[6]	No relevant outcome reported
Bird 1993[7]	No relevant outcome reported
De Groot 2006[8]	Narrative review
Fontana 2007[9]	No relevant outcome reported
Frank 1999[10]	Narrative review
Gallego 2003[11]	No relevant outcome reported
Gir 2005[12]	No relevant outcome reported
Kantrowitz 2005[13]	No relevant outcome reported
Karus 2007[14]	No relevant outcome reported
Pai 2009[15]	No relevant outcome reported
Pontali 2005[16]	Narrative review
Roberson 2009[17]	No relevant outcome reported
Saberi 2012[18]	No relevant outcome reported
Scheyett 2008[19]	No relevant outcome reported
Seal 2005[20]	Narrative review
Small 2009[21]	No relevant outcome reported
Spaulding 2009[22]	No relevant outcome reported
Springer 2004 [23]	No relevant outcome reported
Springer 2005 [24]	Narrative review
Springer 2011[25]	Narrative review
Westergaard 2011 [26]	No relevant outcome reported
White 2006 [27]	No relevant outcome reported

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11. Gallego, O., Corral, A., De Mendoza, C., Gonzalez-Lahoz, J., & Soriano, V. (2003). High rate of resistance to antiretroviral drugs among HIV-infected prison inmates. *Med Sci Monit, 9*(6), Cr217-221.

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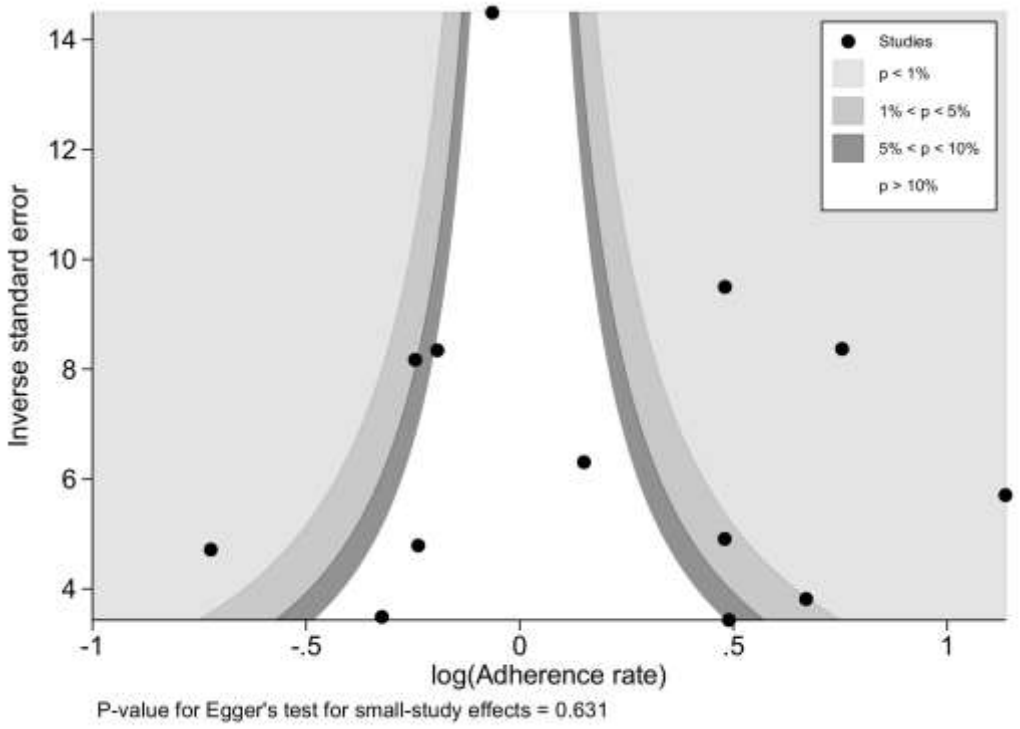
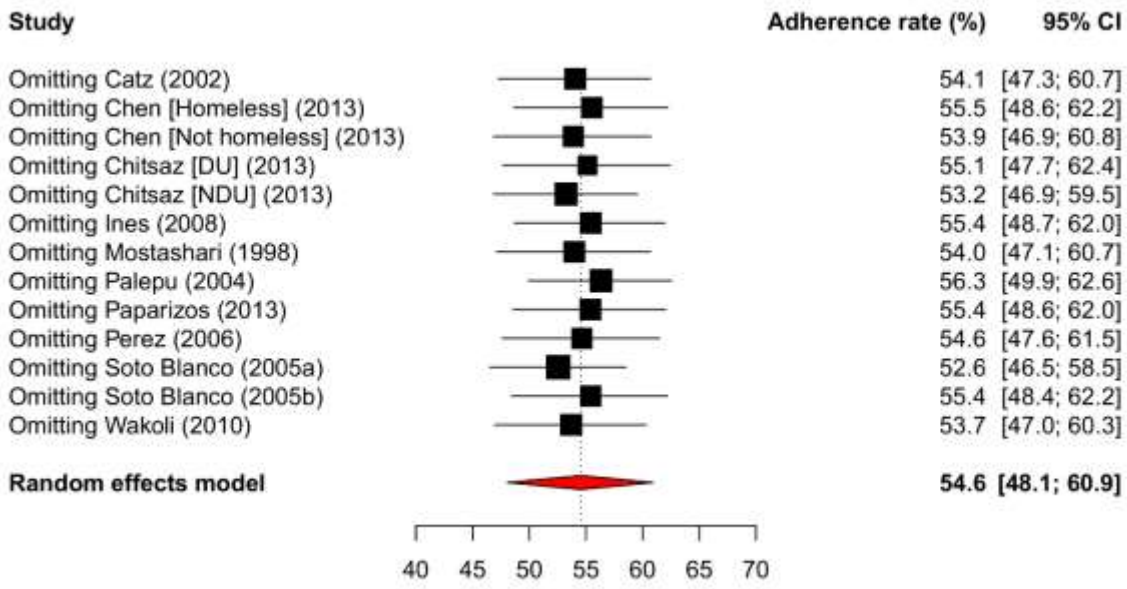
ONLINE ONLY FIGURES

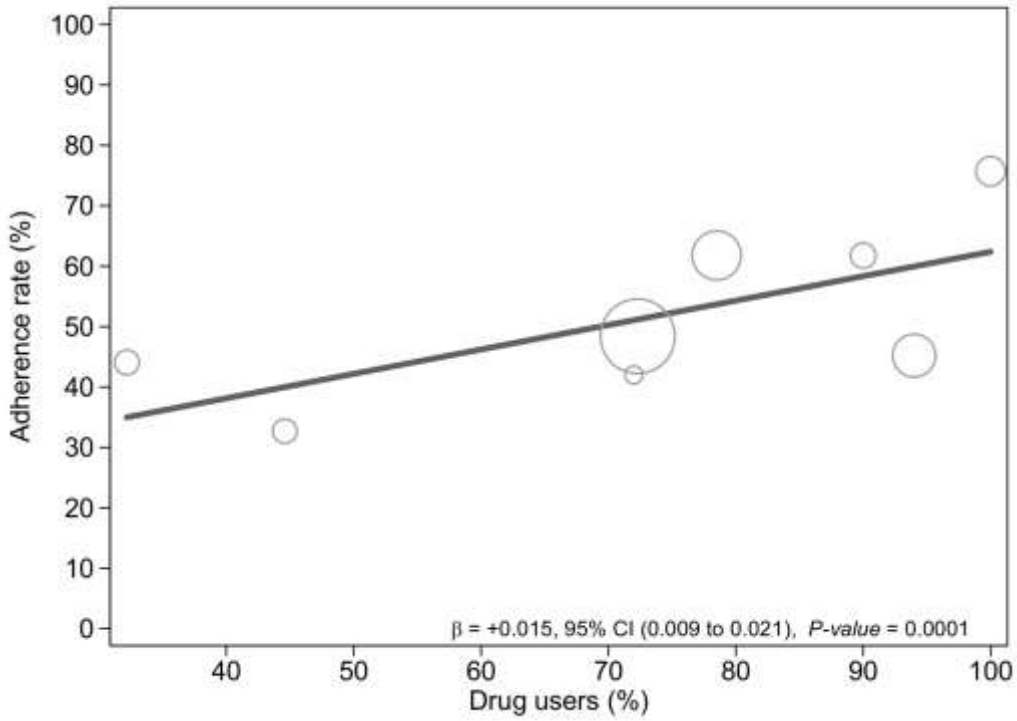
eFigure 1: Contour-enhanced funnel plot



eFigure 2: Leave-one-out sensitivity analyses



eFigure 3: Association between percentage drug users and adherence rate among prison inmates



eFigure 4: Overview of factors associated with adherence as reported by individual studies