WARWICK
THE UNIVERSITY OF WARWICK

A Thesis Submitted for the Degree of PhD at the University of Warwick

Permanent WRAP URL:

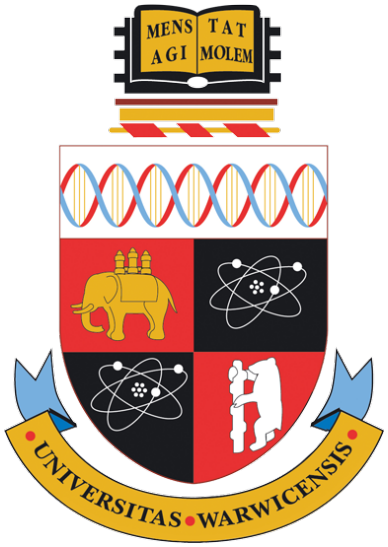
http://wrap.warwick.ac.uk/168617

Copyright and reuse:
This thesis is made available online and is protected by original copyright.
Please scroll down to view the document itself.
Please refer to the repository record for this item for information to help you to cite it.
Our policy information is available from the repository home page.

For more information, please contact the WRAP Team at: wrap@warwick.ac.uk

warwick.ac.uk/lib-publications

WARWICK
THE UNIVERSITY OF WARWICK



Design of medical devices resilient to low-resource settings: from the regulatory framework to the actual design phase

by

Davide Piaggio

Thesis

Submitted to the University of Warwick

for the degree of

Doctor of Philosophy

School of Engineering

October 2021

From Lucretius' De Rerum Natura:

'*Humana ante oculos foede cum vita iaceret*
in terris oppressa gravi sub religione
quae caput a caeli regionibus ostendebat
horribili super aspectu mortalibus instans,
primum Graius homo mortalis tollere contra
est oculos ausus primusque obsistere contra,
quem neque fama deum nec fulmina nec minitanti
murmure compressit caelum, sed eo magis acrem
inritat animi virtutem, ecfringere ut arta
naturae primus portarum claustra cupiret.
Ergo vivida vis animi pervicit, et extra
processit longe flammantia moenia mundi
atque omne immensum peragravit mente animoque,
unde refert nobis victor quid possit oriri,
quid nequeat, finita potestas denique cuique
quanam sit ratione atque alte terminus haerens.
Quare religio pedibus subiecta vicissim
obteritur, nos exaequat victoria caelo.'

From William Ellery Leonard's English translation:

'*Whilst human kind throughout the lands lay miserably crushed before all eyes beneath religion- who would show her head along the region skies, glowering on mortals with her hideous face- a Greek it was who first opposing dared raise mortal eyes that terror to withstand, whom nor the fame of gods nor lightning's stroke nor threatening thunder of the ominous sky abashed; but rather chafed to angry zest his dauntless heart to be the first to rend the crossbars at the gates of nature old. And thus his will and hardy wisdom won; and forward thus he fared afar, beyond the flaming ramparts of the world, until he wandered the unmeasurable All. Whence he to us, a conqueror, reports what things can rise to being, what cannot, and by what law to each its scope prescribed, its boundary stone that clings so deep in time. Wherefore religion now is under foot, and us his victory now exalts to heaven.*'

Contents

List of Tables

List of Figures

Acknowledgments

These acknowledgments will try to be complete but not overly long. Mentioning all the names of the beautiful souls that made the difference in the last 3.5 years of my life would be impossible.
However, you know who you are.
Foremost, I would like to express my sincere gratitude to my supervisor Dr Leandro Pecchia for the continuous support he provided me with throughout my PhD. His friendly advice, patience, motivation, enthusiasm, and, especially, his constructive criticism brought me where I am, as a professional early career researcher and as a more mature person. Thank you for believing in me, allowing me to begin this thrilling adventure.
Besides my supervisor, I would like to extend my acknowledgments to my co-supervisor Dr Ernesto Iadanza, who did not only support my PhD project with his competency, but also provided me with friendly advice and positive criticism.
My sincere thanks also goes to my friends and colleagues (also the temporary visiting students and researchers) at the University of Warwick. Thank you for the time we spent together either in the lab or at the pub or travelling, together we have shared laughs and worries, desperation and joy. I wish you the best in life, may all your dreams come true, because you deserve it.
Never lose that spark in your eyes!
A special mention goes to Rossana, Alessia, Luis, and Martina for the extensive professional and personal support they provided me with.
I would also like to thank all my friends, near and far, for the support you gave me and for all the moments we shared together. For some of you, this goes well beyond the last 3.5 years of my life. Thank you for sticking with me, it is not be taken for granted. For the more recent friends, thank you for deciding

to share with me this adventure called *life*. I wish you all to succeed in life and become the people you dream to be!
Faber est suae quisque fortunae.
My sincere thanks also goes to my family, particularly my mum, dad, brother and grandparents, who have been by my side for all this time, believing in me and making this possible (as well as supporting me with huge parcels of Italian food supplies).
I hope that you are proud of me.
Last but not least, I would like to thank myself for never losing faith and for having come so far. Davide, we both know that this will not be the last accomplishment of your life, because you always aim higher. However, remember to always appreciate yourself and what you have accomplished so far.
Do not take yourself for granted.
I would like to conclude this section by citing Walt Whitman:

O me! O life!

Oh me! Oh life! of the questions of these recurring,
Of the endless trains of the faithless, of cities fill'd with the foolish,
Of myself forever reproaching myself, (for who more foolish than I, and who more faithless?)
Of eyes that vainly crave the light, of the objects mean, of the struggle ever renew'd,
Of the poor results of all, of the plodding and sordid crowds I see around me,
Of the empty and useless years of the rest, with the rest me intertwined,
The question, O me! so sad, recurring—What good amid these, O me, O life?
Answer.
That you are here—that life exists and identity,
That the powerful play goes on, and you may contribute a verse.

Declarations

The work contained in this thesis is based on the author's own work. 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. The work presented (including data generated and data analysis) was carried out by the author except in the cases outlined below:

1. Section 3.1 for which the author was supported in the data collection during a field study by Licia Di Pietro, Busola Oronti, Alessia Maccaro, and Roland Houessouvo, and in the data analysis by Licia Di Pietro.

2. Section 3.2 for which the author was supported and guided in the study in relation to the application of multi-criteria decision analysis techniques by Marco Cinelli.

3. Section 4.1 for which the author was supported in the early stages of image acquisition and processing by Georgy Namm (a former BEng student), and guided by the expertise of Paolo Melillo, who also provided for the videos acquired with the infrared pupillometer, which is available in his lab.

4. Section 4.3 for which the author was supported in the early design phases of the main valves by Scott Hyland (a former MSc student).

5. Section 4.4 for which the author was supported in the design and testing phases of the vest by Mahir Taher (a former BEng student) and by Footfalls&Heartbeats in its manufacturing.

Parts of this thesis have been published by the author [1–7]. Moreover, parts of this thesis are currently submitted to scientific journals [8, 9].

Abstract

This thesis starts from a critical analysis of the current regulatory frameworks concerning medical devices and locations, criticising their non-universality and in-applicability to low-resource settings, and moves on to presenting the main challenges faced by low-resource settings, including the lack of maintenance, the poor supply chain, the scarcity of specialized healthcare professionals, the lack of maintenance, poor plants, low-quality and discontinuous power distribution, etc. In light of such challenges, the use of military standards, which allow a more context-aware approach, together with mHealth, 3D printing, protocycling, and a circular economy and frugal engineering approach are suggested as possible solutions. Subsequently, this thesis presents two original frameworks, namely one for assessing medical locations in low-resource settings which would allow a context-aware design, and one that comprises the criteria for designing medical devices resilient to such settings. Finally, it showcases five use cases, i.e., examples of designs of medical devices or parts of medical devices that were developed throughout my PhD project, following the frugal and contextual philosophy presented in this thesis.

Sponsorships and Grants

Davide Piaggio received support from the University of Warwick with two Warwick Impact Found grants supported by the EPSRC Impact Accelerator Award (EP/K503848/1 and EP/R511808/1).

Acronyms

CEN European Committee for Standardization.

CT Computed Tomography.

DLL Dynamic link library.

ECG Electrocardiograph.

EUDAMED European Databank on Medical Devices.

GNI Gross National Income per capita.

HDI Human Development Index.

HIC High-Income Country.

HRS High-Resource Setting.

HTM Health Technology Management.

ICU Intensive Care Units.

IEC International Electrotechnical Commission.

IP Ingress Protection.

IQR Interquartile Range.

IR Infrared.

ISO International Organization for Standardization.

LIC Low-Income Country.

LMIC Low- and Middle-Income country.

LRS Low-Resource Setting.

MAE Mean Absolute Error.

MAUDE Manufacturer and User Facility Device Experience.

MCDA Multi-criteria decision analysis.

MD Medical Device.

MDR Medical Device Regulation.

MEDDEV Medical Devices Documents.

ML Medical Location.

NCD Non-Communicable Disease.

NHS National Health System.

NTSS-6 Neuropathy Total Symptom Score-6.

PPE Personal Protective Equipment.

RI Relative Importance.

RMSE Root Mean Square Error.

SARS-CoV-2 Severe Acute Respiratory Syndrome CoronaVirus 2.

SDG Sustainable Development Goals.

SSA Sub-Saharan Africa.

UN United Nations.

UV Ultraviolet.

WTO-TRIPS World Trade Organization Agreement on Trade-Related Aspects of Intellectual Property Rights.

Chapter 1

Introduction

The interest of the scientific and political community in low-resource settings (LRSs) and low- and middle-income countries (LMICs), on the wake of the United Nations (UN) 17 Sustainable Development Goals that are part of the 2030 Sustainable Development Agenda [10], has recently increased. The broadness of these goals piqued the interest of experts in different fields, including engineering, medicine, ethnography, philosophy, bioethics, sociology, economics and politics. However, as this is a relatively young and evolving field, the literature related to some specific areas (such as biomedical engineering) is still scarce. The main idea behind this project was conceived by Prof Pecchia after two focus groups held at the International Federation of Medical and Biological Engineering World Congress in 2015 in Toronto, Canada [11], and at Africa Health in 2016 in Johannesburg, South Africa. The focus groups highlighted the inadequacy of the current international standards and regulations of medical devices (MDs) and medical locations (MLs), given the near impossibility of being duly followed and applied in LMICs. After further research, it was discovered that there is a clear need for not only a general inclusive revolution of the Substructure (i.e., the current standards and regulations), but also for a shift of the Superstructure (i.e., the MDs and MLs design criteria) towards a new inclusive, contextualised and user-driven paradigm. This urgent call to arms is widely justified by the numerous challenges that are faced daily by LRSs [1, 2]. Regarding this, it is worth reminding readers that LRSs are not only present in LMICs, but can also be found in some remote areas or in times of catastrophes and crisis in high-income countries (HICs). This was proven further by the recent COVID-19 pandemic, which affected everyone's daily lives and created a generalised condition of LRSs, globally [3]. Accordingly, now more than ever, this is something that should be invested on and researched about further. Hence, this project aimed to analyse the available existing literature, policies, standards, regulations and frameworks to investigate and develop new inclusive, contextualised and

frugal frameworks and methodologies for different purposes, including the design of MDs resilient to LRSs, and the assessment of MLs in LRSs. In particular, the focus was on Sub-Saharan Africa (SSA), given our contacts and collaborations with academics from Benin, Uganda, Ethiopia and South Africa. Moreover, these methodologies were validated and tested through several use cases, in which some MDs were re-designed or designed from scratch, taking into account our underlying framework. Given the wide availability of smartphones and internet globally, and the current shift of the linear economy towards a circular one [12], our approach to these use cases was based on mHealth and additive manufacturing. More specifically, these use cases were divided into three main groups according to their field of application, namely screening, intervention, and clinical engineering, and into two subgroups, namely primary and secondary, based on the amount of individual work spent on them (i.e., for secondary devices, I mainly had support, guidance, and co-supervision responsibilities).
The use cases belonging to the group of screening include:

- **a smartphone-based pupillometer** (Primary), which is a mobile application for testing the pupillary light reflex. This device can be used for screening for the presence and level of possible brain traumas and for the level of anaesthesia in emergency rooms and/or surgical theatres in substitution of/as a complement of specialised doctors. This is relevant for SSA, where there is a lack of expertise and road traffic injuries are very frequent [1]

- **a diabetic neuropathy screening tool** (Primary), which is a smart-tool comprising of a mobile app and 3D-printed parts for the screening of diabetic neuropathies. This is relevant for SSA, as non-communicable diseases (NCDs), including diabetes and the related neuropathies are one of the main causes of mortality and morbidity.

The use cases belonging to the group of treatment include:

- **a 3D-printed condom intrauterine balloon tamponade** (Primary), which is the first of its kind and is used to treat postpartum haemorrhage (PPH) in women. This condition, despite easily treated in HICs, is the cause of death of many women in LMICs. In fact, a woman living in a LMIC is 33 times more likely to die from pregnancy and childbirth complication.

- **a vest for treating jaundice** (Secondary), which aims at monitoring and treating newborns affected by jaundice with blue light. This condition is widespread globally and affects is the 7^{th} cause of neonatal mortality.

The use cases belonging to the group of clinical engineering include:

- **a 3D-printed activated carbon filter for oxygen concentrators** (Secondary), to make up for the chronic lack of spare filters and parts in SSA, which has recently been exacerbated by the COVID-19 pandemic, oxygen concentrators being among the first line treatment for such condition.

For this ambitious purpose, quantitative and qualitative methods related to the fields of engineering and social research were deepened and applied with the help of field experts, including biomedical engineers, clinical engineers, bioethicists, and multicriteria decision analysts.

The following chapters are organised as follows. Chapter 2 - 'Background' presents the background of the thesis along with the identified gaps and possible solutions. In particular, it focuses on the non-universality of standards, regulations and minimum requirements concerning MDs and MLs, on the harsh environmental conditions and frequent challenges that characterise SSA and LRSs, including the dangerous effects on the safe and efficient operationalisation of medical device. Finally, it will introduce the concepts of military standards, ingress protection (IP) codes and circular economy. Chapter 3 - 'Possible tools and methods' presents the tools and methodologies that were created ad hoc describing two frameworks that were developed to assess MLs and to design MDs resilient to LRSs. Chapter 4 - 'Use cases' presents the validation of the tools and methodologies, focusing on the details surrounding the design, prototyping and validation of the above-mentioned devices. Given the width and richness of topics presented in this thesis, to facilitate the reader, Chapters 3 and 4, which rely on previously published papers (or papers currently under consideration), are devised to be self-contained, each presenting their own discussions and conclusions. The latter are then resumed and expanded in Chapter 5 - 'Discussions' and Chapter 6 - 'Conclusions', which conclude this thesis, further commenting on the results and providing a final overview.

Chapter 2

Background, gaps and possible solutions

2.1 Introduction

This introductory chapter lays the basis for the subsequent ones. The aim of this chapter is to introduce the reader to the main challenges and gaps surrounding MD and ML standards, regulations and design with a specific focus on LRSs. The chapter starts with a comparative analysis of the most relevant regulatory frameworks surrounding MDs and MLs, focusing on three main scenarios, i.e., Europe, the USA, and LMICs. After explaining the technical details, the text is also enriched with ethical considerations regarding the non-universality of such frameworks and a brief overview of the social contract theories. A part presenting the main challenges of LRSs and the failure of MDs and MD donations follows. In conclusion, some possible temporary solutions are described, including 3D printing, mHealth and circular economy.

2.2 Post market surveillance, national regulatory agencies, medical device adverse event reports

Post market surveillance can be defined as the systematic process of reporting, monitoring and assessing adverse events or product problems, usually concerning pharmaceutical drugs or MDs, along with the evaluation of other identified possible patient risks [13]. Post market surveillance is crucial to ensure high standards of quality of a product, e.g., of a MD or a drug. National regulatory agencies, among other things, are in charge of the whole MD post market surveillance process that is duly regulated by existing regulations.
Medical device regulations (MDRs) are essential for improving public health outcomes and increasing access to safe, efficient, effective and quality medical

products [14]. However, this need became clear and obtained wide consensus among the international health community only in 1961, when it was discovered that thalidomide caused birth defects [15]. Up to the second half of the Seventies, the existing regulatory frameworks were based predominantly on a national, subjective and prescriptive approach. For example, in the Seventies the Italian MDs had to be made 'a regola d'arte', meaning 'professionally' [16]. Internationally, the situation changed when the Medical Device Amendments of 1976 were approved in the USA. These, aiming to assure the safety and effectiveness of MDs, introduced a three-class risk-based classification for all MDs and established the regulatory pathways for new MDs and for new investigational medical devices to be studied in patients, as well as postmarket requirements, including good manufacturing practices and reporting of adverse events concerning MDs [17]. These Amendments were later on used as a basis for the European 'New Approach', which would constitute the legal foundation of the MD framework of the 1990s, i.e., the Active Implantable Medical Device Directive 90/385/EEC [18] and the Medical Device Directive 93/42/EEC [19] . A similar approach can be found in the early 2000s Japanese Pharmaceutical Affairs Law. Despite an ongoing effort for shifting towards more and more harmonised regulations (e.g., the Global Harmonization Task Force and its successor, i.e., the International Medical Device Regulators Forum[1]), currently, globally, the situation is still fragmented: in fact, the three main existing MDRs are the American Food and Drug Administration (FDA) MDR, the European MDR 2017/745, and the Japanese ones. The latter are currently considered the most important ones, because over three quarters of the MD market is ruled by these three HICs, namely the USA, Europe and Japan [20]. Nonetheless, it is worth mentioning the fact that the MD market shares of these three countries have been diminishing since 2007, when, overall, they accounted for 90% of the global MD market [15]. This is due to the emergence of novel MD markets, which are growing fast, such as China, Canada, Brazil, and India [21]. Also Africa can be included among the fast growing MD markets, with a compound annual growth rate of about 6% [22].

For the sake of completeness, it is worth underlining the fact that there is still a chasm between LMICs and HICs, which can leverage on very demanding MDRs in place as well as national regulatory agenciess (see Figures 2.1, 2.2, 2.3, 2.4), in terms of [23]:

- Pre-market regulations: a MD definition does not exist in the regulatory and legal frameworks of all the countries. In particular, around 35% of the low-income countries (LICs) do not have a definition, while for 42% of them no data is available. LMICs follow with 29% of countries

[1] http://www.imdrf.org/

without a definition and 14.5% countries without available data. Similar trends can be found for the existence of MD risk classes and of essential principles for MDs in the legal frameworks.

- Placing on the market regulations: a registration of establishments is only present in 35% of the LICs, while data is not available for 42% of them. LMICs are not too far with only 33% of countries with registrations of establishments available (data not available for almost 35% of the countries). Similar trends can be seen for the listings of MDs and import controls.

- post-market regulations: similar percentages for LICs and LMICs can be found for adverse event reporting.

The Global Atlas of MDs [23] clearly shows that the African Region is the most problematic one when it comes to either the availability of MD regulatory frameworks or of data.

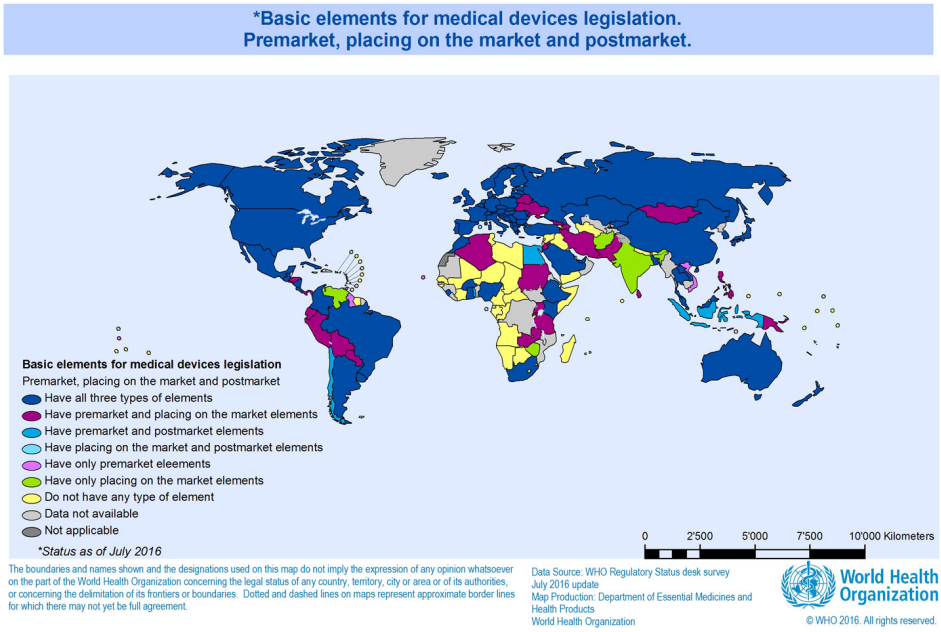


Figure 2.1: The global diffusion of the basic elements for MDs legislations [24].

A brief summary of the regulatory situation in other world regions follows [25]:

- Asia: big markets such as China, Russia and Japan have strict MDRs in place; smaller markets in the south east, belonging to the Association of South East Asian Nations, agreed on a MD directive;

- America (not including the USA): In North America, Canada has its own regulation, issued by Health Canada. In South America, there are

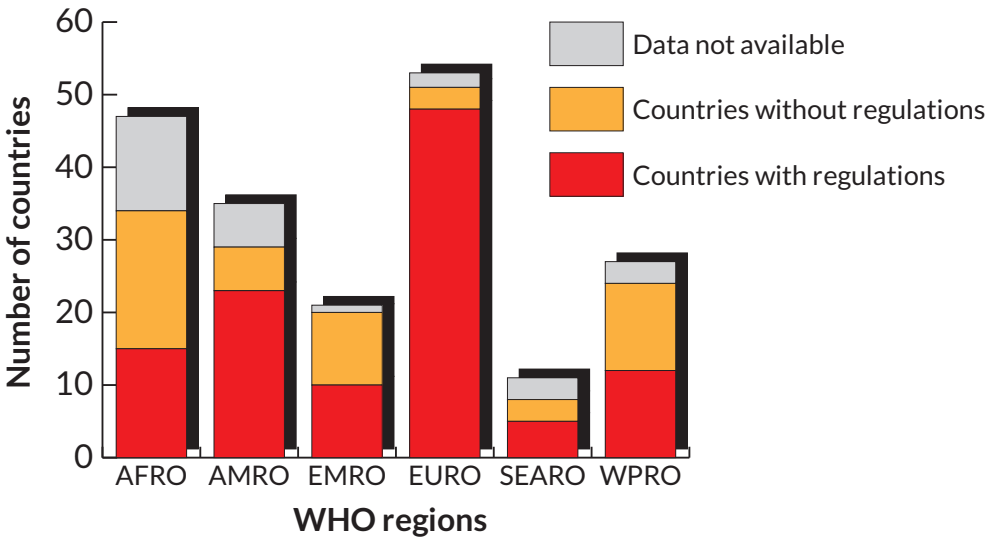


Figure 2.2: Number of countries with a legal framework for MDs by WHO region. Adapted from [23].

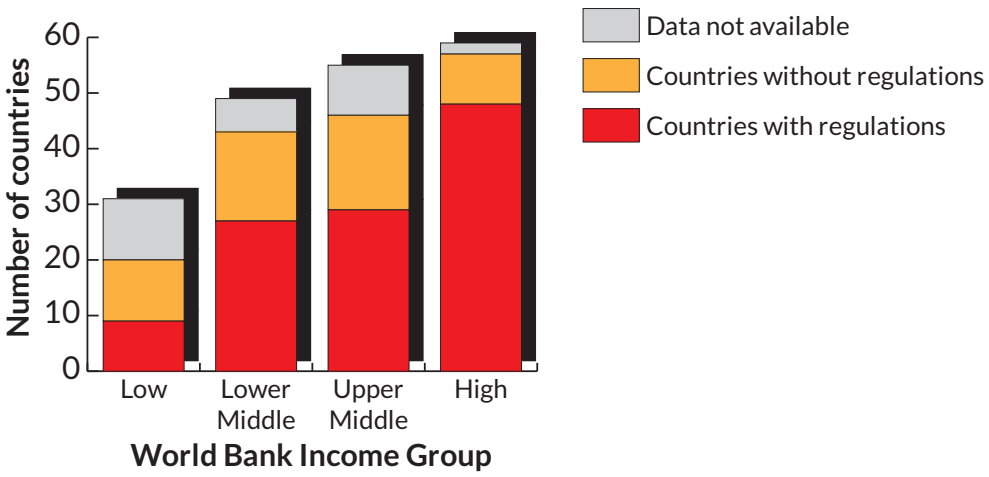


Figure 2.3: Number of countries with a legal framework for MDs by income group. Adapted from [23].

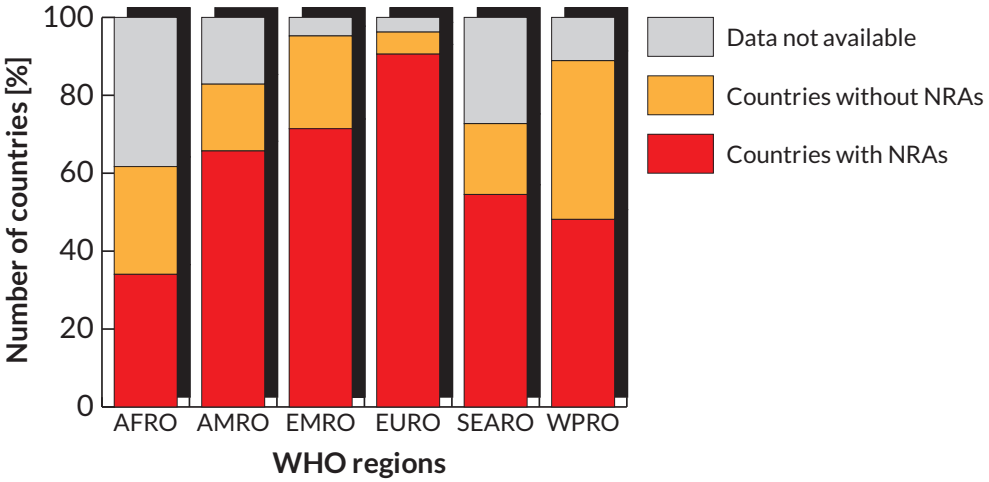


Figure 2.4: Existence of NRAs by WHO region. Adapted from [23].

also strict regulatory systems;

- Africa: Given the wide range of different and complex realities, economic, political and social instabilities, MDRs in Africa are not well defined, unless the scope of the device is related to the treatment of a specific infectious disease such as malaria, AIDS and tuberculosis. In such cases, regulations may be present and strengthened by the national regulatory authorities with the aid of help organizations. Further information on the fragmented situation in Africa will be given in Subsection 2.2.1;

- Oceania: New Zealand and Australia have solid regulations in place, under MedSafe and the Australian Therapeutic Goods Administration.

As regards post-market surveillance, one of the most important parts is that of MD adverse events reporting. Adverse events reporting is crucial to ensure the quality and safe operationalisation of a MD, and to facilitate the intervention of regulatory authorities. It is noteworthy that adverse events reporting focuses on product-related incidents and not on those due to human errors. Accordingly, adverse events related to MD use are distinguished from the ones related to a MD as a product in the regulations of the most prevalent MD markets [15]. A desk survey, involving 194 WHO Member States, conducted by the WHO in 2015-2016, highlighted that only 69% of the 113 countries that have a legal framework also have a regulation regarding adverse events reporting (see Figure 2.5 for further details).

As regards the FDA approach, there are three types of reporting programs, namely the mandatory MD reporting, MedWatch and MedSun.The mandatory MD reporting, introduced only in 1984, obliges manufacturers, importers, and user facilities to report any MD adverse event that may have caused patients deaths or serious injuries. These mandatory reports are submitted

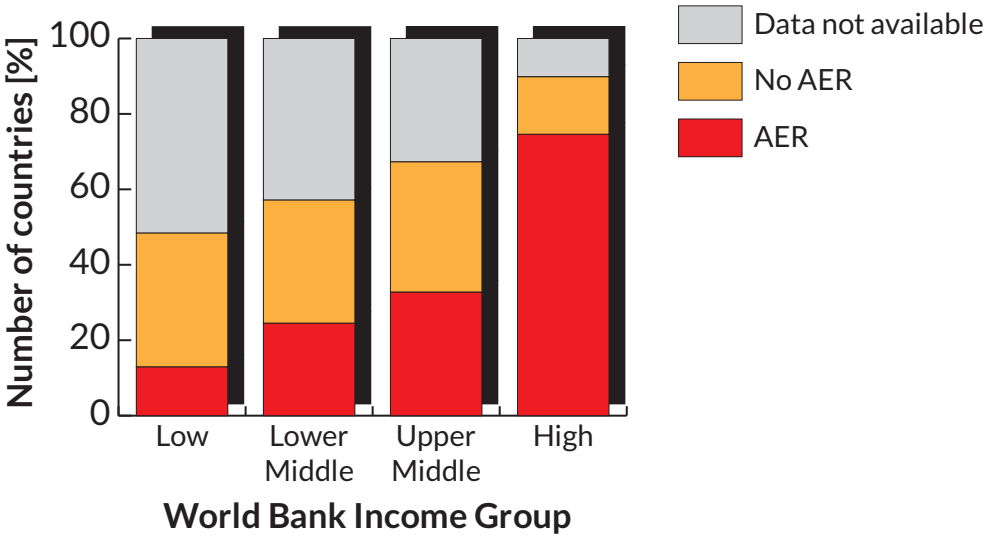


Figure 2.5: adverse events reporting in countries by income group. Adapted from [23].

through a specific form, i.e., Form FDA 3500A [26]. Conversely, MedWatch was introduced by the FDA in 1993 to receive and collect all the voluntary reports surrounding all the FDA-regulated products, including MDs, drugs, food etc. As regard MD-related reports, they can be submitted by anyone excluded by the mandatory reporting regulation, i.e., consumers and healthcare professionals, and they concern quality problems and misuses. These voluntary reports can be submitted in several ways including the Form FDA 3500, electronically, by telephone, fax or mail [13, 26]. It was only in 2002 that MedSun, a 'hybrid' user-facility-tailored and invitation-only program, was launched. According to MedSun, both mandatory and voluntary reports are submitted electronically by trained biomedical and clinical engineers working in the participating facilities and are subsequently reviewed by two groups of analysts [26, 27]. All the above-mentioned reports are open access and available to the public in the Manufacturer and User Facility Device Experience (MAUDE) database [26]. Despite all these adverse events reporting systems and programs available in the USA and the increasing trend of adverse events reporting (see Figure 2.6), underreporting and incomplete reporting are two of their greatest flaws [28].

As regards the European approach, the vigilance system is decentralised and manufacturers are obliged to report adverse events to the national competent authorities of each Member State. These reports are handled and stored independently by each national competent authority. The new MDR 2017/745 also provides for an improvement of an already existing database called European Databank on Medical Devices (EUDAMED), which, among other things, receives and stores the adverse events from the national competent authorities [29]. As Europe is currently under a transition period, whose end

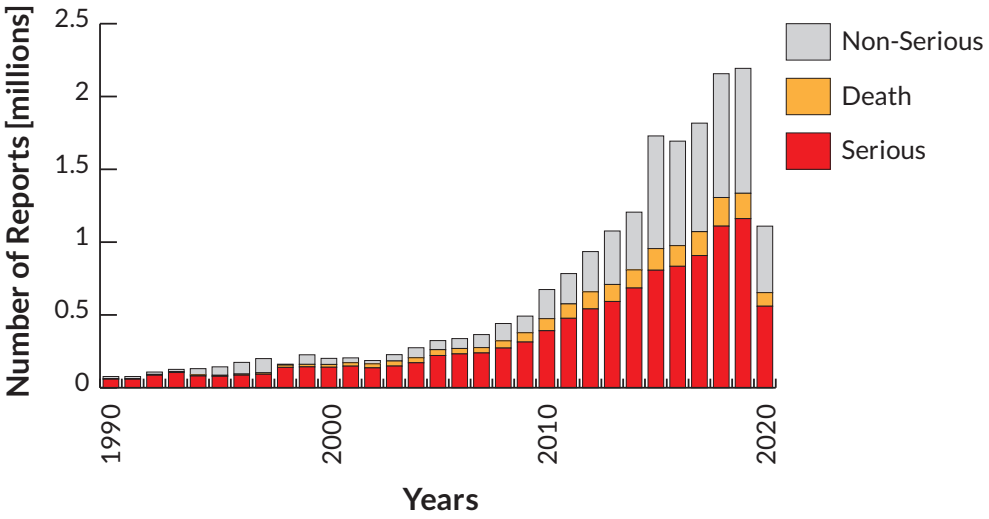


Figure 2.6: FDA adverse event report by year.

has recently been postponed to May 26, 2021 due to COVID-19, reports should currently be made using a tabular format as in Medical Devices Documents (MEDDEV) 2.7/3 Appendix I. However, from May 26, 2021 and only until the use of EUDAMED is available and mandatory, a new tabular format as per Medical Device Coordination Group 2020-10/1, Appendix I, should be used. One of the main issues in the current European post-market surveillance is the fact that there is not an overall collection of the adverse event reports submitted to the national competent authorities and that it is not transparent as it does not allow public access to these data [29]. However, this will be improved by the new provisions of MDR 2017/745, which, among other things, strives for a more transparent approach.

2.2.1 The situation in LMICs: a focus on the African Region

This fragmented situation can also be found in Africa (see Figure 2.1). The African region, in fact, more than other world Regions, is characterised by a complex heterogeneous situation:

- Countries with premarket, placing on the market and postmarket elements: Morocco, Sierra Leone, Burkina Faso, Ghana, Nigeria, Ethiopia, Kenya, and South Africa.
- Countries with premarket and placing on the market elements: Algeria, Sudan, Uganda, Rwanda, Tanzania , Zambia, and Cape Verde.
- Countries with premarket and postmarket elements: Egypt and Togo.
- Countries with placing on the market elements: Zimbabwe.

- Countries without any type of element: Guinea Bissau, Senegal, The Gambia, Mali, Niger, Chad, Libya, Tunisia, Djibouti, Somalia, Ivory Coast, Gabon, Cameroon, Central Republic of Africa, Republic of Congo, Angola, Namibia, Botswana, Lesotho, Eswatini, Burundi, Seychelles, and Madagascar.

- Countries with no data available: Mauritania, Guinea-Conakry, Liberia, Benin, South Sudan, Congo Kinshasa, Eritrea, Malawi, Mozambique, Equatorial Guinea, São Tomé and Príncipe.

As the medical device industry is capital intensive, one may think that richer countries in Africa may present rosier situations. However, even when taking into account the ten African countries with the highest gross domestic product, i.e., Kenya, Nigeria, Egypt, Sudan, Morocco, Angola, Algeria, Tanzania, Ethiopia and South Africa, none of these have specific regulations or regulatory bodies for MDs. Although this is true also for the FDA, the latter can rely on internal divisions and trained personnel for the regulation of the MDs. The above-mentioned 10 African countries, conversely, do not have the same internal organisation and lack skilled personnel [30].

Section 2.2 clearly highlighted a very fragmented situation worldwide, concerning MDRs and, specifically, post market surveillance. It is evident that the lack of efficient or existing adverse events reporting systems brings about a significant underestimation of the problems and challenges surrounding MDs. The lack of negative data, in fact, does not necessarily equate to a perfect condition.

2.3 Regulatory frameworks, international standards and minimum requirements, and their non-universality

Regulation is defined as *'an official rule or law'* or as *'the rules or systems that are used by a person or organization to control an activity or process, or the action of controlling the activity or process'* [31].
Standard is defined as *'an official rule, unit of measurement, or way of operating that is used in a particular area of manufacturing or services'* [32].
Requirement is defined as '*an official rule about something that it is necessary to have or to do*' [33].
In the field of MDs and MLs, standards, regulations and minimum requirements are crucial to warrant and safeguard the conformity, the safety and the efficacy of products. Standards are usually compiled as formal technical documents with international validity by a committee of experts of a regulatory body or

a corporation. From a geographical point of view, there are three levels of standards:

- the international standards have a weight globally and can be adopted by any country; they are compiled by international standards organizations (e.g., International Electrotechnical Commission (IEC), International Organization for Standardization (ISO), etc.) with individual contributions from all the member countries of such organizations.

- the regional standards, followed at a regional level (e.g., Europe), are compiled by appropriate bodies, e.g., the Pan American Standards Commission, the European Committee for Standardization in Europe, the African Organization for Standardization or the Pacific Area Standards Congress.

- the national standards are applied at a national level (e.g., UK, Italy etc.), are compiled by a single recognised national standards body (e.g., British Standards Institution, Ente Nazionale Italiano di Unificazione, South African Bureau of Standards etc.) that is the only member from that country in ISO. The technical content of national standards are usually compiled by national technical societies.

Regional and national standards should be drafted following the ISO/IEC Directives (Part 2) [34] to ensure their universality and worldwide homogeneity. Moreover, sometimes international standards can be adopted at a regional and national level and bypass the respective applicable standards.

As regards MDs, different standards should be taken into account and met while designing them, according to their type, intended use and risk. The following paragraph will focus on the requirements of the new European MDR 2017/745, as it is one of the most relevant worldwide. In particular, MDR 2017/745 allows the manufacturers to respect all, or part of, the essential requirements specified in the regulation, by respecting a certain harmonised standard (e.g., EN 60601 for medical electrical equipment, EN62366 for the application of usability engineering to MDs etc.) or some common specifications, in case harmonised standards were not available. In that case, the manufacturers can avoid to comply with the common specifications if they can prove that they have adopted solutions that ensure a level of safety and performance that is at least equivalent thereto.
As regards MLs, international scientific societies and technical commissions issue standards and requirements in order to harmonise the state-of-the-art for ML design and building (including guidelines surrounding electrical installations, ventilation and filtering, room layouts etc.). Also in this case, as for the regulations surrounding MDs, there is a wide gap among LMICs and HICs.

In most of the HICs, in fact, the standards and minimum requirements are promoted in different ways. For example, in Italy they become law, while in the UK only strong recommendations. Conversely, in most of the LMICs there is both a lack of standardisation and a failure to meet such requirements [1]. Figure 2.7 shows the essential role of international standards and minimum requirements for the safe and efficient functioning of MDs.

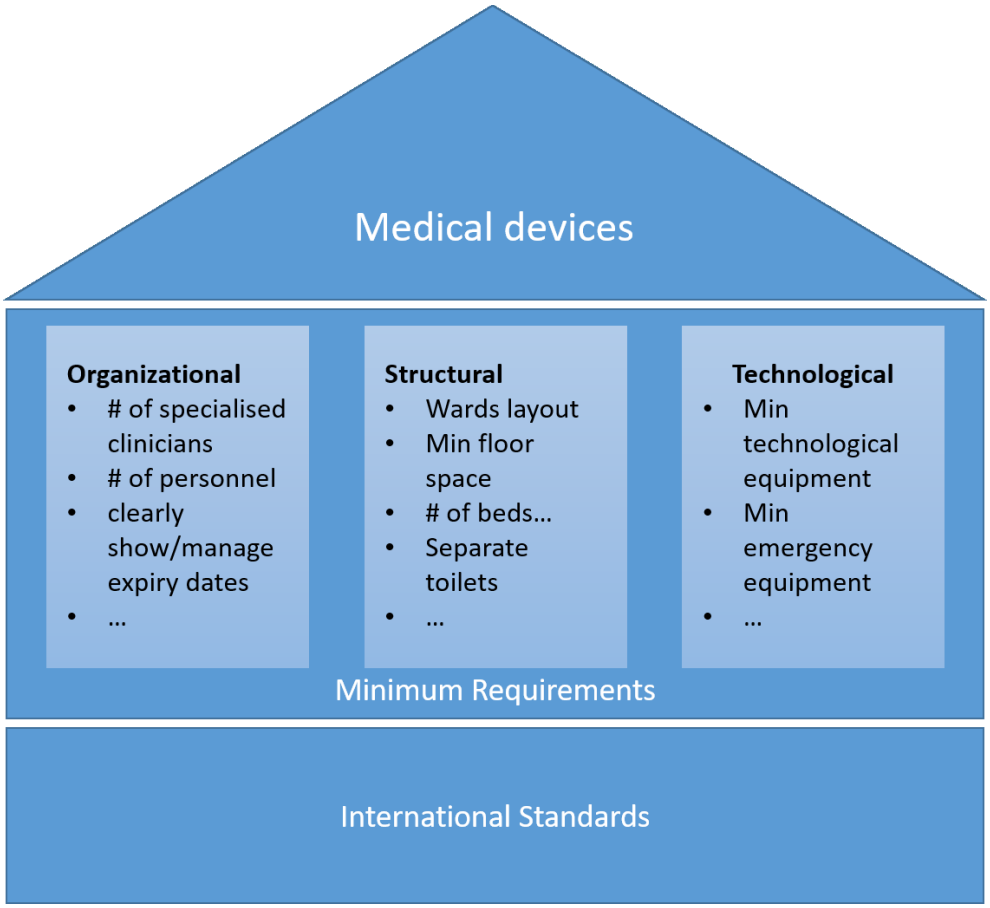


Figure 2.7: The essential role of international standards and minimum requirements for the safe and efficient functioning of MDs [1]

Always in Figure 2.7 it can be seen that the minimum requirements can be divided into structural, organisational and technological [35]. Some examples related to the minimum requirements for activities of diagnostic imaging were selected from the Italian Legislative Decree n. 484 and are reported hereby [1]:

- Structural - a diagnostic imaging ward should have, among other things, a room for radiodiagnostics, with annexed spaces/changing room for users, a room/storage for clean materials and a room/storage for dirty materials and separate toilets for staff and users.
- Organisational - a diagnostic imaging ward should have, among other things, a number of healthcare operators and/or technicians appropriate

for the complexity of the services offered and a quality control system.

- Technological - a diagnostic imaging ward should have, among other things, a high voltage generator (> 30 kW) and a console table and a double focus rotating anode X-ray tube.

A similar scenario can be found in the Health Building Notes from the Department of Health and Social Care in the UK. The latter, together with the Health Technical Memoranda, offer best practice guidance for designing and planning new healthcare buildings and for adapting or extending existing facilities [36]. The Health Building Notes are divided into 17 core subjects including cardiac care, in-patient care, surgery, emergency care etc. Taking as an example Health Building Note 04 (in-patient care) part 02 (critical care unit), the different requirements surrounding critical care units can be found. For instance, mixed-sex accommodation are to be avoided if possible, or the highest standards of privacy and dignity are to be maintained, otherwise; critical care units should be located centrally, very close to imaging facilities, operating theatres, the hospital pharmacy and microbiology laboratory; each bed space, with a minimum size of 25.5 m^2, should include an electric bed fitted with a pressure-relieving mattress, and a ceiling-mounted pendant, that should feature, among other things, 3-4 oxygen outlets, two 4-bar air outlets, a computer with flat-screen monitor, a multi-parameter patient monitoring equipment, 3-6 infusion pumps etc. Health Building Notes are generally complemented by figures and floor plans such as the one shown in Figure 2.8. As it will be further proved in Sections 2.3.1 and 2.5.4, most of these requirements are not inclusive of LRSs and are too strict and demanding for their healthcare facilities.

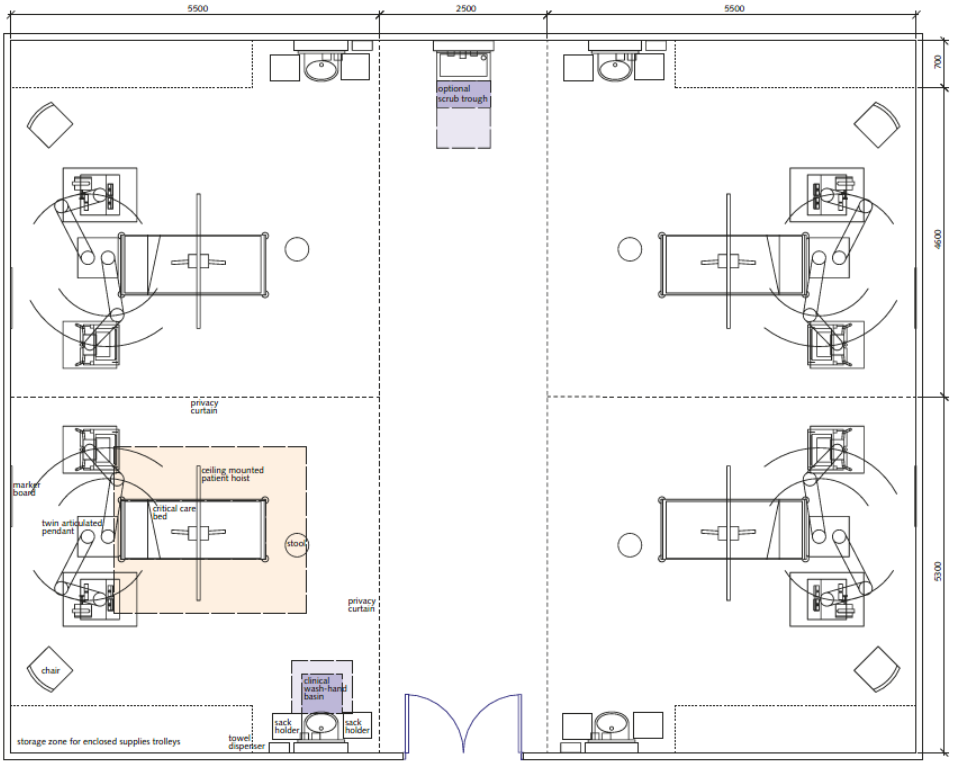


Figure 2.8: A floor plan of a critical care 4-bed bay [36]

2.3.1 Locke's social contract and Nussbaum's capability approach: the non-universality of international standards and minimum requirements, and possible solutions

Hereby an extract of the Second Treatise of Government by John Locke [37]: '*Men being, as has been said, by Nature, all free, equal and independent, no one can be put out of this Estate, and subjected to the Political Power of another, without his own Consent. The only way whereby any one devests himself of his Natural Liberty, and puts on the bonds of Civil Society is by agreeing with other Men to joyn and unite into a Community, for their comfortable, safe, and peaceable living one amongst another, in a secure Enjoyment of their Properties, and a greater Security against any that are not of it.*'

Among the modern fathers of the social contract theories, on the wake of Thomas Hobbes, John Locke clearly states that given the intrinsic free, independent and equal nature of men, no one can lose his/her status and be subjected to the political power and dominance of another, without his/her own consent. The only case in which a man can renounce to his Natural Liberty is when he/she puts it aside in favour of a new Civil Society, through the so-called 'Social Contract'. In addition, Locke asserts that the stipulation of a social contract is the natural course of events when it comes to human interactions.

This is because a man creating and joining a community can lead a comfortable and peaceable life among one another, safe from those who are not part of it. It should be noted that the social contract should be stipulated in the state of nature, i.e., when no man is different from another. In fact, the structure of a political society resulting from a starting point that assumes no antecedent advantages on the part of anyone cannot be other than fair. Likewise, the principles bargained among a fair society cannot be other than fair and will protect the interest of all. However, as good as these theories are ideally, they also present many points of criticism, such as their limited applicability. Martha Nussbaum effectively presents two questions that cannot be ignored: '*By whom are society's basic principles designed*?' and '*for whom are society's basic principles designed*?' This is where the issue lies: the contracting parties, i.e., those settings the basic principles, should be the same citizens who will live together in respect of the chosen principles. Nonetheless this is not the case for many realities, in which some categories (e.g., disabled people) are excluded from the first stipulation of the contract. Although their interest may be taken into account at a later stage, Nussbaum argues that this is likely to affect the completely equal treatment of such citizens [38]. The same social contract theory can be applied at an international level: nations will tend to form a community for the safe and peaceable living, laying down some basic principles. However, in this case it will be the less powerful nations, mainly those whose developmental stage is pre-industrial or so, who will be left out of the initial contracting group and will need to adapt to a new community, which is not tailored to their needs and capabilities [38].

In my opinion, these social contract theories can be perfectly applied to the situation surrounding the regulatory frameworks, international standards and minimum requirements about MDs and MLs. These international standards can be seen as 'basic principles' to promote quality healthcare worldwide to the global community. However, even in this case, some communities, i.e., the poorer nations, the South of the World, have always been excluded or not taken into account when drafting such legal and technical documents. In other words, the legal and regulatory frameworks surrounding MDs and MLs are all based on the wrong starting point, i.e., not all the states were stripped naked of their wealth, when forming the contract. Only at a later stage, the interests/limits of the excluded nations were partially taken into account and this led to initiatives (more like sops) such as donations of MDs, which, as shown in Section 2.5.4, are not an ideal solution and can become a burden for the people and the environment. This trend of displacing and imposing a body of norms and laws from its country of origin to another external country is a phenomenon better-known as 'legal transplantation' [39]. Legrand, arguing that Watson's views on legal transplants [40] are simplistic and, therefore, fallacious, comes

to the conclusion that legal transplants are impossible. In fact, he claims that rules cannot travel, because they always need an interpretation, which is subjective and depends on the particular culture and traditions of the context of application. However, I believe that this cannot be completely applied to international standards and regulations concerning MDs and MLs. In fact, these cannot be misinterpreted at a local level. Rather, they could be difficult to implement in countries with contexts that are very different from those taken into consideration when drafting such standards and regulations. Also in this case a legal transplantation could not be possible and should not be needed. In fact, a more inclusive approach should be followed, including also LRSs in the selection and drafting of such standards and regulations.
An interesting approach in this direction is the so-called 'capability approach' [38, 41], introduced by Nussbaum and Sen. This approach, as suggested by the name, focuses on human capabilities, i.e., what people are actually capable of doing and being, and fights discrimination and unequal treatment, being a fully universal approach. More specifically, among the central human capabilities that are necessary for a life worthy of human dignity, there are:

- Life: 'Being able to live to the end of a human life of normal length; not dying prematurely, or before one's life is so reduced as to be not worth living.'
- Bodily Health: 'Being able to have good health, including reproductive health; to be adequately nourished; to have adequate shelter.'

According to Nussbaum, this approach can be used to generate political principles by the joint effort of economists, policymakers, political scientists and so on, supported by multinational corporations, global economic policies, agencies agreements, international bodies and non governmental organisations. In fact, she strongly believes that each country can pragmatically leverage its capabilities, keeping in mind the Sustainable Development Goals (SDGs), for a fairer world.

2.4 An example of the inadequacy of the current regulatory frameworks: personal protective equipment and COVID-19

This section reports on how the current regulatory frameworks are not only inadequate to LRSs but also to higher resource ones in times of emergency and crisis (e.g., COVID-19). The complete findings are reported in a previously published article [3].

2.4.1 Introduction

Since early 2020, the world has been stricken by COVID-19 pandemic [3] caused by a new strain of Coronavirus, previously unknown to mankind, denominated Severe Acute Respiratory Syndrome CoronaVirus 2 (SARS-CoV-2). SARS-CoV-2, similarly to other viruses [42], seems to have spilled over to humans from wild animals [43]. As a consequence, the human immune system, having never been in contact with such a virus, lacks the ability to fight against the pathogen [42], which can have particularly dangerous effects on subjects with already weak immune systems, or immunosuppressed or elderly subject with existing preconditions. The COVID-19 outbreak impact on European countries was twofold. First, the supply chain of personal protective equipment (PPE), MDs, consumables and spare parts revealed its frailty in its dependence on China's capability to produce them, severally hindered by the lockdown since January 2020. Second, this pandemic has been causing an unprecedented demand of hospitalizations, especially in intensive care units (ICUs), since its early stages. This set off a chain reaction affecting a number of other routine hospitalizations (e.g., elective surgeries), which were postponed giving priority to ICU beds in terms of resources (spaces, personnel, equipment) Moreover, healthcare staff is highly exposed to the risk of catching COVID-19 themselves, due to the inner nature of their daily routine, which exposes them to physical contact with patients. While this condition was already familiar to low- and middle-income countries, COVID-19 has overwhelmingly created LRS conditions in HICs, such as Europe, the USA and Japan, for the first time since World War II [44]. The combination of a frail supply-chain and an unprecedented demand of ICU beds demonstrated the extent to which countries were not prepared to tackle global disasters, such as the current pandemic. This is particularly evident in Europe, where many healthcare systems (e.g., France, Italy, Spain and the UK), being rated among the best ones in the world (11), are being heavily overburdened by the ever-increasing number of patients needing hospitalization or intensive care [45–48]. The national health systems, in fact, lack essential resources for dealing with COVID-19, including MDs (e.g. surgical masks, ventilators, infusion pumps), PPEs [49] and healthcare personnel (who is being reduced by the disease itself). For the first time after decades, the progressive scarcity of devices, equipment and resources has raised also in HICs the problem of resource allocation and prioritisation. The latter could expose a part of the population, probably the most disadvantaged individuals, to further difficulties in accessing healthcare services [50]. The urgent need for equipment directly affects the role of clinical engineers, professionals who are in charge of verifying that all the medical and electro-medical devices are compliant with the essential requirements imposed by the national laws, before authorising

their use in hospital settings. In Europe, this means compliance with the European framework of directives and regulations certified by the presence of the CE mark. Strictly following international standards is the regular path chosen by the manufacturers in order to guarantee the compliance of their products to the above-mentioned requirements, in terms of performances and safety. The current situation has highlighted the flaws of the regulations. For instance, the non-universality of regulations, norms and international standards is clearly evident in these situations of emergency. The problem of non-universality of technical norms is well-known in the context of LRSs, especially in the context of LMICs as highlighted by the authors of this paper who have been extensively acting to overcome this issue [1, 35]. The COVID-19 pandemic, is dramatically demonstrating that this limit is paramount also in HICs during emergencies. The international standards, indeed, proved to be often too generic and demanding, resulting difficult to be implemented in many countries, in terms of time, costs and overall effort required, thus jeopardizing a prompt response to emergencies. This is everyday evidence in lower-income countries, and it is becoming now clear also in high-income ones. In this critical context, this paper shares relevant considerations on the necessity of identifying a set of minimum requirements to test PPEs for use in hospitals during the COVID-19 pandemic. Hopefully, this contribution may be relevant for readers, helping them navigate the variegated context of PPEs regulatory framework. The proposed approach reflects a minimum set of tests that should always be considered despite the waivers issued by several states. This discussion should then be continued, once this crisis will be over, especially with regard to lower-income countries, where the inadequacy of international norms is clear also in everyday conditions. For the sake of conciseness, this section will not report the details of the relevant standards for PPE and the subset of suggested standards that was proposed. Should the reader be interested in such, they may refer to the published paper [3]. However, it will still report background information on the PPE regulation and its fallacies, as well as an analysis of the similarities between the situation caused by the COVID-19 pandemic and that typical of LRSs.

2.4.2 PPE regulation in EU and its inadequacy for COVID-19

The first European directive on the design, the manufacture and the marketing of PPEs was published in December 1989, exactly 30 years before SARS-CoV-2 was first identified in China (Directive 89/686/EEC). This Directive was superseded in 2016 by Regulation (EU) 2016/425, which outlines legal obligations in order to guarantee the highest quality and efficiency of the PPEs

circulating in the EU internal market. The compliance with such regulation is assured by the CE marking. As per semantics, the change from directives to regulations was not trivial and implied a tougher and more harmonized approach. Directives, in fact, are EU instruments requiring member states to legislate accordingly and enforce them at a National level by relevant laws with a certain flexibility. Vice versa, EU Regulations are simultaneously enforced in each member state after a transitional period, imposing clear and detailed common rules, which do not give room for divergent transpositions by member states [51]. The Regulation (EU) 2016/425 itself refers to harmonized standards, developed by a recognized European Standards Organization (e.g., the European Committee for Standardization (CEN)) as a way in which manufacturers or Notified Bodies can assess the conformity of a product. As of Personal Eye Protection and Respiratory Protective Devices, EN166:2001 and EN 149:2001+A1:2009 are the respective harmonized standards. The pathway that manufacturers can take for achieving the CE Marking of PPE are different, depending on the PPE risk-category. For PPE used in low-risk conditions, manufacturers can rely on internal labs and tests to demonstrate that their products are compliant with the harmonised standards requirements, issuing self-certifications. When dealing with protection against SARS-CoV-2 virus, the PPEs are framed in the highest risk class (class II or III), requiring the involvement of external notified bodies. Notified Bodies are appointed under the Article 28 of Regulation (EU) 2016/425, and their responsibilities include confirming that PPE have an adequate level of health and safety in accordance with the essential requirements laid down for that product in harmonised standards. According to the number of PPE produced, Notified Bodies may be requested to repeat this test several times per year. This may include testing few samples that manufactures send to the Notified Body, as well as inspections in the manufacturing farms. A key point is that there is a series of tests that need to be performed according to the relevant standards, depending on the type of device and equipment, to prove that the designed solutions fulfil the minimum requirements in terms of performance and safety. This series of tests is not specific for hospital settings, but it is general, aiming at including all the working conditions to which PPE could be exposed, including testing the robustness of PPE after having been exposed to extreme temperatures (e.g., 70°C), which are never reached in hospitals due to harmonised standards for medical locations. Therefore, when dealing with general standards, their generality becomes a too stringent constraint in emergency situations. For example, PPEs such as face shields or particle filtering face masks (e.g., FFP2 or FFP3 masks) are also (and more often) required in settings other than hospitals, such as in carpentry or soldering activities, in conditions very different from the ones needed by hospital settings. The tests required by the international norms reflect these extreme

working conditions, which are different from the ones that can be found in hospitals. Some national standards developing organisations and some notified bodies, aware of the fact that requiring redundant tests is not strictly necessary in conditions of emergency, reconsidered the whole procedure for testing PPEs and reduced it to a subset of essential tests and minimum requirements that should be met for the use in a COVID-19 hospital department. Confirming this criticism, on the 13th March 2020 the EU Commission published the Recommendation EU 2020/403 (non-legislative act), providing guidance for conformity assessment and market surveillance procedures within the context of the COVID-19 threat. This recommendation has proved the resiliency of the European Commission and its outstanding capability to react to crisis, while confirming the inadequacy of European Regulation for crises and scarce resource scenarios. Amid this widespread confusion, the scientific community has to make clear the fact that, especially during a crisis, PPE should meet the highest possible quality standards, in accordance to the 'As Low As Reasonably Possible' risk management principle [52].

2.4.3 Amateur solutions and the importance of international standards and CE marking

The importance of meeting high-quality standards, guaranteeing the efficiency of MDs and equipment and the safety of their users, is evident now more than ever. During this pandemic, we are witnessing growing proliferation of amatorial initiatives (i.e., quick fixes) aiming at providing for the above-mentioned needs. These initiatives, amplified through social media, although certainly driven by good intentions, may beget a series of solutions potentially as harmful as the problem they are trying to solve, if not properly mentored. The innumerable solutions one can come across on the internet span from using baking paper to reproduce a (surgical!) face mask to 3D printing filter facial masks using cotton filters, claiming that they are effective in filtering the virus. The lack of any risk assessment, albeit minimal, poses major risks for the user. Using materials from vacuum cleaner filters to realize filtering face masks, for example, could be a threat for the user's safety, in case of presence of dangerous glass microfibers [53].

Also in this context, regulations and standards are essential, as they sum up the state of the art, resulting from a series of field experiences, aimed at guiding the manufacturer in designing and producing devices with high levels of safety. In this regard, visual inspections performed by experienced technicians are the first approaches that can be used to evaluate if the obtained prototype is safe-by-design. For example, even a small abrasion or defect due to sub-optimal materials or inappropriate manufacturing processes, can

potentially lead to discomfort and skin irritation or lesions in the long run. This possibility, potentially dangerous in normal working conditions, is even more risky in extraordinary working conditions. In severe working conditions (due to extended/more frequent shifts for lack of personnel and to stressful conditions), mistakes or distractions are even more likely. A robust design is thought to be resilient to these conditions as well.

2.4.4 Similarities between the COVID-19 pandemic and LRSs

COVID-19 pandemic and LRSs have deep differences, but also many commonalities. LRSs are common in LMICs, but also exist in rural and remote areas of many high-income ones. Contrary to the common belief, the main problem of low-resource settings lays beyond the lack of funding. Several studies have in fact highlighted the fact that if this had been the main problem, donations would have solved it [1, 54]. Conversely, modern medicine requires much more than budget, as it is evident especially in the remit of MDs and equipment, included PPE. In fact, LRSs are often characterised by the lack of clinical knowledge, lack of specialised clinical personnel and technical staff, scarcity of MDs, drugs and spare parts due to a jeopardised supply-chain [1, 55]. As argued above, COVID-19 has simultaneously hindered the supply-chain, increased the ICU hospitalization demand and reduced staff. This created de facto conditions that are quite common in low-resource settings, especially in LMICs. The COVID-19 pandemic demonstrated the lack of knowledge and lack of preparedness of many high-income countries, aggravated by the slowness in perceiving the complexity of the situation faced by other countries, affected by the COVID-19 months in advance. For instance, before facing the COVID-19 outbreak in Milan metropolitan area, Italian authorities and experts of virology failed to understand the complexity of the situation in China and failed to acknowledge the great work done by Chinese colleagues. The same inertia has affected many north European Countries, which failed to appreciate the complexity of the COVID-19 disaster in Italy, despite the prompt response of Regional Institutions, especially in the South. While I write this paper, it seems that the USA reaction is again demonstrating some degree of inertia, failing again to acknowledge the severity of the situation in many European Countries, despite the effort that those countries are putting into the limitation of this pandemic. Despite the deep differences, the shift of methodology from LRSs to the COVID-19 pandemic response may help speeding-up the response to the emergency, also in high-income countries. After all, shifting from domains where we lack solutions to a domain where we have established methods and tools has been one of the most powerful engineering

solutions. An example could be the application of transformations such as Laplace transform to differential problems, bringing them in a domain where the equations become algebraic and can be easily solved in analytic form, and then shifted in the original domain using an anti-transform.

2.4.5 Conclusion

The COVID-19 outbreak has shown clearly the unsuitability of PPEs' regulatory framework, body of norms, and international standards to extreme conditions. This was evident to the professionals working in LRSs, such as LMICs and it emerged now powerfully also for high-income countries during the COVID-19 pandemic. The European regulatory framework evolved in the Nineties, mainly to protect European manufacturers from the unsustainable competition from manufacturers producing abroad. This evolution has been also driven by the manufacturers' need to produce PPEs for the widest market possible, therefore following the principle of generalism (i.e., PPE tested to be used in any context) as opposed to particularism (i.e., PPE tested to be used in a specific context, such as nurses working in hospital wards). The prevalence of generalism over particularism resulted in a loss of universality, and in the fact that norms that can be sustained in normal conditions, at least by HICs, become unsustainable in times of crisis. These norms, which are often assumed as standards de facto also in many non-EU countries (e.g. in many African countries), are clearly not sufficiently universal for the contexts of low- and middle-income countries. In the published paper, two examples of simplified protocols starting from existing harmonized norms are presented and discussed. Similar exemplifications are currently accepted by European notified bodies in some EU Countries and could guide the realisation of tests in LMICs. Starting from this unprecedented crisis, HICs will have to reconsider the nature of this regulatory framework and of these norms and international standards. The main lessons that our community should learn from this terrible experience is that there is a major need for an evidence-based regulatory framework, responding to the need of lead and lay users, rather than those of the market itself.

2.5 Main challenges for low-resource settings and the failure of MDs and MD donations

2.5.1 Chronology of the main events: field studies, focus groups etc.

The founding ideas at the base of my PhD project and of the use cases presented in this thesis were conceived and kept evolving amid several conferences, focus

and working groups, and field studies taking place between 2015 and 2019. This series of events (see Figure 2.9) is hereby reported for the sake of completeness and for guaranteeing easy reading of the following sections.

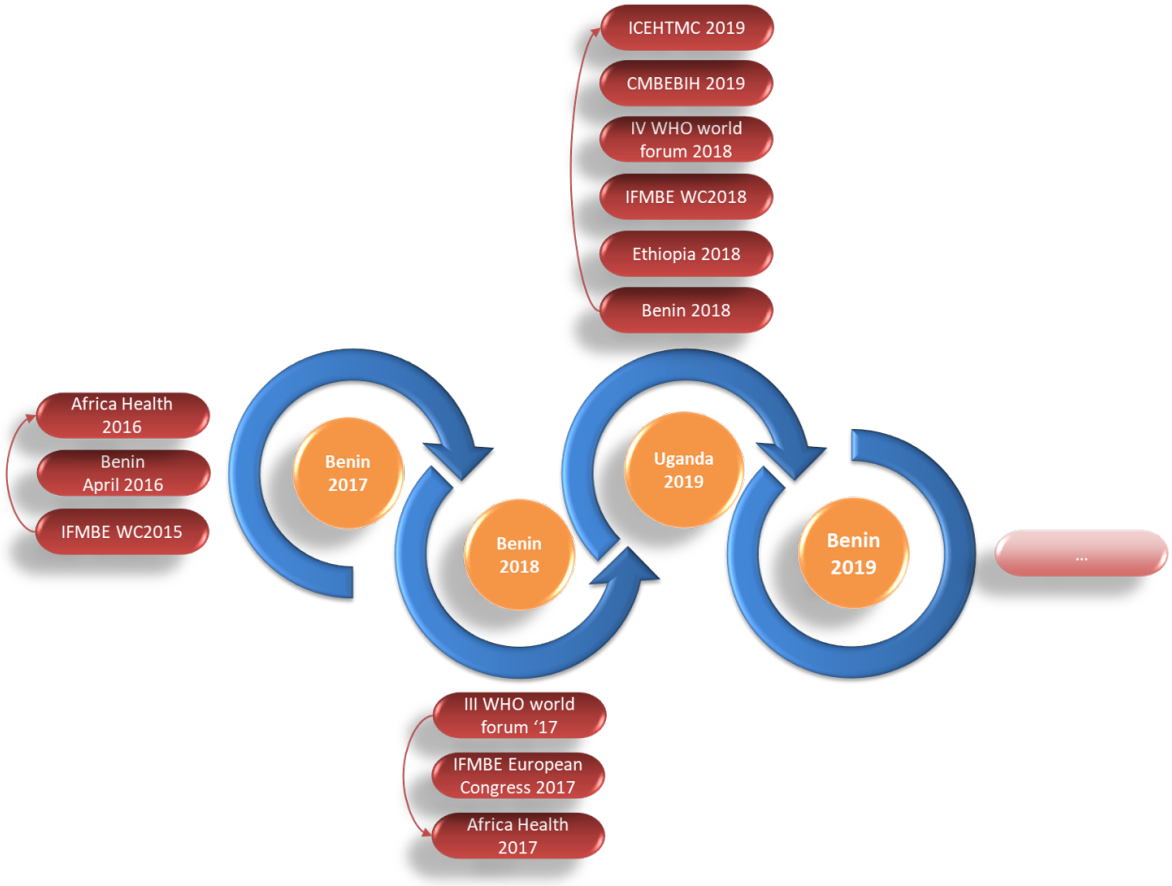


Figure 2.9: A timeline of the events and milestones of the design process: the red ovals represent the focus groups and the conferences where the results were presented, the orange circles represent the field studies.

Five focus groups were held with world leading experts of biomedical and clinical engineering during international conferences: the first one was held in Toronto in June 2015 during the International Federation of Medical and Biological Engineering World Congress on Medical Physics and Biomedical Engineering 2015 [11], the second one was held in Geneva in May 2017 during the WHO Third Forum of Medical Devices [56]; the third one was held in Tampere in June 2017, during the International Federation of Medical and Biological Engineering European Congress [35]; the fourth was held in Prague in June 2018, during the International Federation of Medical and Biological Engineering World Congress on Medical Physics and Biomedical Engineering 2018 [57], and the fifth one was held in Visakhapatnam in December 2018,

during the WHO Fourth Forum on Medical devices [58]. The contextualisation in SSA was performed designing, piloting and administrating surveys and holding focus groups with biomedical and clinical engineers from SSA countries. Five focus groups were held in SSA: 1. two in South Africa, respectively in June 2016 and June 2017, during the AfricaHealth Conferences, organised by South-African societies of HTA and Clinical Engineering and attended by delegates from more than 20 SSA countries; 2. two in Benin in April 2016 and February 2018 with Scholars from the Department of Biomedical Engineering, Ecole Polytechnique d'Abomey-Calavi, University of Abomey-Calavi; 3. one in Ethiopia in April 2018, organised by the International Federation of Medical and Biological Engineering, and attended by representatives of Biomedical Engineering or Clinical Engineering Scientific Societies from 12 SSA Countries: Ethiopia, Burundi, Democratic Republic of the Congo, Mali, South Africa, Ghana, Nigeria, Uganda, Tanzania, Kenya, Cameroon, Benin. Three field studies were conducted in Benin in April 2017, January 2018 and November 2019 and one field study was run in Uganda in October 2019. During these studies, several aspects of MDs and MLs were analysed. This included electrical measures in hospitals, examinations of MDs and inspections of medical locations (i.e., ambulatories, surgical theatres, one intensive care unit, wards etc.). Focus groups were organised in collaboration with the International Federation of Medical and Biological Engineering, and in particular with the its Clinical Engineering Division[2], its Health Technology Assessment Division[3] and its Working Group on BME in Africa[4].

2.5.2 Harsh environmental conditions

Among the main issues plaguing LRSs there are the harsh environmental conditions, which severely challenge the safe and efficient functioning of MDs, as they are designed and developed to work in certain normal ranges (e.g., Respironics Everflow oxygen concentrators require the operating temperatures to be 13°C to 32°C). High humidity, extreme temperatures, dust, vermin are the most typical ones. Once again, Respironics Everflow oxygen concentrators would not be working properly in LRSs, where temperatures are often greater than 32°C and there is condensing humidity. MIL-STD-810H, Environmental engineering considerations and laboratory tests [59], is a military standard surrounding the design criteria, specifications and testing of military equipment with a stress on the conditions that it will experience throughout its service life. Part Three of this standard presents an overview of the global climatic regions, that can be divided into Hot (Hot Dry, Hot Humid), Basic (Constant High

[2]http://cedglobal.org/
[3]http://htad.ifmbe.org/
[4]http://2016.ifmbe.org/wp-content/uploads/2018/05/News-No103.pdf

Humidity, Variable High Humidity, Basic Hot, Intermediate, Basic Cold), Cold and Severe Cold. Table 2.1 shows a summary of the climatic conditions for these regions. The reported high temperatures, were observed during strong sunshine and fairly light winds, in standard meteorological instrument shelters, representing the temperature of free air in the shade 1.5 m above the ground. The related temperatures on the ground will reach temperatures 15 to 30°C higher depending on radiation, wind, conduction and turbulence. Figures 2.10 and 2.11 show the distribution of these climatic zones and the maximum absolute temperatures.

Table 2.1: The typical temperatures and humidity of Climatic Zones [59]; ARH stands for Ambient relative humidity.

Climatic Zone	**Daily Cycle**	**Air Temp. [°C]**		**ARH [%]**
		Daily Low	**Daily High**	
Hot	Hot Dry	32	49	8 to 3
	Hot Humid	31	41	88 to 59
	Const. High Humidity	24	24	95 to 100
	Var. High Humidity	26	35	100 to 74
Basic	Basic Hot	30	43	44 to 14
	Intermediate	28	39	78 to 43
	Basic Cold	-32	-21	Saturation
Cold	Cold	-46	-37	Saturation
Severe Cold	Severe Cold	-51	-51	Saturation

2.5.3 The instability of the electrical supply

Another main challenge for LRSs and for SSA is the instability and unreliability of the power supply, other than the scarcity of functioning safety systems, such as equipotential nodes and ground systems [2]. As Chawla et al. [60] states, energy is essential for achieving global health goals, since electricity is used for the basic functioning of hospitals. Indeed, the actual size of the problem can be better understood when looking at the African regional average percentage of hospitals with reliable electricity (i.e., 39.1%). Moreover, although generators are often used as a solution, less than 2/3 of hospitals providing surgical care can rely on continuous electricity or a generator. This unsafe context that hinders the correct and safe functioning of MDs, and increases the risk of micro/macro-shocks, can be dangerous for users and patients. For a mere comparison, Table 2.2 shows the electrification rate as a percentage of the population and the quality of electricity supply. The latter ranges from 1 (extremely unreliable) to 7 (extremely reliable).

Table 2.2: Electrification rate and quality of electricity supply for some HICs and LMICs [2]

Country	Electrification rate	Quality of electricity
UK	100%	6.7/7
USA	100%	6.5/7
Italy	100%	5.9/7
Cameroon	53.7%	2.1/7
Benin	43%	2.06/7
Uganda	22%	3.43/7

These data is further supported by the results of our field studies [2] in SSA (2016-2019), during which several aspects of MDs and MLs were analysed. This included electrical measures in hospitals, examinations of MDs and inspections of medical locations (i.e., ambulatories, surgical theatres, intensive care units, wards etc.). The preliminary results from these field studies were presented at the Fourth WHO Global Forum on MDs in Visakhapatnam in 2018 [61], at the International Conference of Medical and Biological Engineering (CMBEBIH 2019) in Banja Luka in 2019 [1] and at the International Clinical Engineering and Health Technology Management Congress (ICEHTMC 2019) [62] in Rome in 2019.

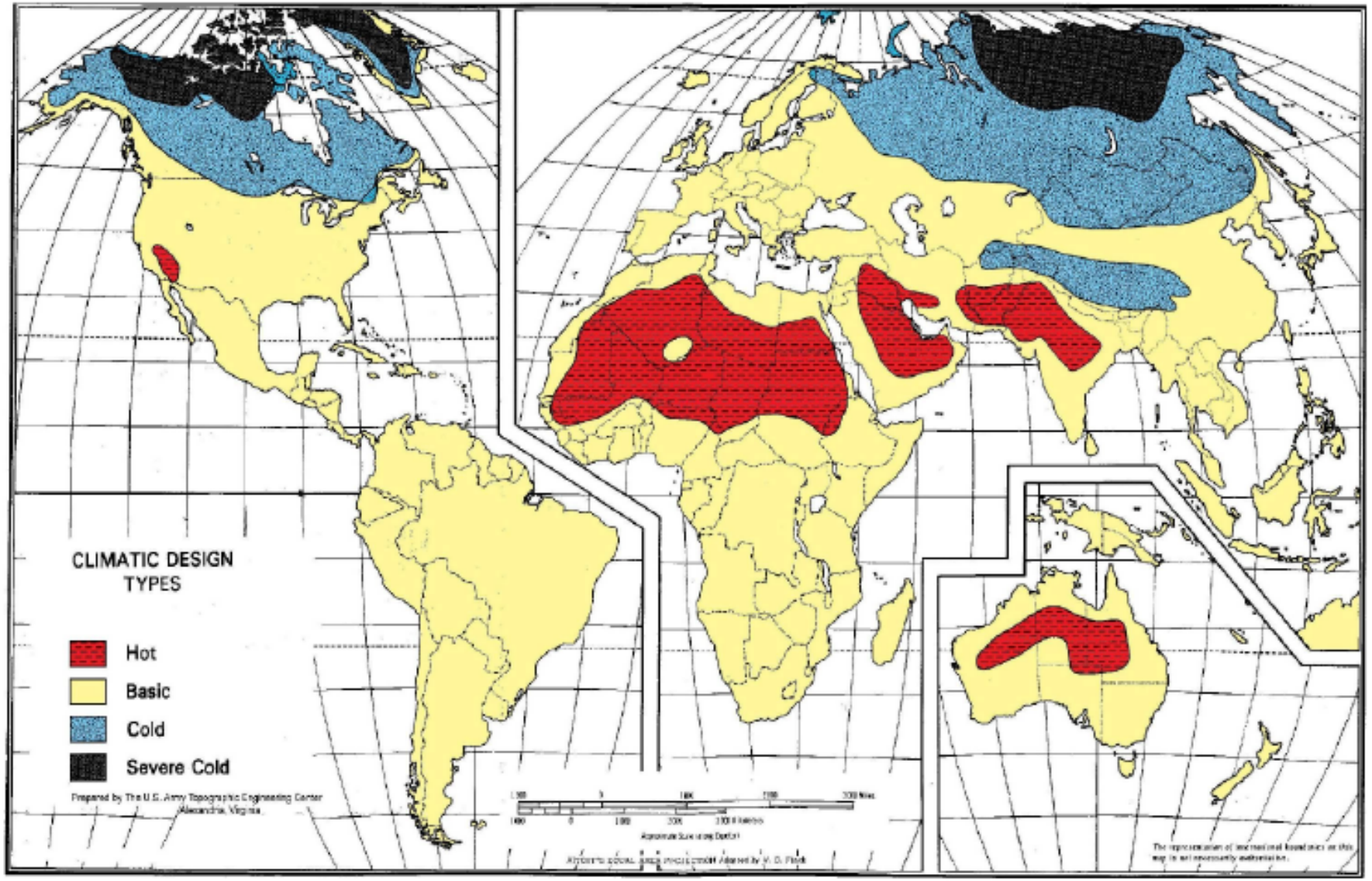


Figure 2.10: Distribution of the climatic zones [59]. Red zones refer to Hot zones, yellow ones refer to Basic zones, light blue ones refer to Cold zones, and black zones refer to Severe cold ones.

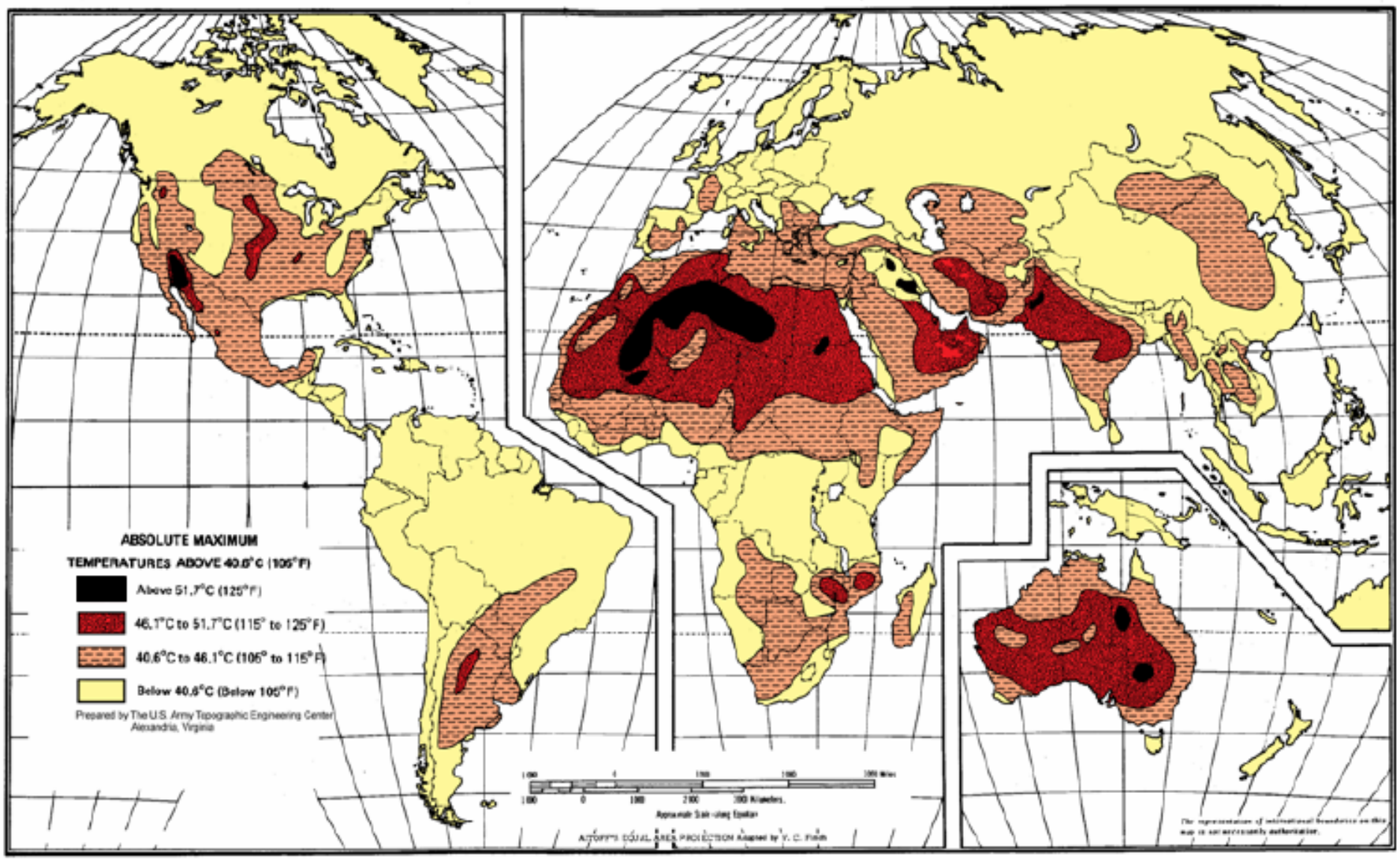


Figure 2.11: Distribution of the maximum absolute temperature [59]. Black zones refer to temperature above 51.7°C, red ones to temperatures between 46.1°C and 51.7°C, orange ones to temperatures between 40.6°C and 46.1°C, and yellow ones to temperatures below 40.6°C.

2.5.4 Other challenges and failure of MDs and MD donations

The challenges faced by LRSs do not end here. Among other impelling issues, there are the lack of funding and of essential MDs, specialized doctors, an efficient maintenance program, management systems, biomedical engineers and technicians, a limited supply chain (i.e., deficiency of spare parts/disposables) [4, 63–66] and a failure to define and meet minimum requirements for MDs and MLs. Besides, the situation can change significantly among city centers and peripheries. All of these factors negatively influence the efficacy, safety, and duration of the MD [1].

It is common belief that donations of MDs, as they are now, are a good solution to this dire situation. However, it has been proven otherwise [1, 54]. In fact, 80% of the MDs in SSA are donated, and over 70% are broken or non-functional because of different reasons. In many cases these donations do not only become an environmental burden (i.e., when the MD ceases to work, it is abandoned in the hospital or in the surrounding environments) as highlighted by McDonald et al. [67], but also a financial burden for end-users, who have to allocate their scarce resources towards fixing or getting rid of the equipment, as claimed by Williams et al. [54]. The latter also proved that this situation is inconvenient also for donors: in fact, out of 1 dollar spent on medical equipment, up to 87.54 cents are wasted.

During our field studies, I was able to visit several hospitals including vocational ones. Although vocational hospitals may represent only a part of the scenario, they are a significant part of the healthcare systems of LRSs. Figure 2.12 shows an example of the conditions of some of the visited hospitals, including, for instance, dust over the wiring and equipment, which could become conductive and cause short circuits and damage to equipment in case of wet weather. Electric panels, power transformers, UPS, cables and electric cabins were not installed, maintained or services as expected (Figures 2.12a,b,c,d). Vermin is clearly apparent, with a wasps nest being on one of the pieces of equipment (Figure 2.12e) [1].

Figure 2.12: The conditions of the electrical panels, wiring and equipment in one of the hospitals [1].

Subsections 'X-ray machine' and 'Oxygen concentrator', adapted from [1], will explain in detail what were the issues that I encountered with some donated MDs.

2.5.4.1 X-ray machine

Figures 2.13 show an X-ray machine that was inspected upon request in a vocational hospital during one field study. Although the equipment was perfectly working before being disassembled in a European hospital and was shipped with 5 sheets of instructions (see Figure 2.13d), the local technician was not able to assemble the parts, because the instructions were written in a language non-locally spoken. Even if the local technician had tried to install the machine, he concluded that one of the non-fused terminal blocks was damaged (see Figure 2.13c). Thus, he decided to send the supposedly broken part to Nigeria in order to replace it. Some members of the Applied Biomedical Signal Processing Intelligent eHealth Lab of the University of Warwick were able to stop this process, retrieving the part. During the following field study, they came back with an experienced retired X-ray technician, who helped install the machine correctly collaborating with the local technician, promoting capacity building (see Figure 2.14).

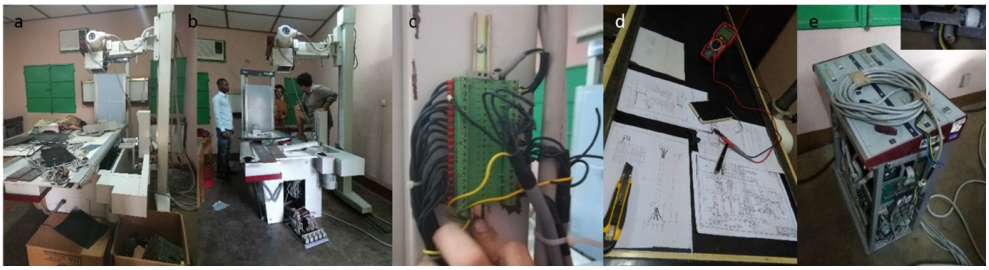


Figure 2.13: **a**, **b** and **e** show the donated X-ray machine; **c** shows one of the non-fused terminal blocks; **d** shows the set of instructions [1].

2.5.4.2 Oxygen concentrator

Figure 2.15 shows an oxygen concentrator, i.e., a MD used to deliver oxygen to patients who need it. During a field study, a nurse asked for our help, because she suspected that oxygen concentrator they had was not working properly (i.e., when switching the switch from 1 to 2, the flow of oxygen was not doubling). After inspecting the device, the fault was identified in the filters. This kind of MD is designed taking into consideration the previously mentioned international standards and minimum requirements (see Section 2.3). In the case of the oxygen concentrator, this kind of device has two types of filters, external and internal. The external filters should have been washed weekly and had never been, while the internal filters should be changed after 4380 hours of

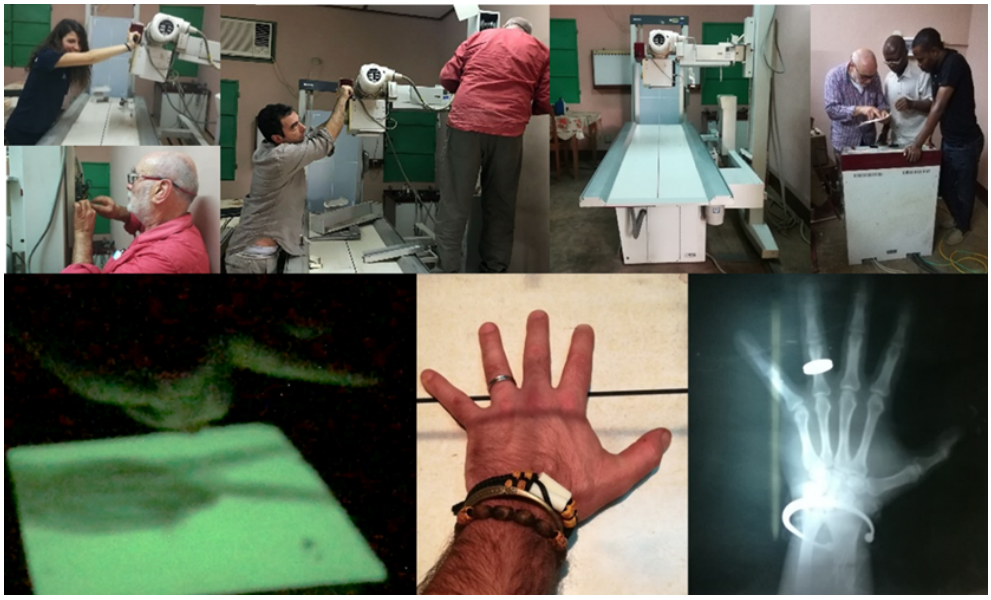


Figure 2.14: Members of the Applied Biomedical Signal Processing Intelligent eHealth Lab along with the local and the experienced technicians assembling and testing the X-ray machine [1].

work (as per instructions manual) and had already been working for 6501 hours without having been changed. It is useful to remind that these requirements are based on high-resource settings (HRSs), where strict standards regarding ML are respected (e.g., the air in a surgical room has to be filtered at a 99.97% level). This situation is utopic for many LRSs, where there is a lot of dust, no filtering or not to a 99.97% level. Consequently, the minimum requirements regarding the filters of the oxygen concentrator should be even stricter or these devices should be redesigned to be more resilient.

Figure 2.15: **a**, **b** Oxygen concentrator and its components; **c**, **d** details of dust and filters; **e** display with the number of hours that the device had been working [1].

Table 2.3 shows an example of inventory of the MDs that are used by Medecins Sans Frontieres in field hospitals in Niger, along with their status. By looking at this figure, it is possible to notice that all these MDs are those designed for working in ideal conditions (HRSs), apart from the one that reads 'tropicalisé', i.e., 'tropicalised', i.e., made suitable for use in tropical

regions, especially in regard to protection against the destructive effects of moisture and fungi, which, however does not take into consideration all the other aforementioned challenges. Overall, it is clear that a revolution in the way of designing MDs towards a more user-driven and contexualised approach is urgent as well as a harmonisation of the regulatory frameworks surrounding MDs and MLs between Europe and Africa, if not internationally. In order to be a more effective solution, donations should be made more carefully and could be regulated by the viability model presented by Williams et al. Moreover, they should be supported by an underlying solid structure comprising a working local management system (either paper based or computerised), in order to keep track of the devices, their status and maintenance schedule, and installation and maintenance support in order to avoid problems such as those mentioned above [1].

Table 2.3: An inventory of the devices used by Doctors without Borders in a field hospital in Niger, kindly provided by Mr Marcos Grau (logistician for Doctors without Borders.)

Status	**Device**	**Manufacturer**
ACTIVE	ANALYSEUR CHIMIE CLINIQUE	REFLOTRON
ACTIVE	ANALYSEUR HEMATOLOGIQUE (Sysmex XP 300)	SYSMEX
ACTIVE	ASPIRATEUR MECANIQUE (Twin Pump)	AMBU
ACTIVE	AUTOCLAVE 39 l (All American), sans réchaud	ALL AMERICA
ACTIVE	AUTOCLAVE TBM 90 l, vertical	AFTECH
ACTIVE	CENTRIFUGEUSE électrique (Hettich EBA 200)	HETTICH
ACTIVE	CONCENTRATEUR O2 (DeVilbiss 525KS)	DEVILBISS
ACTIVE	CONCENTRATEUR O2 (New Life Intensity) 10l	NEW LIFE
ACTIVE	CONGELATEUR (Vestfrost MF314) 323l	VESTFROST
REASSIGNED	DETECTEUR RYTHME CARDIAQUE FOETAL	EDAN
BROKEN	GLUCOMETRE, lecteur glycémie (Nova StatStrip)	NOVA
ACTIVE	LAMPE D'ECLAIRAGE, EXAMEN (LID medical)	LID
UNDER REPAIR	MICROSCOPE (PrimoStar iLED), lumière & fluorescence	ZEISS
ACTIVE	NEBULISEUR + COMPRESSEUR (PariMobile S)	PARIBOY
ACTIVE	OTOSCOPE, halogène + SPECULUMS	0
ACTIVE	OXYMETRE DE POULS (Masimo RAD-5)	MASIMO
BROKEN	OXYMETRE DE POULS (Masimo RAD-5)	MASIMO
ACTIVE	PHOTOMETRE HEMOGLOBINE, tropicalisé	HEMOCUE
ACTIVE	RECHAUFFEUR NEONATAL (Ceratherm 600-3)	CERATHERM
ACTIVE	REFRIGERATEUR (Vestfrost MK304) 204l	VESTFROST
ACTIVE	REFRIGERATEUR (Vestfrost VLS200A) 60l	VESTFROST
ACTIVE	REFRIGERATEUR (Vestfrost VLS350A) 127l	VESTFROST
ACTIVE	REFRIGERATEUR BANQUE DE SANG (MB3000G)	DOMETIC
ACTIVE	REPARTITEUR pédiatrique (Sureflow)	AIRSEP
ACTIVE	SPECTROPHOTOMETRE (Humalyzer 2000)	HUMALYSER
ACTIVE	SYSTEME PCR TEMPS-REEL (GeneXpert GX-IV)	GENEXPERT
ACTIVE	UNITE DE PHOTOTHERAPIE pour NOUVEAU-NE	ARDO

2.6 Possible solutions

Apart from a complete revolution of the design paradigm, some quick and feasible solutions to the aforementioned issues could be the use of military standards and IP rating to improve the ruggedness of MDs, of circular economy and mHealth, and a frugal innovation approach. The following sections will briefly present these topics.

2.6.1 Military standards and IP code

As already mentioned in Section 2.5.2, military standards set how things are to be designed, built, and tested in a controlled, known, and acceptable manner so that they are standardised for military use [68]. Military (defense) standards are officially defined as [69]:

'*A document that establishes uniform engineering and technical requirements for military-unique or substantially modified commercial processes, procedures, practices, and methods. There are five types of defense standards: interface standards, design criteria standards, manufacturing process standards, standard practices, and test method standards.*'

MIL-STD-810H, Environmental engineering considerations and laboratory tests [59], duly explains how to design and test military equipment against numerous harsh environmental conditions, using chamber test methods reproducing the effects of environments on the equipment rather than the environments themselves [70]. Among the most relevant ones for MDs and LRSs, there are: No. 501 High temperature (see Appendix A), No. 503 temperature shock, No. 505 Solar radiation, No. 506 Rain, No. 507 Humidity, No. 510 Salt and Dust, and No. 516 Shock.

Another relevant existing standard that is currently used to describe the degree of protection of the devices against the ingress of particles is IEC 60529. The latter describes the IP code, which officially comprises 3 digits and 2 letters [71]:

1. the first digit indicates the solid particle protection (see Table 2.4) and is mandatory;
2. the second digit indicates the liquid ingress protection (see Table 2.5) and is mandatory;
3. the third digit indicates the mechanical impact resistance and is no longer used;
4. the fourth and fifth letters indicates other protections (see Tables 2.6 and 2.7) and are optional;

Interestingly, in the '90s Adler et al. [72] presented and described the application of some military standards to the design of MDs for military use. This did not seem to get as much attention as the current trend followed by the Information Technology industry, which is adopting the IP code and military standards (specifically, MIL-STD-810H) to design and manufacture "ruggedised" devices, which are sturdier and more resilient to harsh working conditions. For example, an iPhone 7 has an IP67 rating and an iPhone 12 has an IP68 rating. However, their design did not consider any military standard. On the contrary, some brands offer devices designed also with military standards in mind: for example, a CAT S41 or a Doogee S60 follow military standards and have an IP68 rating. Also computer brands such as Dell offer rugged versions. The price of these 'upgraded' versions is not much higher and is completely balanced by the longer duration of the device itself throughout the years. The application of similar standards in the design and development of MDs to be deployed in LRSs would greatly increase the lifespan and the safe and efficient use of the MD.

Table 2.4: The explanation of the first digit of the IP code.

Level	**Effective against**	**Description**
X	—	No data available to specify a protection rating
0	—	No protection against contact and ingress of objects
1	>50 mm	Any large surface of the body
2	>12.5 mm	Fingers
3	>2.5 mm	Tools, thick wires
4	>1 mm	Wires, slender screws
5	Dust protected	Ingress of dust is not entirely prevented, but it must not enter in sufficient quantity to interfere with the satisfactory operation of the equipment.
6	Dust-tight	No ingress of dust

Table 2.5: The explanation of the second digit of the IP code.

Level	Protection against
X	No data available to specify a protection rating
0	None
1	Dripping water
2	Dripping water when tilted at 15°
3	Spraying water
4	Splashing of water
5	Water jets
6	Powerful water jets
6K	Powerful water jets with increased pressure
7	Immersion, up to 1 meter (3 ft 3 in) depth
8	Immersion, 1 meter (3 ft 3 in) or more depth
9K	Powerful high-temperature water jets

Table 2.6: The explanation of the fourth letter of the IP code.

Letter	Meaning
A	Back of hand
B	Finger
C	Tool
D	Wire

Table 2.7: The explanation of the fifth letter of the IP code.

Letter	Meaning
H	High voltage apparatus
M	Motion during water test
S	Stationary during water test
W	Weather conditions

2.6.2 Circular economy

The first approach to a primitive form of circular economy was imposed by a natural scarcity of resources and followed the maxim 'Use it up, wear it out, make it do or do without'. The situation changed drastically when, with the Industrial Revolution, the society was able to overcome scarcities of shelter, food and objects [73] transitioning to the current linear economy (see Figure 2.16). However, as Bompan et al. [73] point out this was a double-edged sword: indeed, it freed human beings from the limitations imposed by nature, but it also alienated them from nature. The risk associated with this human conquest is the fact that any abuse of the environment could destroy the human beings themselves. In fact, mass production brought about a plethora of waste.

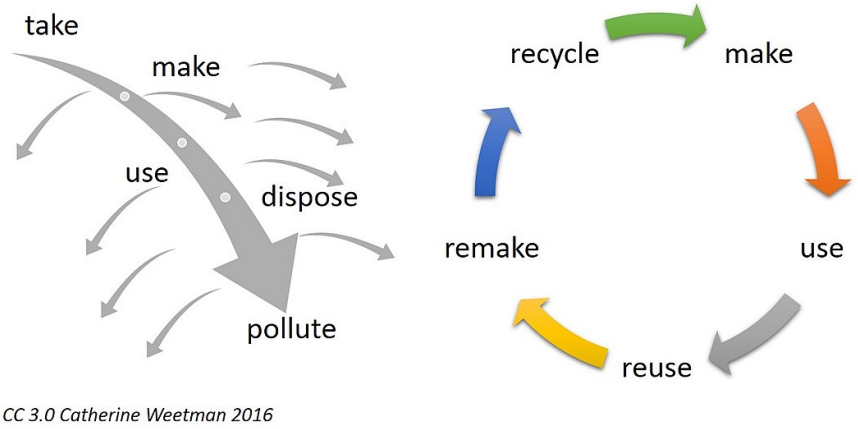


Figure 2.16: A comparison of the linear economy model with the circular economy one [74].

Nowadays, there is a current shift of paradigm towards a new circular economy approach. In fact, the circular economy has been gaining increasing attention as a tool to increase the lifespan of products, optimise resource usage, and reduce waste, energy consumption, and emissions [75]. Although the idea behind the circular economy is linked with that of sustainable development, the two concepts are somewhat different as it can be noticed in the following definition given by the Ellen MacArthur Foundation [73].
Circular economy is '*a generic term used to define an economy that is designed to regenerate itself. In a circular economy the flows of materials are of two types: biological, and therefore able to be reinserted into the biosphere, and technical, which can be revalued without entering the biosphere*".
Sustainable development is '*the process of change whereby the use of resources, the direction of investments, the focus of technological development and the changes in institutions are made coherent with the needs of present and future generations*".

On the wake of Walter Stahel, one of the founding fathers of circular economy [76], Robert U. Ayres, a physicist, compared circular economy to thermodynamics, underlying that, as the first principle of thermodynamics states that in a closed system the sum of all forms of energy remains constant, the principle behind the conservation of resources states that all the material taken from the environment has to equal the amount that has to be returned, excepting those that are temporary parts of goods (e.g., cars) [73].

From this, it can be stated that circular economy is based on a 3-R principle: Reduce, Reuse, Recycle [77].

New technologies, such as 3D printing and protocycling can foster this paradigm shift towards more and more self-sustained communities. In our case, a circular economy approach and competent and experienced artisans can be used wherever there is a need for goods to be substituted. This approach would overcome one of the main issues of LRSs, that of the limited supply chain. Local communities, in fact, empowered by circular economy and the creation of new jobs, would be able to close the loop and extend the lifespan of many MDs.

2.6.3 mHealth

The WHO defined mHealth (an abbreviation for mobile health), a component of eHealth (an abbreviation for electronic health), as "*a medical and public health practice supported by mobile devices, such as mobile phones, patient monitoring devices, personal digital assistants and other wireless devices*" [78]. During their second global survey on eHealth, they documented the existent mHealth activities within the Member States, what kinds of activities, their status and the barriers to their implementation. As shown in the report, many countries reported up to 6 mHealth programs per country, and Africa (where 80% of the countries reported at least one mHealth programs) does not differ much from Europe (90%) (see Figure 2.17).

These programs range from health call centres to decision-support systems. Globally, the most frequently reported types were health call centres/healthcare telephone helplines (59%), emergency toll-free telephone services (55%), emergencies (54%), and mobile telemedicine (49%). Health surveys, surveillance, awareness raising and decisions support systems were less reported (19-26% each) (see Figure 2.18 for a global overview) [79].

Recently, mobile phones and smartphones' users in LMICs have been exponentially increasing: 28% of people in Kenya with secondary-level or higher education now own a smartphone, and 88% of Nairobi medical students do too [80]. As a mere comparison, Benin, which has 87.7 mobile phone subscriptions per 100 inhabitants, along with other Sub-Saharan countries, is

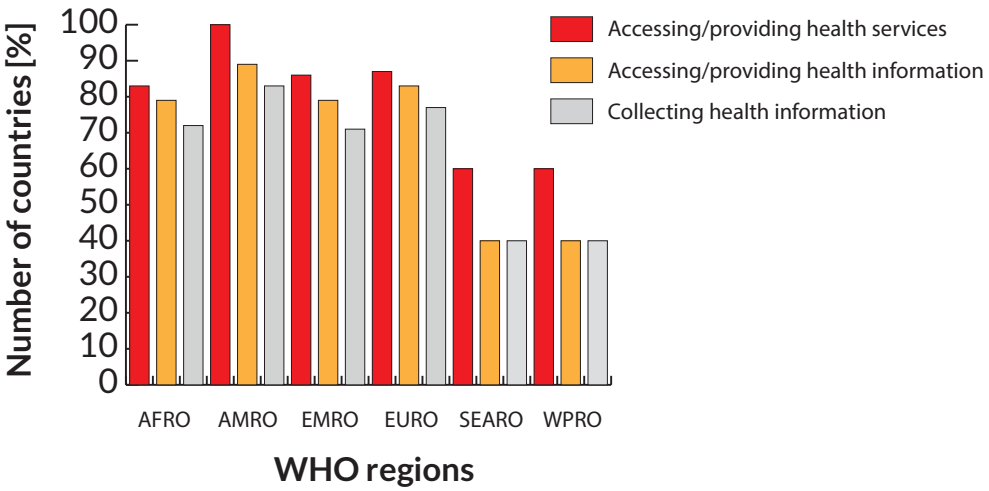


Figure 2.17: Percentage of countries that reported at least one type of mHealth program within the three main program categories, by WHO region [79].

not that far from the UK (118.36 per 100 inhabitants). The data looks more impressive when compared to Canada (92.5 per 100 inhabitants) [81].

In the past years, the increase in the mobile phone subscriptions was greater in the developing world, which, in 2015, reached an average of 92 per 100 inhabitant mobile phone subscriptions. Similarly, active mobile broadband subscriptions have been and are increasing rapidly, overtaking global fixed broadband subscriptions in 2008 and fixed telephone lines in 2012. Thanks to this spread adoption of technology worldwide, mHealth and smartphones are a possible medium to improve healthcare in different ways.

2.6.3.1 mHealth as an educational tool

One of the main limitations of LRSs is the scarcity of skilled personnel, which is linked to the lack of access to health education, according to Rusatira [64]. Many authors suggested mHealth as an educational tool aiming to train medical students, update physicians and allow them to share their knowledge with their colleagues via dedicated forums or chats. In particular, Rusatira [64] asserts that an ideal app should allow a quick reference for evidence-based consultation, have language support and enable more rapid decisions with a lower error rate. Similarly, Edgecombe [80] states that mobile devices have several unique features which may help share information, retain knowledge and assist during training. The paper shows that different healthcare training apps have been developed to date and they can be divided into two categories. Some apps replicate existing teaching strategies, by providing exam practice or displaying textbook graphics. Others take advantage of smartphone-specific features (e.g., the interaction with animations, accelerometry, augmented reality, etc.) to enable practice and assessment of medical procedures (e.g., the resuscitation

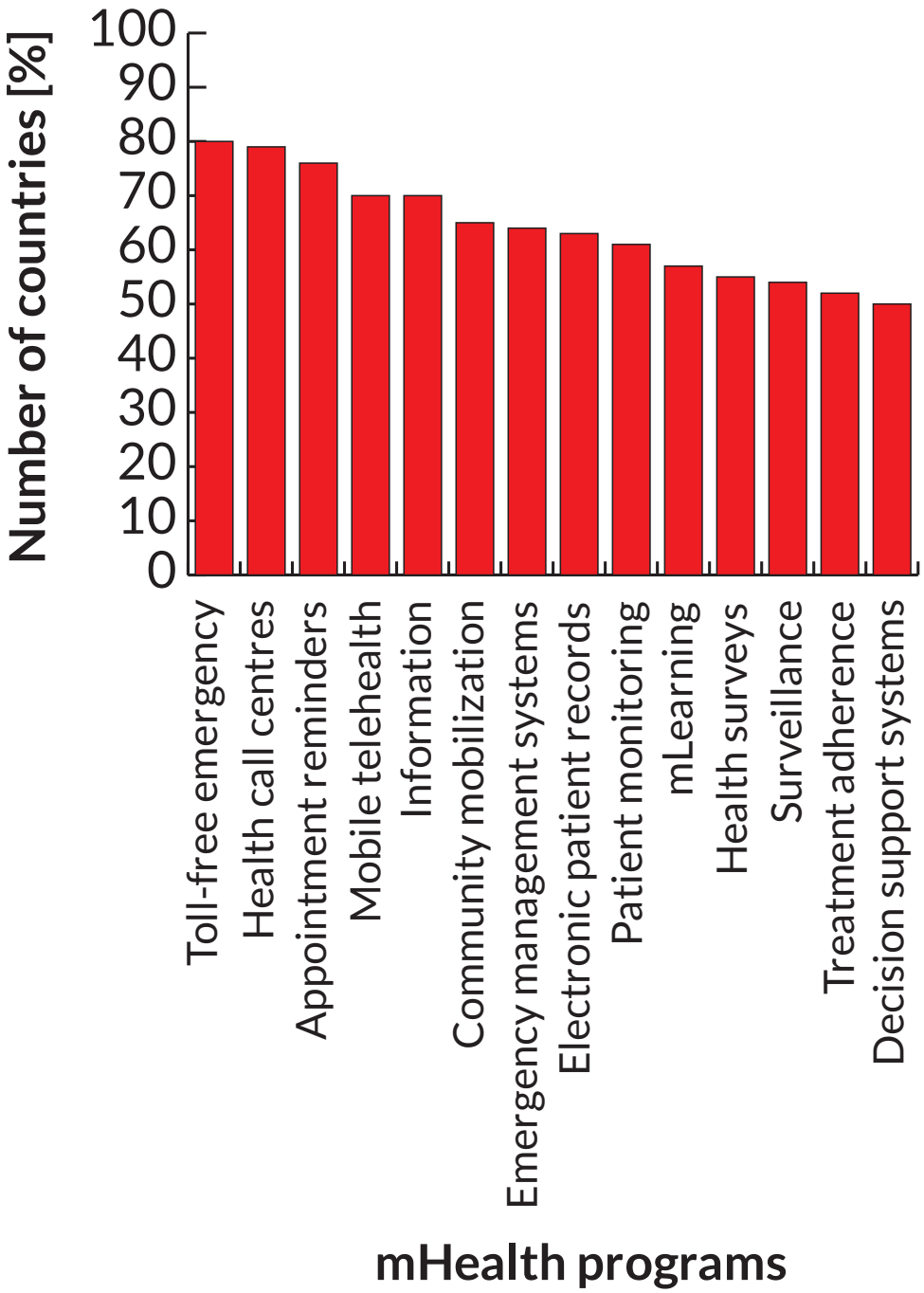


Figure 2.18: Number and percentage of countries that reported employing an mHealth program, by type [79].

algorithm).

2.6.3.2 mHealth as a substitute for MDs

Universal health coverage, a priority for WHO, strives for universal access to needed health services (e.g., prevention, treatment, rehabilitation, etc.) of sufficient quality to be effective, ensuring that the user is not exposed to financial hardship [82]. Hence, many affordable mHealth applications have been developed to reproduce more accessible MDs. Cremer [83] stated that portability, durability, and efficiency are primary requirements for a successful MD in LMICs. In 2014, for example, a smartphone-powered cloud-enabled portable electrocardiograph (ECG) was developed. It allowed physicians to acquire ECG readings of patients in remote areas and send it to colleagues for feedback/diagnosis. The device itself was powered via smartphone, which could be recharged beforehand or with solar energy. In 2013, an application was developed to provide accurate and accessible audiogram screen, optimised diagnosis and care through remote review and tracking [82]. In 2016, during a cohort study of eye disease in Kenya, Bastawrous [84] validated Peek (see Figure 2.19, a portable eye examination kit. The author, also, pinpoints the main problem for healthcare in Africa, in particular: a comprehensive examination (in this case eye examination) is not straightforward in remote areas with poor or no road access and no electricity. At the same time, he also suggests that the mobile phones, with their widespread use, are a great way of allowing some medical tests that otherwise would be impossible to do. The paper focuses on the app that allowed an important screening test for the eye thanks to an m-health approach to telemedicine. In fact, it allows not only a visual acuity test but also to examine the retina using a smartphone, thanks to a low-cost smartphone adapter and remote experts' reviews (i.e., telemedicine).

2.6.3.3 Weaknesses and limitations of mHealth

There is a shared thought among some authors regarding possible limitations and weaknesses of mHealth technologies. Blaya [85] affirms the deficiency of scientifically rigorous data regarding the efficiency, effectiveness, cost-effectiveness of eHealth systems in developing countries. The author, in fact, states that up to 2010 most studies were academic and were small and focused on process indicators rather than on patient outcomes. Aranda [86] is of the same mind: she ponders whether the increasing use of mHealth in developing countries is reliable for health outcomes. As regards limitations, she claims that long-term results are still uncertain and need to be investigated further and that mHealth is strongly affected by infrastructure availability (e.g., a reliable internet connection and a reliable power source). On the other hand, Edgcombe [80] focuses

Figure 2.19: An example of the application of Peek on a patient [84]

on the educational value of mHealth and argues about the educational effectiveness of mobile technologies. In the paper, she acknowledges that there are aspects of training which are not compatible with mobile-assisted techniques: for instance, learning motor skills is impracticable without expensive haptic feedback technology; communication and team-working skills are similarly not easily taught via these technologies.

2.6.4 3D printing and its applications in healthcare

The creation of a three-dimensional (3D) object from a CAD model or a digital 3D model is known as '3D printing', which is one of the branches of additive manufacturing. 3D printing dates back to the 1980s, when it was called 'rapid prototyping'. The first patent in this field related to a stereolithography apparatus and belonged to Charles Hull, who then co-founded 3D System Corporation, a leading company in the field today. Currently, 3D printing is based on diverse processes, including stereolithography (laser and photopolymer resin based), digital light processing (conventional light source and photopolymers), fused deposition modelling (deposition of melted plastic filament), inkjet, selective deposition lamination (based on standard copier paper and adhesive), electron beam melting (metal and laser) [87]. The remaining part of this section will focus on fused deposition modelling, as it is the most known and versatile kind of 3D printing. Fused deposition modelling consists in melting a plastic filament and laying it down layer by layer, consequently, until the final

object is created. There are several kinds of materials (thermoplastic polymers) that can be used, each with different properties, e.g., polylactic acid, ULTEM, polycarbonate, polyphenylsulfone, and acrylonitrile butadiene styrene. Usually, in healthcare applications, polylactic acid, polyamide and polyetheretherketone are used, because they are biocompatible [88, 89]. Indeed, 3D printing currently offers a significant possibility to assist pharmaceutical and medical companies in developing more precise medications, as well as enabling the quick creation of medical implants, allowing the introduction of new methods and tools for healthcare delivery by healthcare workers. Hence, 3D printing has been introducing more and more applications in this field contributing to better health for all. Many are the fields of medicine in which it is currently being used, such as cardiology, gastroenterology, neurosurgery, ophthalmology, vascular surgery, etc [90]. Overall, the most important applications of 3D printing in healthcare relate to:

- personalised presurgical/treatment and preoperative planning (e.g., physical 3D model of the patient anatomy)
- customise surgical tools and prostheses
- medical education
- bioprinting (e.g., 3D printing of synthetic skin for transplantation to patients with burn injuries)

3D printing, with its advantages, makes a good candidate solution for bypassing some of the challenges faced by LRSs (such as the lack of spare parts), on the wake of a frugal engineering approach [91]. In fact, paired with protocycling, which allows for the recycling of the used filament to produce new material that can be reutilised for print, 3D printing is the possible key towards a more circular economy approach, which would be more suitable to these settings. It is noteworthy that 3D printing was also utilized in higher resource settings to cope with the scarcity of medical devices, their spare parts, and PPE during the COVID-19 pandemic [92]. Nonetheless, it shall be noted that the use of 3D printing in healthcare is still limited due to a lack in clear and detailed regulatory guidance on the matter. As of now, in fact, 3D-printed devices are classes as custom-made devices within the Regulation 2017/745. Despite its young age, the regulation still does not give enough space nor detail to the use of 3D printing in healthcare, which is necessary to safeguard the safe and efficient use of 3D-printing technology [90].

2.6.5 Frugal innovation/engineering

Although Carlos Ghosn, ex CEO of Renault and Nissan, coined the term 'frugal engineering' defining it as 'achieving more with fewer resources", this concept finds its roots in the appropriate technology movement of the 1950s. Frugal strategies have become increasingly popular also among Western companies, to face the uncertainty due to COVID-19 crisis [93]. In 2016, Weyrauch et al. [94] tried to sum up the paramount pillars of frugal innovation, via a literature review as well as via interviews with mangers from companies and researchers from different research institutions. As a result of their analysis, their findings can be related to one of three principal categories, i.e., cost reduction, core functionality, and optimised performance level.

- Cost reduction entails reducing both the purchasing and ownership costs, as well as minimising the usage of material and financial resources. As the main idea behind this lies in the concept of affordability, then it is worth highlighting that the envisioned cost reduction should always be from a customer's perspective.

- Focusing on core functionalities means reducing complexity and responding to some essential need with extreme efficiency. This concept does not only allow for a cost reduction but will also increase the user-friendliness and ease of use of a product.

- Aiming at optimised performance level means investigating the relevant required characteristics to be optimised, e.g., power, durability, accuracy, which largely depend on the context of application. This level should be optimised and tailored to the intended purpose and specific requirements of the contexts of use of the innovation (e.g., since car horns are used excessively in India, car horns in Indian cars should be designed to withstand greater strain and have better performance than those of European cars).

Among the several applications of frugal engineering in healthcare, the Jaipur foot, which is a prosthetic leg for people with below-knee amputations made of rubber coming from irrigation piping, and the Thermoplan Lung ventilator, a simplified machine based on 80% of coffee machine components which allowed a mass production of up to 800 units per week at a quarter of the cost of an original ventilator, are worth mentioning (see Figures) [93].

2.6.5.1 Possible limitations

It might be argued that frugal engineering and, specifically, some frugal technologies (e.g., smartphones and apps) are affected by fast obsolescence and

this may clash with the time required by context-aware design. However, the concept of obsolescence itself is contrasting with the pillars of frugal engineering. As explained in this subsection, frugal engineering is based on cost reduction, core functionality, and optimised performance level. It entails re-inventing technologies possibly taking into account low costs, while efficiently focusing on users and essential functionalities, and performance levels optimised to the context of use. The focus is shifted, therefore, more on a technology that works for a specific context and population, rather than on the use of cutting-edge technologies (e.g., Jaipur foot). It is indisputable that novel technologies face rapid obsolescence right after their release, but this applies to any kind of design, not only the context-aware one. Being aware of this, we also should note that, considering the equipment replacement rate – especially in the biomedical field – the useful life is a few years. Because mHealth solutions are software-based, they can easily undergo frequent perfective maintenance (software updates), to be adapted to the novel technologies (e.g., new and better sensors). Finally, a context-aware approach to design, leveraging the correct tools and methodologies (e.g., AGILE, web-based collaborative design platforms such as Ubora or Mirò, Quality Function Deployment, etc.), can indeed help save a lot of time and resources compared to designing being 'blind' to the constraints of the context.

2.7 Discussion

Chapter 2 reported the main challenges concerning LRSs, as well as possible solutions. Sections 2.2 and 2.3 highlighted the deficiencies of the current regulatory frameworks and their tools (e.g., adverse event reporting), to a point where even higher resource settings demonstrated to be suffering from that in times of resource scarcity (e.g., pandemic) (Section 2.4). The role of this thesis in respect to this is to raise awareness about and denounce this issue, in the hope that policymakers will take such matters into considerations when drafting the new set of regulations and standards, hopefully relying on a similar approach to that suggest by Nussbaum (Section 2.3.1). Sections 2.5 and 2.6 focus on the recurrent challenges of LRSs and possible solutions. This part can be used by MD designers to attempt to design MD resilient to LRS conditions. In particular, the findings presented in these sections should offer a set of solutions and approaches that designers can use. Starting from a contextualised approach, the main point here is that, a thorough need and context analysis performed as a first step of the design phase, should highlight the main needs that need solutions, as well as the most relevant criteria that need to be taken into account (e.g., high temperatures for countries in SSA, or other factors). With those in mind, it will be possible to design,

or at least attempt to, a more resilient solution. IEC 60529 (IP Code) and MIL-STD-810H can guide this process, providing details on how the future context of deployment (the external environment) can be taken into account early during the design phase. Overall, an approach based on contextualised frugal engineering and circular economy seems a feasible way to foster not only the design of MD resilient to LRSs, but also capacity building, as well as to empower local communities, and start a positive trend of self-sustained supply chain of simple spare parts for MDs, if not devices themselves. From an analysis of what available in literature and from the authors' field notes, it seems that within this macro-area of contextualised frugal engineering and circular economy, mHealth, 3D printing and protocyclings are viable options to meet the *desiderata*. Engineers who would like to design MD resilient to LRSs, should then surely consider these options as possible ways of developing their designs.

Chapter 3

Possible tools and methods

This chapter introduces several methods and tools that were created ad-hoc and validated, and that can be applied to overcome parts of the challenges duly presented in Chapter 2. In particular, this chapter will focus on the presentation of two frameworks, namely for the assessment of MLs in LRSs, and the design of MDs resilient to LRSs. The work presented in this chapter is already published [2, 4].

3.1 A Framework for Assessing Healthcare Facilities in LRSs: Field Studies in Benin and Uganda

3.1.1 Introduction

For brevity, this subsection is not reporting the whole text of the related publication. Shall the reader be interested, they could find more information in the published paper [2]. As presented in Chapter 2, disparate challenges hinder the safety and effectiveness of MD, jeopardizing the life of patients and healthcare workers. These non-ideal conditions cause frequent failures and trigger a higher demand for spare parts, which are expensive and difficult to find, making the maintenance of MDs as problematic as their acquisition [95]. These challenges are also exhacerbated by the underlying structures and conditions of the buildings of the local hospitals [96–101] (see Figures 3.1,3.2,3.3).

Given the paucity of information on the conditions of LRSs, several authors have performed reviews, interviews and observations, aimed at assessing the adequateness and appropriateness of local hospitals to deliver surgical care [96, 97], or intensive care [98–101] or to manage NCDs [102] such as hypertension [103]. In 2011, Hsia et al. [96] ran a survey based on the WHO list of essential

Figure 3.1: Details of a surgical room in CHU d'Abomey-Calavi. The windows are neither sealed nor filtered.

Figure 3.2: Details of a surgical room in CHU d'Abomey-Calavi. Entrance and exit to the surgical room.

Figure 3.3: A dump within the Naguru hospital in Kampala, Uganda.

surgical services, analysing hospitals in Kenya, Rwanda, Tanzania, Uganda and Ghana, focusing on different variables, including basic infrastructure, medicine storage capability and quality systems. The authors concluded that none of the analysed countries had the proper infrastructures for delivering surgical care. The same problems along with supply chain difficulties in terms of equipment and supplies, old infrastructures not big enough for the ever-growing population, a limited number of beds and monitored beds, were identified by Albutt et al. [97]. They also stressed the fact that the equipment, if present, is outdated and works intermittently, lacking maintenance. In some cases, the situation is exacerbated by the differences between rural and urban areas [101, 102]. Accordingly, it was decided to implement and test a systematic framework, consisting in semi-structured interviews with qualified personnel and direct measurements campaigns, for the assessment of health centres and hospitals in LRSs, given the lack of a standard protocol and of tangible, quantifiable and comparable information regarding these settings. The following subsections present the framework and its application during two field studies performed in Uganda and Benin. This study was performed in accordance with ethical approval REGO-2018-2283.

3.1.1.1 Two LICs: Uganda and Benin

The UN created the Human Development Index (HDI) to evaluate the development of a country, based on different factors, including economic growth, life expectancy at birth, education and the standards of living [104]. A developing country, or a LMIC, is a country with few resources, a low HDI compared to other countries, and a gross national income per capita (GNI) below 4035$. Uganda, an Eastern African country with a GNI of 620$, and Benin, a Western African country with GNI of 870$, are both ranked as low-income countries (LICs) and are among the 25 poorest countries in the world [105]. Table 3.1 summarises some relevant data for both countries in comparison with a typical HIC.

Table 3.1: Relevant data for Uganda, Benin, and Italy [2].

	Uganda	**Benin**	**Italy**
Area (Square km)	241037	114763	301338
HDI	0.528	0.52	0.883
Population (Millions)	42.86	11.49	60.48
GNI ($)	620	870	34456
HIV prevalence (% among 15-49 years old)	5.7	1.13	0.3
Life expectancy at birth (years)	60	62	83
% of population using an imporved drinking water source	79	77.9	100
Physicians per 1000 inhabitants	0.09	0.16	3.95
Houses with centralised electricity supply (%)	22	43	100
Quality of electricity	3.43/7	2.06/7	5.91/7

The Ugandan national health system. Uganda is organized into four administrative regions (i.e., Northern, Eastern, Central and Western), which are further divided into 134 districts and one city (the capital city of Kampala). The National Health System (NHS) in Uganda comprises both a private and a public sector. The public sector includes all Government of Uganda health facilities under the Ministry of Health, and other ministries. The private health sector, which plays an important role in the delivery of health services in Uganda, includes Private Not for Profit, Private Health Practitioners, and Traditional Contemporary Medicine Practitioners. The provision of the health system is decentralised with districts and health sub-districts playing a key role in the delivery and management of health services at those levels. The health services are structured into National Referral Hospitals and Regional Referral Hospitals, Fourth level General Hospital Health Centres, Third level Health Centres, Second level Health Centres, and Village Health Teams [106].

The Beninese national health system. Benin is divided into 12 departments, 77 communes, and 546 districts, all referring to 34 sanitary zones. Its

most important departments are Oumé, with the official capital (Porto-Novo), and Littoral, where the economic and administrative capital (Cotonou) is located. Specifically, also for Benin, the NHS is decentralised, based on a pyramidal structure comprising of 3 levels:

1. central: the Ministry of Health and General Secretariat are in charge of defining policies, strategies and directives;
2. intermediate: the Departmental health directorates are in charge of implementing and coordinating the governmental health policies;
3. peripheral, including Health zones, Commune Health Centres, village health units and private hospitals, which are the operational units.

The multifaceted realities of the departments are difficult to map out and present differences, mainly between the north and the south of the country. In addition to the ordinary health structures, there are numerous vocational hospitals spread around the country [55].

3.1.2 Methods

3.1.2.1 Selection of health facilities

Benin and Uganda were selected as first destinations, because of our previous experiences and the networks. Local contacts were able to link us with the hospitals, where I performed our assessment. The selected health structures were:

1. Kawolo General Hospital (Buikwe, Uganda) (H1)
2. Mengo Hospital (Kampala, Uganda) (H2)
3. Naguru General Hospital (Kampala, Uganda) (H3)
4. Hôpital La Croix (Zinviè, Benin) (H4)
5. Centre Hospitalier Universitaire (CHU) de Zone Suru-Léré (Cotonou, Benin) (H5)
6. CHU de Zone d'Abomey Calavi (Abomey Calavi, Benin) (H6)

3.1.2.2 Questionnaire preparation and validation

The questionnaire was drafted during focus groups among experts of MD design, contextualised design, health technology assessment and management and clinical engineering (see 3.4). During these focus groups, relevant literature was used and integrated by the experts' knowledge to define the different

questions and sections of the questionnaire: in particular, the sections on the general characteristics of the facility, electrical access, human resources and facility environment were based on refs. [107, 108], those on medical electrical equipment on refs. [109, 110] and the one on patient data management on ref. [55]. At first, the questionnaire was conceived to be online, but I realised that more relevant information could be captured if it was administered in person as a semi-structured interview (see Figures 3.5, 3.6, 3.7). The first draft of the questionnaire was circulated among the participants of the first focus group, for internal validation and possible corrections. Once the final version was ready, it was tested for further validation on an anaesthesiologist with working experience in hospitals in Sierra Leone (with Emergency).

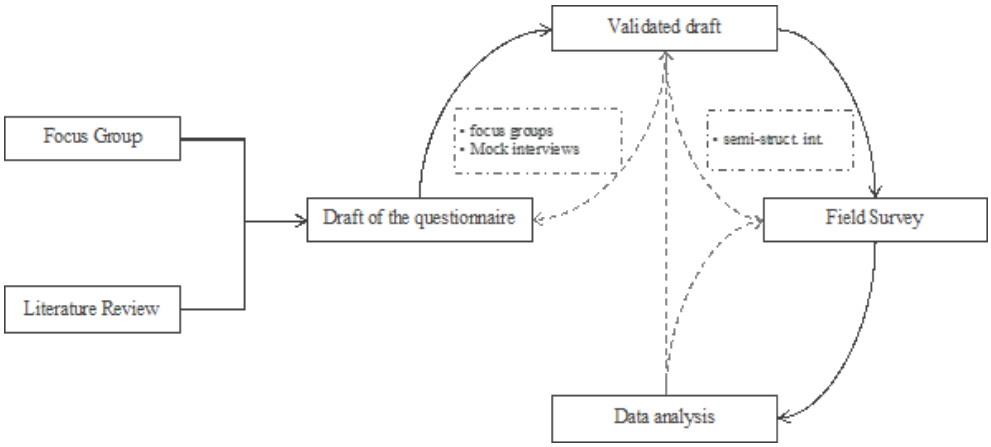


Figure 3.4: The diagram shows the methodologies used for the development and administration of the questionnaire [2].

3.1.2.3 Electrical safety measures

Electrical safety measures were carried out in accordance with IEC 62353-2015, using an electrical safety analyser (ESA620) by Fluke (see Figures 3.8,3.9,3.10, 3.11). The MDs analysed were selected depending on availability at the health centres at the time of the assessment. Our inspection protocol included:

- Voltage and earth check on the main power supply;
- Visual inspections to check the integrity of the devices, the cables and the accessories;
- Protective earth measurement;
- Insulation resistance measurement;
- Leakage currents measurement;
- Functionality tests (e.g., ECG wave simulation).

Figure 3.5: Semi-structured interviews being held with a local biomedical technician in Uganda

Figure 3.6: Semi-structured interviews being held with a local biomedical engineer in Uganda

Figure 3.7: Semi-structured interviews being held with the director of one of the hospitals in Uganda

Figure 3.8: Electrical safety measurements

Figure 3.9: Electrical safety measurements

Figure 3.10: Electrical safety measurements

3.1.3 Results

3.1.3.1 Questionnaire

The final questionnaire (see Appendix B.1) consisted of 71 questions, organised in 9 sections: Introduction and Authorisation, Personal Information, Facility Information, Facility general characteristics, Electrical Access, Human Resources, Facility Environment, Medical Electrical Equipment, and Database. The questions were of different type (e.g., Yes/No, multiple choice etc.) and part of them was quantitatively assessing some dimensions, others were assessing how some dimensions were perceived by the interviewee. The latter had six possible answers, based on a 5-step Likert-type scale, i.e., "Very low", "Low", "Middle", "High", "Very high", "Do not know". The six interviewees, one per hospital, were all males (21-50 years old), had a college or university degree and were 4 biomedical engineers, 1 medical doctor and 1 nurse. All had been working in those roles for an average of 7 years.

General information about the facility. All the assessed hospitals are public and third-level structures (urban), but the one in Zinviè, which is private and a second-level structure (semi-urban). All the hospitals rely on piped water, but H1, which relies on tanker water (also available in H2, H3 and H6), or water from a well (also available in H4, H6). H1 also has structures for

Figure 3.11: Electrical safety measurements. Details of a socket grounding that does not meet the standards, in a surgical theatre in Benin.

collecting rainwater. Only some of the structures have a functioning landline telephone (H2, H3, H5). Other basic facilities are: a mobile phone (H1, H2, H3, H5), a short wave radio (H2), a computer (all but H4), an internet service (H2, H3, H5, H6), an ambulance (all but H5). As regards the access to electricity, all the hospitals can rely on the central supply, most of them have a generator (H1, H2, H4, H5, H6) and some of them have a solar electric system (H1, H2, H6) (see Table 3.2 for further information). All the hospitals reported a certain degree of incompatibility among the local sockets and the plugs of donated MDs (see Figure 3.12).

Table 3.2: Summary of the information and the ratings of the electrical access, reliability, and safety. EG: electrical grounding, EN: equipotential node, and IT: isolation transformer.

Hospital	**Power outages per month**	**Rating of access to the main source of electricity**	**Rating of the quality and reliability of the electricity of the facility**	**Available and functional systems for electrical safety**	**Rating of the electrical safety in the facility**	**Rating of the compatibility of the working voltage and frequency required for the MDs and those available at the facility**
H1	4-6	Acceptable	Poor	EG	Poor	Good
H2	1-3	Acceptable	Very good	EG, EN, IT	Good	Very good
H3	1-3	Good	Acceptable	EG, EN, IT	Very good	Good
H4	10+	Poor	Poor	EG, EN	Acceptable	Poor
H5	10+	Good	Poor	EG, EN, IT	Acceptable	Very good
H6	10+	Acceptable	Acceptable	EG, EN	Good	Very good

Human resources. All the facilities reported a chronic lack of doctors (1 for more than 30 patients), clinical officers (1 for more than 30 patients), of nurses (with an average of 1 nurse per 20 patients), and laboratory technicians. In general, most of the interviewees judged this situation as “poor” or “very poor”.

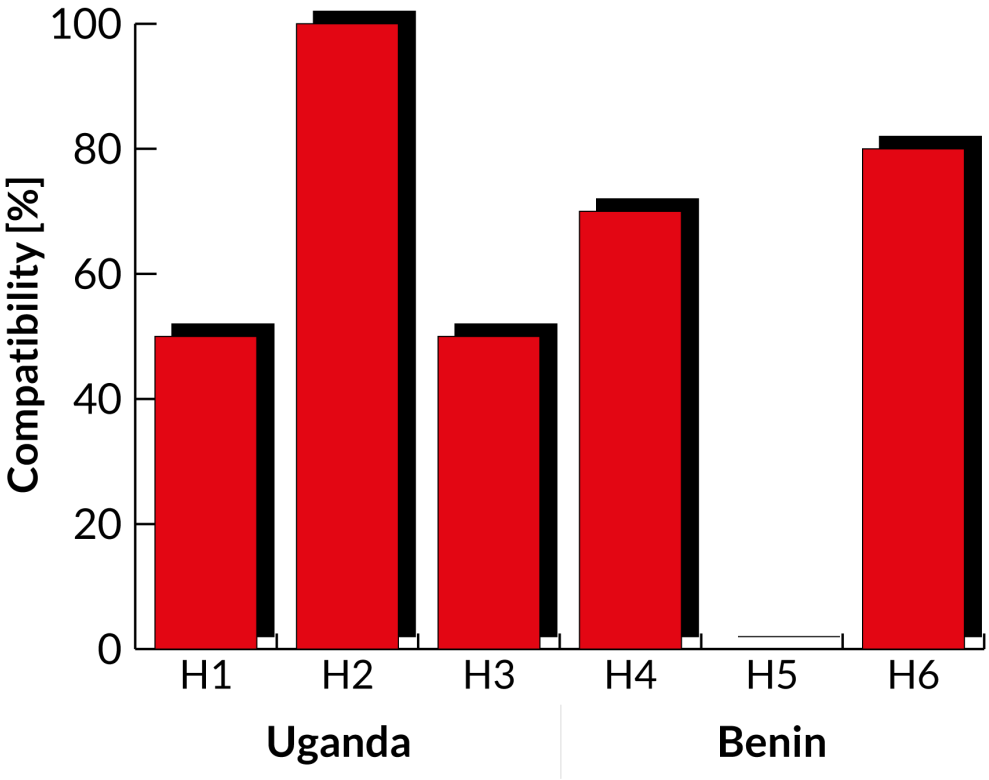


Figure 3.12: The compatibility between the local sockets and the plugs of donated MDs for Uganda and Benin [2].

Facility environment. In general, most of the facilities were judged by the interviewee as poorly insulated or distant from dust, smoke, and undue noise. A better situation was found regarding the insulation or distance from foul odours, the lighting, and the adequateness of ventilation (see Table 3.3). Similarly, the disposal of different kinds of waste (e.g., non-risk waste, infectious waste, sharps etc.) was mostly rated as "very good", apart from H1, for which it was rated as "very poor". All the hospitals' environments are cleaned 5+ times per week.

Table 3.3: The ratings of the insulation or distance of the structures from undue noise, dust, foul odors and smoke

Hospital	Undue noise	Smoke	Dust	Foul odours
H1	Very poor	Very poor	Very poor	Very poor
H2	Very poor	Very poor	Very poor	Acceptable
H3	Very poor	Very poor	Very poor	Very poor
H4	Acceptable	Acceptable	Poor	Acceptable
H5	Good	Good	Acceptable	Good
H6	Good	Poor	Acceptable	Good

Medical electrical equipment, maintenance, and management. Figure 3.13 shows the distribution of essential MDs and services within the six hospitals. The list is ordered from the least available piece of equipment to the most available one. Complex devices like colonoscopes, mammographs, CT-scanners and X-Ray machines are a rare find, compared to blood pressure machines, thermometers, pulse-oximeters, scales, and patient monitors. All the hospitals have a biomedical engineering department, except H1 and H4. The approach to MD maintenance varies depending on the facility. Most of the structures that have a biomedical engineering department are in charge of the preventive and the corrective maintenance (H2, H5, H6), with the exception of H3 that only follows corrective maintenance practices. However, the structures that do not have a biomedical engineering department (H1, H4) are only relying on on-call biomedical engineers/technicians, thus following only corrective maintenance practices. The most recurrent challenges resulted to be the lack of funding, of essential MD, of spare parts and consumables, of expertise. One of the hospitals (H1) also denounced the nonexistence of a policy regulating the donation of MDs. As regards the management, all the hospitals but one (H4) have a form of inventory: 3 hospitals have a paper-based one (H1, H2, H3) and 2 have or are transitioning to a computerised one (H5, H6). The most recorded information regards the year of manufacture, the type, the serial number, the year of acquisition, the class function, the date of service, the routine servicing, the reason for acquisition and the technical characteristics.

3.1.3.2 Electric safety measurements

We were able to perform these measurements in 4 hospitals (1 in Uganda, 3 in Benin). As regards the intensive care unit of H2, the inspected sockets were up to standards (voltage on the mains of 238 V; voltage between the neutral and the ground of 0.2 V). In H2, out of the five tested devices (i.e., 1 defibrillator, 3 patient monitors and 1 ECG), two of the patient monitors[1,2] (see Table 3.4) did not pass visual inspection because they were lacking respectively the blood pressure cuff, the ECG cables and the power cable, and the ECG cable. Moreover, the ECG cables of the defibrillator[3] were not working (see Table 3.4), in fact, when inputting a simulated signal nothing was showing on the screen. All the other devices passed the inspection. As regards H4, the Hôpital La Croix in Benin, the sockets of the surgical room I inspected were up to standards (voltage on the mains of 240 V; voltage between the Neutral and the Ground of 2.6V). H6 had functional sockets in the ambulatory, however the maintenance lab and two surgical theatres had no ground, with voltages between the neutral and the ground of 89.9-134.5 V. Throughout the different buildings I noticed that the grounding system was a common problem, along

Country	Uganda	Uganda	Uganda	Benin	Benin	Benin
Hospital	H1	H2	H3	H4	H5	H6
Colonoscope	0	1	0	0	0	0
Mammograph	0	0	1	0	0	0
CT-scanner	0	1	1	0	0	0
Gastroscope	0	1	2	0	0	0
Infant reanimation centre	0	0	1	0	1	1
X-Ray Machine	1	3	1	1	1	1
Ambulance	0	3	1	2	0	2
Defibrillator	2	4	NA	3	2	0
Ventilator ICU	0	4	8	0	2	1
Hemocytometer	1	4	1	8	4	1
Ultrasound machine	0	8	2	4	2	3
Oxygen systems/cylinders	10	10	1	0	0	0
Syring pump	0	8	0	2	8	8
Autoclave for sterilisation	2	8	10	2	4	1
Operating theatre with basic equipment	3	8	3	8	3	2
Suction pump	1	8	10	0	8	1
Infant warmer	0	8	8	4	8	0
Anasthetic machine	1	10	8	0	2	8
Fetal monitor	1	8	10	0	8	2
Neonatal incubator	8	10	1	3	4	4
ECG machine	0	4	8	10	8	2
Patient monitor	1	10	10	10	8	10
Scale for adult	0	10	10	10	10	10
Scale for newborns	0	10	10	10	10	10
Pulsoximeter	2	10	10	10	10	10
Thermometer	8	10	10	10	10	10
Blood pressure machine/cuff	10	10	10	10	10	10

Figure 3.13: The distribution of essential MDs and services within the 6 hospitals. The ranges were substituted with the average value. The value 10 stands for 10 or more. Red circles individuate a low availability of the MD, yellow circles a medium availability, and green circles a high availability [2].

with the inversed polarity of the sockets. In H5, all the inspected departments (i.e., Biochemistry, Haematology, HIV lab, new equipment room) presented troubles with the earth system (with voltages between the Neutral and the Ground between 8 and 43 V), but the department of radiology. Table 3.4 reports the findings on electrical safety.

3.1.4 Discussion and conclusions

This paper introduces a framework to assess clinical locations, specifically in LMICs, through a semi-structured interview and electrical safety measures. Such a framework, tested in Uganda and Benin, is crucial for mapping out the different realities of healthcare locations of LRSs. Many developing countries still lack access to MDs and equipment that are appropriate for their specific clinical needs because of poor regulatory controls [111]. More importantly, what they do have is often inappropriate due to a mismatch between working conditions and design constraints. In Africa, for example, competent authorities, who control the quality and safety of MDs, often lack adequately trained staff for consultation [112] due to limited human capacity in Biomedical Engineering [113]. We believe that the problem of existing standards is that of generalism, or of a non-inclusiveness, which does not take into consideration all the specific realities and that, for this reason, is not reachable by them. This dilemma, however, can be addressed with an inductive method, which, by examining specific situations, can inform the writing of new regulations and standards that are more inclusive and universally applicable. It is only by studying and taking into account different contexts and types of users that the design of a safe and high-quality MD for LRSs can be successful [114]. It is true that many challenges are common to these settings, but it is also true that each of them has its own identity and peculiarities. According to this, open-source and collaborative methods have the potential to improve the design of needs-based MD, offering specific solutions to problems not properly considered by current standards, oriented to well-structured healthcare environments. When properly deployed, the open design paradigm has the potential to increase access to medical technologies, reducing the management, maintenance, and repair costs due to the open-access of device blueprints [115]. In this context, UBORA, the open Biomedical Engineering e-platform for collaborative design, can be effectively used to develop safe and effective MDs, and the relative spare parts [116], the analysis of the technical needs, the risk management process, legal aspects, safety criteria and performance data, fundamental for maintaining the compliancy of the repaired devices with the MDR[1]. As shown by the results of the questionnaire, all the analysed facilities are inefficiently built, with poor

[1] https://platform.ubora-biomedical.org/

Table 3.4: The report of the electric safety measurements in some of the hospitals. NC meaning normal conditions. † denotes devices that did not pass completely or partially the inspection. †† denotes the measures not respecting the standard. § denotes the devices for which no electrodes were available. * denotes measures that were taken on ECG cables as applied parts. PE means protective earth, AP applied part, NE equipotential node

Hospital	**Equipment**	**Protective earth (Ohm)**	**Insulation (MOhm)**					**Leakage current (μA)**	
			Mains-PE	AP-PE	Mains-AP	Mains-NE	AP-NE	Equipment	AP
H2	Defibrillator[3†]	NC	Infinite	NA	NA	NA	NA	0.2*	5.4*
	Patient Monitor[2†]	0.075	Infinite	NA	NA	Infinite	NA	NA	NA
	Patient Monitor[1†]	–	–	–	–	–	–	–	–
	Patient Monitor	0.065	Infinite	Infinite	Infinite	Infinite	–	0.3	5.2
	ECG EDAN SE 1200 Express	0.043	Infinite	100.6	Infinite	Infinite	100.7	0.2	8.8
H4	Patient Monitor	1.23††	Infinite	98.4	Infinite	Infinite	98.2	0.2	7.7
	ECG Schiller AT 102	0.126††	Infinite	96.2	Infinite	Infinite	96.2	0.1	20.7
H6	Patient Monitor[§]	1.7††	Infinite	Infinite	Infinite	Infinite	Infinite	0.5	3.8
	Bionet Fetalcare ECG	0.34††	Infinite	Infinite	Infinite	Infinite	Infinite	0.65	0.5
H5	Biobase Centrifuge	0.125††	Infinite	Infinite	Infinite	Infinite	Infinite	0.5	NA
	Mindray Bs200 Analyzer	0.633††	Infinite	Infinite	Infinite	Infinite	Infinite	34.2	NA
	Heamatology analyser	0.073††	Infinite	Infinite	Infinite	Infinite	Infinite	0.2	NA
	Sysmex coagulation system	0.166††	Infinite	Infinite	Infinite	Infinite	Infinite	0.7	NA
	Edan Patient Monitor	NC	Infinite	99.5	Infinite	Infinite	Infinite	0.9	8
	Aspel ECG	NC	Infinite	Infinite	Infinite	Infinite	Infinite	0.2	18.6

isolation from foul odours, smog and undue noises, and unstable and unsafe power supplies. The scarcity of essential MDs, spare parts and consumables, together with a poor maintenance system, bolstered by the chronic lack of biomedical engineers, technicians and healthcare personnel (from nurses to specialised doctors), hinders the safe and efficient care of patients, impeding universal health coverage. The electrical safety measurements confirmed the results of the questionnaire, highlighted the common issue of too high protective earths of some MDs, and, above all, clearly proved that in Benin there are problems with the grounding systems. One limitation of the study is that it was not always possible to test MDs, because of the lack of authorisation or because they were all being used for the care of patients. Nevertheless, the availability of the technical staff, who allowed the measurements and the interviews on the field, made us understand the urgency for the locals of the problems highlighted in this paper. Therefore, this study is an important starting point to frame the problem and present the framework which favoured a thorough investigation in the field and facilitated the subsequent processing of the data, showing itself a suitable, exportable and repeatable tool to offer an overview of healthcare locations in specific contexts. The study will be expanded to include more hospitals around Uganda, Benin and other LMICs in order to provide the basis for promoting awareness of the issues they face and towards global policy changes for health equity.

3.2 A multi-criteria decision analysis (MCDA) framework for designing MDs resilient to LRSs: an application for LMICs

3.2.1 Background

For brevity, this subsection is not reporting the whole text of the related publication. Shall the reader be interested, they could find more information in the published paper [4]. As already clearly set out in Chapter 2, LRSs face several challenges that hinder the safety and effectiveness of MDs. In the 2010s, some studies started relating this situation to a design problem. For instance, Aranda et al. [117], similarly to Kortum et al. [118], stated that healthcare facilities are in poor conditions in terms of basic infrastructure due to designers' failure. Aranda et al. [117] also asserted that these inequalities could be efficiently tackled with a well-planned, user-driven and contextualized design. Although it is clear that user-needs and the context of use are essential for manufacturing safe, efficient and effective MDs, they are rarely considered during design [35]. In the literature, there have been attempts to identify the crucial criteria for the design of MDs resilient to LRSs [117, 119–121].

Arasaratnam et al. [119] gave an overview of the past trend, better known as “glocalization”. This term, not to be confused with the currently misused term “globalization”, arises from the combination of the latter with the term “localization”. It is used to describe a phenomenon of contextualization of some products or services, universally distributed but adjusted to accommodate the user or consumer of local markets. Glocalization was a typical trend of the industries, which removed some features from high-tech products that were designed for more developed countries to make them accessible to LRSs. Nowadays, it is widely recognized that this trend is not sufficient to adjust medical technologies to LRSs. Thus, the new trend is the so-called ’frugal innovation‘ [122]. The paper by Aranda et al. [117], relying on the views of some experts, identified some essential criteria in the durability, the robustness, and cost of ownership over time and the simplicity of use. The same criteria along with accuracy, reliability, size, weight, materials, power requirements, ease of manufacture, language barriers, availability of facilities and population dynamics were pointed out by Nimunkar et al. [120]. The latter also agreed with the widely shared belief that special considerations should be made when designing MDs for developing countries. Similar results were obtained by Gauthier et al. [121] through a literature review and an analysis of the state of the art of the MDs designed for lower resource settings. Beyond the already mentioned criteria, Gauthier et al. [121] also pinpointed more criteria such as appropriateness, functionality, spare parts, personnel, management, and public policy. In [121] the authors also asserts that the primary focus should be on affordability, durability, and materials. Interestingly, in the ’90s Adler et al. [72] presented and described the application of some military standards to the design of MDs for military use. This did not seem to get as much attention as the current (2021) trend followed by the Information Technology industry, which is adopting the IP Code (presented in the IEC standard 60529) and military standards (specifically, MIL-STD-810H) to design and manufacture “ruggedized” devices, which are sturdier and more resilient to harsh working conditions. Nonetheless, overall, there is no agreement on a framework including a set of criteria that support the design of MDs for LRSs. The aim of this study is to contribute to filling this research gap by systematically developing a general framework that could guide designers in their complex tasks. In particular, this study aims to identify, classify and weigh the essential criteria to be considered while designing MDs resilient to LRSs. The framework was initiated starting from the MDs presented in the WHO compendium of innovative health technologies for LRSs [123]. Our goal was pursued inductively, i.e., by inferring the general set of essential criteria from observations/data. A triangulation of qualitative and quantitative methods was used, in fact, as Pope et al. affirms [124], the former can complement the

latter when used as an essential preliminary to quantitative research and can also be supplementary information to validate the quantitative results further. Such methods, which will be thoroughly described in the paper, included: focus groups, field studies, content analysis for drafting and validating a set of essential criteria, pilot tests, semi-structured interviews, a Delphi survey, and MCDA for developing and validating a questionnaire, and analysing the results. As a result, in fact, the final version of the questionnaire (see Appendix B.2) was issued to a pool of experts to complete. As a result, a set of essential criteria was obtained and used to develop a framework, i.e., a multi-criteria decision system for designing MDs resilient to LRSs. This work could lay the basis for the creation of novel and contextualised international standards, which could empower LMICs, enabling them to enforce import restrictions according to the World Trade Organization Agreement on Trade-Related Aspects of Intellectual Property Rights (WTO-TRIPS), and creating "an indigenous medical equipment manufacturing capability"[95]. Thus, this would force manufacturers to design and manufacture products in line with the new consensus standard to give them the opportunity to market their products in LMICs.

3.2.2 Methods

The inductive method, which implies the generation of theories starting from numerous observations [125], was used to develop the set of essential criteria. In particular, a triangulation of qualitative and quantitative methods was used to develop a framework of criteria for the design of MDs resilient to LRSs and for its validation through the convergence of information [124, 126]. Figure 3.14 shows a summary of the phases of the project along with their main objectives, methods, people involved and outcomes. In particular, purposive sampling [124, 127] was used for the methods that required sampling. The latter is a non-random technique that consists in the deliberate choice of participants by the researcher, based on the information they can provide relying on their knowledge or experience (23).

3.2.2.1 Criteria identification

The identification, classification and weighting of the fundamental criteria for the design of MDs for LRSs were achieved with a series of nested closed loops involving relevant scholars and experts (see Figure 3.15) from five continents. All the steps presented in Figures 3.14 and 3.16 are interdependent. After analysing the criteria for the design of MLs and MDs, essential criteria for the resilient design for LRSs were identified by reviewing systematically existing scientific literature. These initial criteria and the rationale of this study were

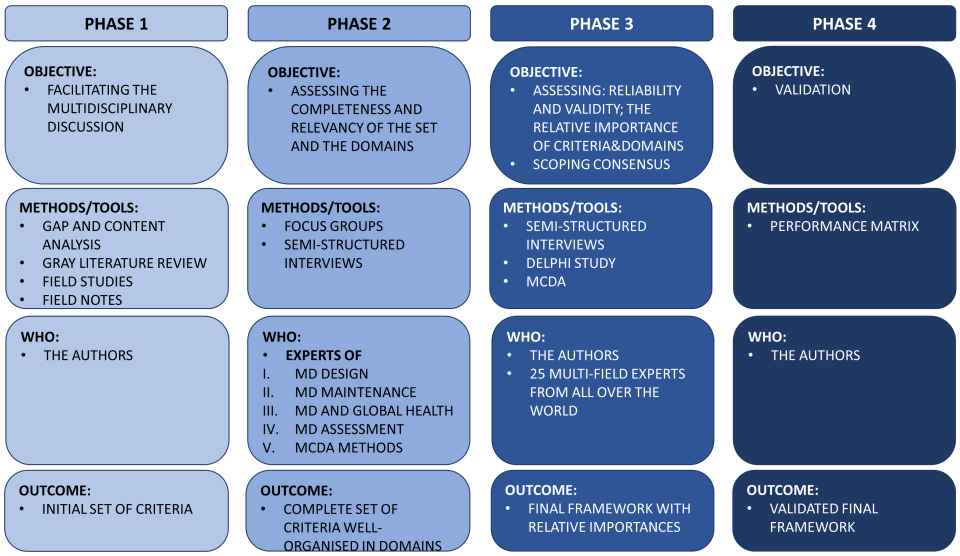


Figure 3.14: A summary of the phases, their objectives, methods, people involved and outcomes.

presented during the AfricaHealth Conference (Johannesburg, June 2016), where they were discussed in a focus group with biomedical and clinical engineers from 15 Sub-Saharan Africa countries. In November 2016, the essential criteria were reviewed during a 3-day meeting organized in Warwick in collaboration with the International Federation of Medical and Biological Engineering HTAD division[2] working group for the preparation of guidelines of the Health Technology Assessment of MDs [128]. During the meeting, 14 experts from 8 nations and 1 WHO representative participated in a focus group to analyse the interdependencies among working environments and MD safety and effectiveness [35]. During this focus group, the essential criteria were enriched with experts' feedback and a grey literature review on LRSs, design of MDs and MLs. Particular attention was given to the WHO compendium of innovative health technologies for LRSs [123]. Two authors (Davide Piaggio, Sara Cinelli) analysed the compendium reporting the MDs that are supposedly resilient to harsh environments. The recurrent design criteria were noted, narrowed down and, finally, enriched with the experts' views.

3.2.2.2 Hierarchy of criteria

The identified criteria were clustered in meaningful domains defining a hierarchy framework. The hierarchy was piloted in Africa with several field studies, each followed by an additional focus group. In fact, two field analyses were carried out in Benin (May 2017 and January 2018) performing visual inspections of MDs and testing on ML plants [1], aiming at evaluating the relevance and the

[2]http://htad.ifmbe.org/

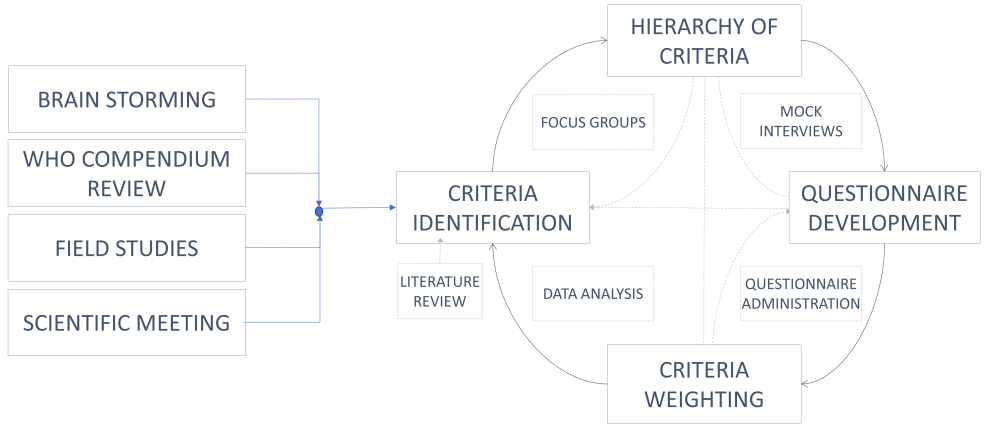


Figure 3.15: Block diagram of the study process and methods used.

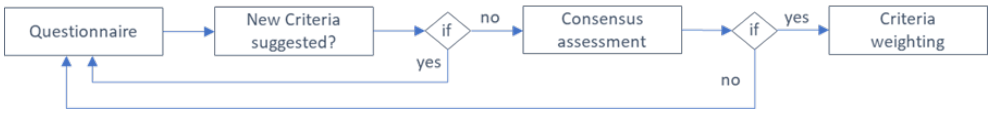


Figure 3.16: Diagram showing the steps taken from the questionnaire development to the weighting of the criteria.

suitability of the essential criteria set. The former field study was followed by a focus group with experts from SSA during the AfricaHealth2017 (Johannesburg, South Africa). The latter field study was followed by a focus group held in Addis Ababa, Ethiopia, during the kick-off meeting of the International Federation of Medical and Biological Engineering Working Group on BME in Africa, in February 2018 [129]. Additionally, in 2019 two extra field studies were carried out in Benin and Uganda [2].

3.2.2.3 Survey

Once the set of essential criteria was consolidated as described above, one investigator created the first draft of a questionnaire, aiming at confirming the set of criteria, exploring consensus among scholars and domain experts and weighting criteria relative importance. The survey was pilot-tested in two stages. Firstly, it was administered to the participants of the first focus group in Warwick for possible disambiguation and correction of content and language. Secondly, it was tested with in-person semi-structured mock interviews at the International Union for Physical and Engineering Sciences in Medicine World Congress (Prague, June 2018) recruiting scholars not involved in the previous steps. In particular, during the Congress, one of the authors conducted semi-structured interviews and collected the answers of biomedical and clinical

engineering experts, whose feedback helped us refining our questionnaire and enrich it with one additional criterion. Eventually, another focus group was held to review the criteria and to create the final version of the questionnaire. The final questionnaire was sent with a bilingual email invitation, linking to two online questionnaires, one in English and one in French, to improve the reachability of African experts from francophone countries. One reminder was sent to the panellists who did not reply, after one month. Due to our extensive network of institutions, responders were identified amongst the ones collaborating with the International Federation of Medical and Biological Engineering Health Technology Assessment, Clinical Engineering divisions and speakers selected by the WHO for the sessions on MD design and management in LMICs of the Fourth WHO Global Forum on Medical Devices. Finally, authors of relevant scientific papers were invited, which were independent of the above institutions. Figure 3.16 shows the steps from the questionnaire development to the criteria weighting.

Responders were identified through the international scientific society of biomedical engineering (i.e., International Federation of Medical and Biological Engineering), among corresponding authors of relevant papers, through authors partners from Africa, and via WHO regional representatives. Responders were recommended based on their experience with health technologies, including design, development, testing, implementation, maintenance of MDs. The study received full ethics approval by the University of Warwick Ethical BSREC Committee (REGO-2018-2283).

3.2.2.4 Delphi survey design

Named after the famous oracle at Delphi, the Delphi study is one of the several consensus methods available, other than nominal group process and consensus development panels [130]. It is an iterative multistage process that aims to elicit and reinforce experts' opinions via group consensus with a series of structured questionnaires which the experts fill in. This can be conducted in two main ways. The questionnaire can be anonymous, i.e., the respondents' identity is private and they cannot see the others' answers; or it can be blinded, i.e., the respondents' identity is only known by the investigators and they are still "blind" to others' answers. This allows every participant to freely express their own opinions, minimizes the "bandwagon effect" (i.e., the phenomenon in which people tend to do something just because other people do it, regardless of their own beliefs or opinions [131]) preventing the authority or reputation of some participant from dominating others [132]. In this study, I conducted a blind online Delphi survey, which allowed reaching expert panellists all around the world. Our study aimed to obtain consensus merging the panellists' different

opinions through group dynamics, rather than to achieve statistical power. Therefore, a priori power analysis to calculate the minimum sample number of panellists was not evaluated for this study. However, I referred to the existing literature that suggests that a panel should include 10 to 18 experts [133].

3.2.3 Delphi process

The questionnaire was composed of 42 questions, organized in 9 sections: 1 regarding the responder's professional experience, 7 weighting the importance of design criteria clustered in different domains, and one to weigh the relative importance of such domains. Each section closed with an open question to gather suggestions about new criteria, if any. All the acronyms of the questionnaire were duly explained. Definitions were given for some of the criteria. In fact, given the respondents are experienced in the domain of MD design with a special focus on LRSs, I assumed that well-established concepts in this domain needed no further explanation (i.e. maintenance frequency, maintenance cost, the need for consumables or spare parts, etc.). Conversely, for the criteria that were not deemed self-explanatory, examples/definitions (please see Appendix B.2) were added in brackets in the questions of the questionnaire as in the following examples:

- For "reliance on medical location air", examples were given such as "filtering, temperature, humidity, etc."
- For "end users' background", examples were given such as "doctors, nurses, biomedical engineering technicians"
- For "ease of use", examples were given such as "the medical device requires a high specialised personnel, any operator can use it, or it is so intuitive that anyone can use it" etc.)

The questions regarding the design criteria were asked with a repetitive formula, namely "What is the importance of considering "CRITERION 1" during the design of MD which will be used in low-resource settings?". Such questions had six possible answers, converted in integer number based on a 5 steps Likert-type scale, i.e., 'Very low' (1), 'Low' (2), 'Middle' (3), 'High' (4), 'Very high' (5), 'Do not know' (' '). A new criterion would be included in a next Delphi round if proposed by at least 30% of the respondents (24). Regarding the iteration stopping criteria, I decided not to iterate the questionnaire if all of the criteria and domain reached consensus defined as follows. For all the criteria, the first and third quartiles and their relative distances 'Δ', i.e., the interquartile ranges, were calculated in order to rank the criteria consensus with a "Sufficient" range ($2 \geq \Delta \geq 1$), "Fair" range ($1 \geq \Delta > 0$) or a "Full consensus" range ($\Delta = 0$).

3.2.3.1 Data analysis

Reliability. When performing a survey, it is crucial to assess the reliability of the responses. Low reliability affects negatively the validity of the results [134]. Reliability measures how the criteria are part of the same domain and are, thus, relevantly measuring the same overarching concept. This is fundamental since also experienced experts may provide inconsistent answers due to tiredness or distraction. Following the procedure previously employed in other studies [135, 136], reliability was estimated through ordinal alpha and the use of polychoric matrices. The latter are optimum tools for analysing test reliability in case of ordinal data (such as Likert-scale based questionnaires) because Cronbach alpha is based on the assumption of continuous data [137] and could lead to underestimation [138]. Ordinal alpha scale, in particular, ranges from 0 to 1, with values over 0.7 being "Acceptable" [135]. Polychoric correlation matrices and the consequent ordinal alphas were calculated in R (version 3.5.1) with the functions polychoric and alpha for each domain. As suggested in [139], once the ordinal alphas were calculated, internal consistency was rated according to the values reported in Table 3.5. Then, the alpha drop was also calculated for the domains that showed low internal consistency. The latter is a measure of how the alpha would change if a criterion of the domain were dropped. This helps identify the problematic elements of the questionnaire, if any.

Table 3.5: The values of α and their interpretation

Alpha	**Internal consistency**
$\alpha \geq 0.9$	Excellent
$0.8 \leq \alpha < 0.9$	Good
$0.7 \leq \alpha < 0.8$	Acceptable
$0.6 \leq \alpha < 0.7$	Questionable
$0.5 \leq \alpha < 0.6$	Poor
$\alpha \leq 0.5$	Unacceptable

Validity. Validity is an essential component of survey evaluation; in fact, it tests whether the scale is measuring what it is intended to measure [135]. In this case, validity was tested during the pilot test, in which additional comments were asked to the interviewees and also tested during the Delphi survey. Each domain contained a final question asking to suggest criteria, their ranking, and possible comments. New criteria would be added if suggested by at least 30% of the panellists.

3.2.3.2 Ranking

In order to find the final importance of each criterion derived from the answers to the questionnaire, the relative index was calculated. The relative index is defined by the following equation [135]:

$RI = \sum_{i=1}^{5} \frac{w_i * f_i}{N}$

where w_i is the weighting factor calculated by dividing the rating score by the highest score (i.e., 5), f_i is the frequency of the responses and N is the total number of responses. Once the relative indices were calculated, the criteria were sorted in decreasing order and were divided into subclasses according to their importance, namely Fundamental, Important and Relevant.

Correlations among criteria. Correlations among criteria in the same domain were assessed with Goodman and Kruskal's gamma, which was calculated with the following equation [135]:

$\gamma = (SOP - IOP)/(SOP + IOP)$

Where SOP stands for "same order pairs" and IOP for "inverse order pair". Gamma ranges from -1 to 1 and in this case values greater than 0.5 or lower than -0.5 were considered to highlight a strong correlation, whose significance depends on the p-value. In this case, I selected a p-value of 0.05.

3.2.3.3 Validation and use of the framework

Once identified, the relevant criteria were combined in a framework that could be used to help inform the design of MDs resilient to LRSs. Afterwards, a protocol was developed to test this framework of criteria with a subset of MDs and to show its possible uses. All the criteria were reported and divided into two sets: discriminatory and non-discriminatory criteria. 3 criteria were added a posteriori of our field studies, under the "Reliance on external factors" domain. A total of 8 MDs was randomly extracted from the WHO compendia of innovative health technologies for LRSs, 4 from the 2014 version [82] and 4 from the 2017 one [140]. After analysing the selected devices, information regarding each of the criteria was used to score them with the help of a performance matrix (similarly to the concept of Pugh matrix [141]). The criteria from the cost and lifetime domains, i.e., non-discriminatory criteria, were excluded from this analysis, as they cannot be scored qualitatively. A qualitative three point-based measurement scale was used. Adopting the well-known traffic light colour code, red was used for the worst cases, yellow for the intermediate performance and green for the best one. Consequently, two trends were evaluated:

1. Which criteria feature mainly green cells (i.e., a good assessment) irrespective of the device? In this case, only the criteria reaching a good

assessment in at least 5 out of the 8 MDs were selected.

2. Which of the selected MDs resulted efficient (i.e., criteria prevalently coded as green), which averagely efficient (i.e., criteria prevalently coded as yellow) and which not really efficient (i.e., criteria prevalently coded as red)?

3.2.4 Results

3.2.4.1 Focus group and pilot

The results from the second focus groups and brainstorming are summarised in Figure 3.17, which shows the final version of the hierarchy of essential criteria for the design of MDs resilient to LRS working conditions. The criteria were grouped into seven main domains, namely user type, health technology management (HTM), design, reliance on external factors, material, cost and lifetime. Moreover, the piloting phase led to the addition of one criterion, namely "the capability of the user to understand the technical and clinical impact of the technology".

3.2.4.2 Delphi Survey

Characteristics of panelists. I invited 56 professionals, with a background spanning from biomedical engineering to clinical engineering and public health, to participate in the final survey, and an overall 25/56 (44.6%) answered the questionnaire. The 25 panellists represented 19 countries, 7/25 (28%) of them represented Europe, 12/25 (48%) Africa, 2/25 (8%) North America, 2/25 (8%) East Asia, 1/25 (4%) Central America, and 1/25 (4%) South America (see Figure 3.18). As far as Africa is concerned, the involved countries were the Democratic Republic of Congo, Ethiopia, Tanzania, Mozambique, Benin, South Africa, Ghana, Kenya, and Burundi. The fields of expertise of the respondents are several and summed up in Table 3.6. Since some respondents had more than one area of expertise, the different areas of expertise were counted as separate entries. The average years of expertise of the responders were 18.6 years and the standard deviation 12.2 years.

Consensus on Criteria. The median, interquartile range (IQR) (i.e., the range containing 50% of the data, obtained by subtracting the first quartile from the third quartile) and its interpretation, and the number of panellists for each recommendation are shown in Table 3.7. All the criteria reached the consensus threshold.

Table 3.6: A summary of the areas of expertise of the panellists. The numbers are out of 29 respondents as more than one respondent stated more than one area of expertise. The different areas of expertise were counted as separate entries.

Area of Expertise	**Percentage**
Biomedical engineering	9/29 (31.0%)
Clinical engineering	6/29 (20.7%)
Medical devices & Instrumentation design	7/29 (24%)
Life cycle management of MDs	4/29 (13.7%)
Health technology assessment	2/29 (6.9%)
Other	1/29 (3.4%)

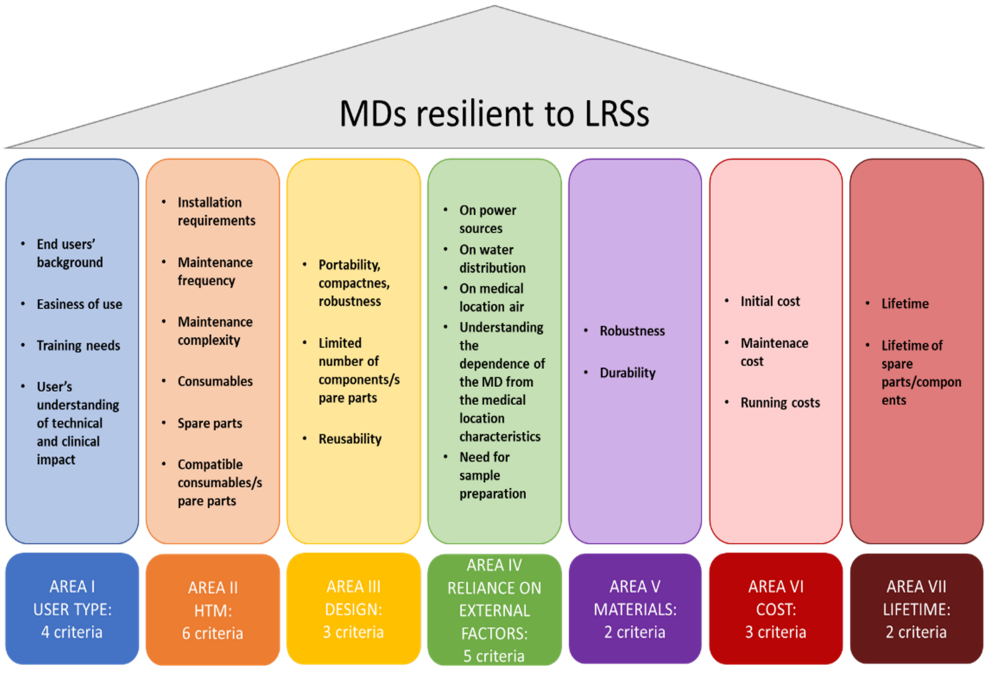


Figure 3.17: The final draft of the essential criteria for the design of MDs resilient to LRS working conditions. The criteria are grouped into 7 domains.

Table 3.7: Design criteria with median, interquartile range, its interpretation and the number of panelists.

Criteria	**Median (IQR)**	**IQR interpretation**	**# of Panellists**
End users' background	5 (4,5)	Fair Consensus	24/25
Easiness of use	4 (4,5)	Fair Consensus	24/25
Training needs	4 (4,5)	Fair Consensus	25/25
User's understanding of the technical and clinical impact	4 (3,5)	Sufficient Consensus	25/25
Installation requirements	5 (4,5)	Fair Consensus	25/25
Maintenance frequency	4 (4,5)	Fair Consensus	25/25
Maintenance complexity	4 (4,5)	Fair Consensus	25/25
Need for consumables	5 (4,5)	Fair Consensus	25/25
Need for spare parts	5 (4,5)	Fair Consensus	25/25
Compatible consumables/spare parts	4 (3,5)	Sufficient Consensus	25/25
Portability, compactness, robustness	5 (4,5)	Fair Consensus	25/25
Limiting the number of components/spare parts	4 (4,5)	Fair Consensus	25/25
Reusability	4 (3,5)	Sufficient Consensus	25/25
Reliance on power sources	4 (4,5)	Fair Consensus	25/25
Reliance on water distribution	4 (3,5)	Sufficient Consensus	24/25
Reliance on medical location air	4 (3,4)	Fair Consensus	25/25
Understanding/stating the dependence of the MD from the medical location characteristics	3 (3,4)	Fair Consensus	20/25
Need for sample preparation	4 (3,4)	Fair Consensus	24/25
Robustness of the material	4 (4,5)	Fair Consensus	25/25
Durability of the material	4 (4,5)	Fair Consensus	25/25
Initial cost	4 (4,5)	Fair Consensus	25/25
Maintenance costs	5 (5,5)	Full consensus	25/25
Running costs	5 (4,5)	Fair Consensus	25/25
MD lifetime	4 (4,5)	Fair Consensus	25/25
Lifetime of MD parts/components	4 (4,5)	Fair Consensus	25/25

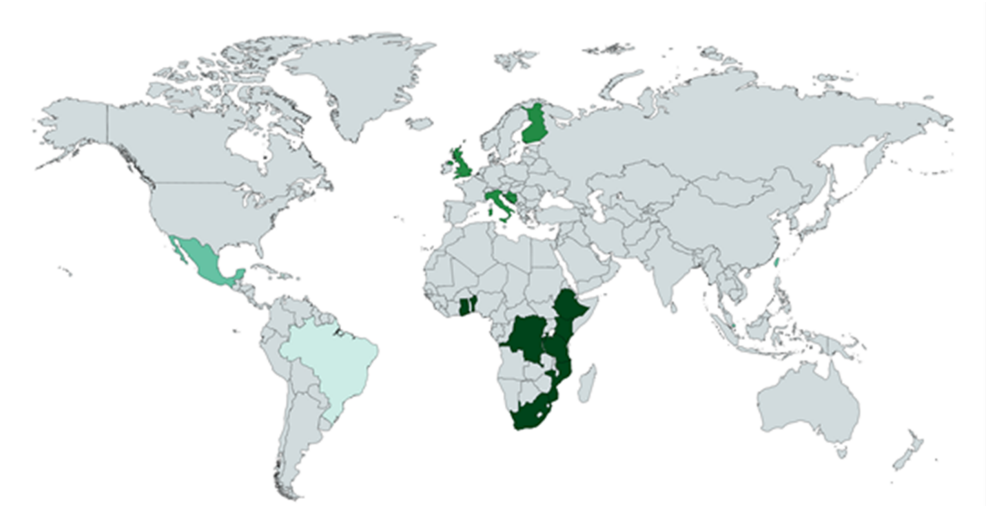


Figure 5. The map shows the countries represented by the panellists. The higher the colour intensity, the higher the percentage of respondents from that geographical area.

Figure 3.18: The map shows the countries represented by the panelists. The higher the colour intensity, the higher the percentage of respondents from that geographical area.

3.2.4.3 Reliability analysis

Six domains out of seven showed a high internal consistency (see Table 3.8). This means that all the identified domains included a coherent and relevant set of criteria. Only the User Type domain showed a low ordinal alpha (0.58). In this case, I also performed further analysis to study how the ordinal alpha would change if one criterion would be omitted. As a result, not considering the easiness of use would lead the ordinal alpha to an acceptable value of 0.76.

Table 3.8: Summary of the reliability analysis.

Statistics	**User Type**	**HTM**	**Design**	**Reliance on ext. factors**	**Material**	**Cost**	**Lifetime**
# of replies	24	25	25	20	25	25	25
Scale Reliability	0.58	0.92	0.7	0.9	0.96	0.9	0.84
Interpretation	Poor	Excellent	Acceptable	Excellent	Excellent	Excellent	Good
# of criteria	4	6	3	5	2	3	2
Changes applied after pilot survey	1 criterion added	-	-	-	-	-	-

3.2.4.4 Validity

The pilot study helped to refine how questions were presented and one criterion was added during the piloting. Moreover, although the respondents to the final survey suggested some additional criteria through the open questions, none

of these was supported and shared by more than 3/18 respondents (16.7%) (<30%).

3.2.4.5 Ranking and correlations

All the relative indexes that were calculated were over 0.5, implying that all the criteria raised a great interest in the panellists. Moreover, all of the indexes are very close to each other, highlighting the great importance of each domain, which in decreasing order were 0.888 for cost, 0.848 for lifetime, 0.84 for HTM, 0.832 for design, 0.824 user type, 0.824 for materials and 0.792 for reliance on external factors (see Figure 3.19).

In particular, the next subsections will show the results grouped by domain (see Table 3.9 and Figure 3.20).

Cost. Maintenance cost (6.1), running costs (6.2) and initial cost (6.3) are 'Fundamental', although the initial cost is seen as slightly less important with respect to the first two.

Lifetime. Both the lifetime of the MD (7.2) and its parts/components (7.1) are 'Fundamental' and correlated. The lifetime of a MD depends on the functionality of its parts, the more the components, the more likely a breakdown.

HTM. The need for consumables (2.1) is number one in this domain and is positively correlated with the need for spare parts (2.2), the installation requirements (2.3), and the maintenance complexity (2.4) and frequency (2.5). This stresses the recurrent problems reported in the literature, in which the lack of spare parts and consumables or existent or functional maintenance are very common [63, 65, 66].

Design. Portability, compactness, and robustness (3.1) and limiting the number of components/spare parts (3.2) are ranked as 'Fundamental' and are correlated. Portability and compactness are greatly influenced by the number of components or spare parts. Limiting the latter would improve the durability of a functional device, because the fewer components, the less the chance of any breakdown.

User type. The end-users' background (1.1) ranks at the top of this domain and is positively correlated with the users' understanding of the technical and clinical impact (1.4). The latter is dependent on the former: a solid background is a key to a complete understanding of technical and clinical impacts. As regards the easiness of use (1.2), negatively correlated with the end-users' background (1.1) (although not significantly), it was discarded because of how negatively it affected the overall reliability of the user type domain. In this case, this variable could be re-assessed by the panelists to see if the results may change. **Materials.** Both the durability (5.1) and the robustness (5.2) of the material are "Fundamental" and are correlated.

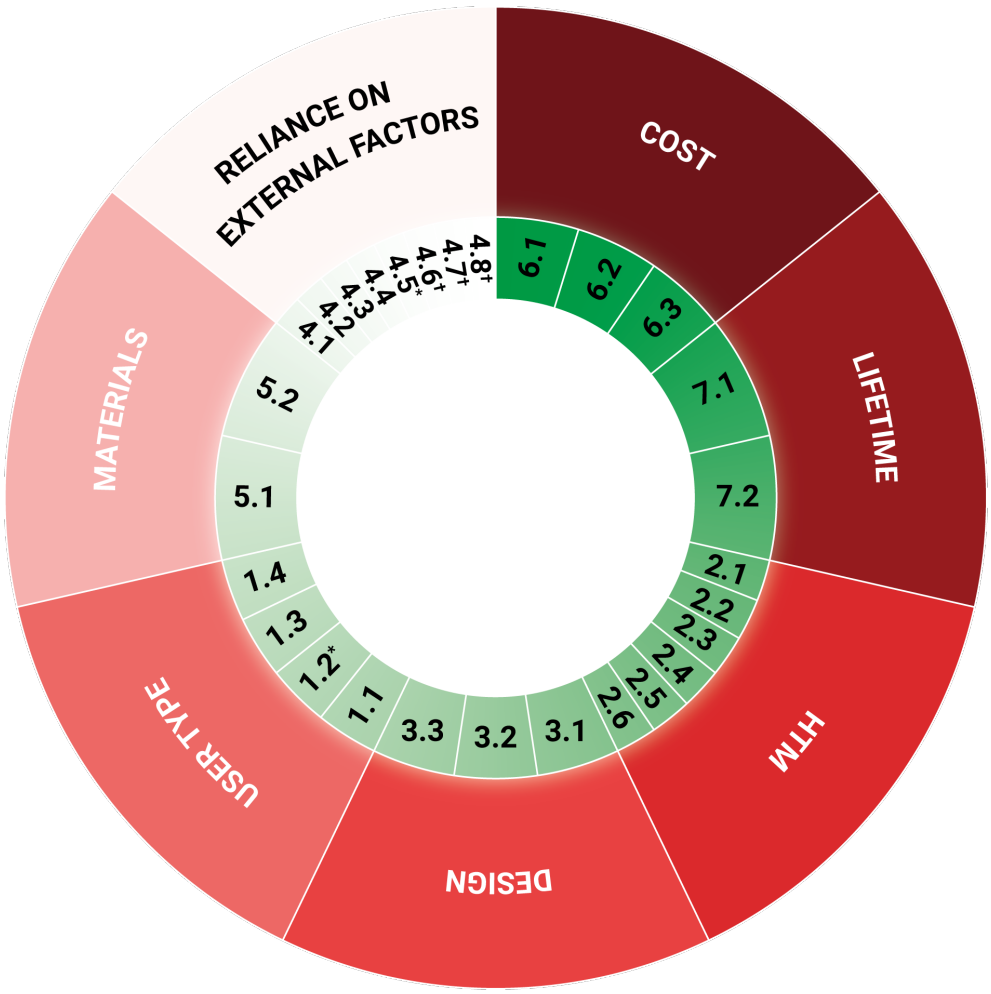


Figure 3.19: The final framework containing the domains and the criteria ranked according to the level of importance. The domains, although approximately sharing the same importance, are presented in descending order of importance starting from cost, clockwise. Each criterion is presented in the same descending order within each domain, too. *Criterion 1.2 is the criterion that was excluded after reliability/internal consistency analysis. *Criterion 4.5 is the criterion that was excluded because deemed of Medium importance. †Criteria 4.6, 4.7 and 4.8 are the criteria added a posteriori of our field studies and they are not currently ranked.The legend for the criteria in this figure can be found in Table 3.9

Table 3.9: The correlations of the criteria grouped by domain. Correlation was reported only if "strong" (i.e., gamma greater than 0.5) and if the respective p-value was less than 0.05. The number specified in the correlation column refers to that of the correlated criteria. The "+" indicates a positive correlation, the "-" a negative correlation. †Criteria 4.6, 4.7 and 4.8 are the criteria added a posteriori of our field studies and they are not currently ranked. For this reason, also correlations are not calculated nor reported (NA).

Criteria	**Correlation**
6. Cost	
6.1 Maintenance costs	6.2,6.3(+)
6.2 Running costs	6.1(+)
6.3 Initial cost	6.1(+)
7. Lifetime	
7.1 Lifetime of MD parts/components	7.2 (+)
7.2 MD lifetime	7.1(+)
2. HTM	
2.1 Need for consumables	2.2,2.3,2.4,2.5(+)
2.2 Need for spare parts	2.1,2.3,2.4,2.5(+)
2.3 Installation requirements	2.1,2.2,2.4,2.5(+)
2.4 Maintenance complexity	2.1,2.2,2.3,2.5,2.6(+)
2.5 Maintenance frequency	2.1,2.2,2.3,2.4(+)
2.6 Compatible consumables/spare parts	2.4(+)
3. Design	
3.1 Portability, compactness, robustness	3.2(+)
3.2 Limiting the number of components/spare parts	3.1(+)
3.3 Reusability	-
1. User type	
1.1 End users' background	1.4(+)
1.2 Easiness of use	-
1.3 Training needs	1.4(+)
1.4 User's understanding of the technical and clinical impact	1.1(+)
5. Material	
5.1 Durability of the material	5.2(+)
5.2 Robustness of the material	5.1 (+)
4. Reliance on external factors	
4.1 Reliance on power sources	4.2,4.3,4.4(+)
4.2 Reliance on water distribution	4.1,4.3,4.4(+)
4.3 Reliance on medical location air	4.1,4.2,4.4,4.5(+)
4.4 Need for sample preparation	4.1,4.2,4.3,4.5(+)
4.5 Understanding/stating the dependence of the MD from the medical location characteristics	4.3,4.4(+)
4.6 Resilience to dusty environments†	
4.7 Resilience to high-temperature environments†	NA
4.8 Resilience to high-humidity environments†	

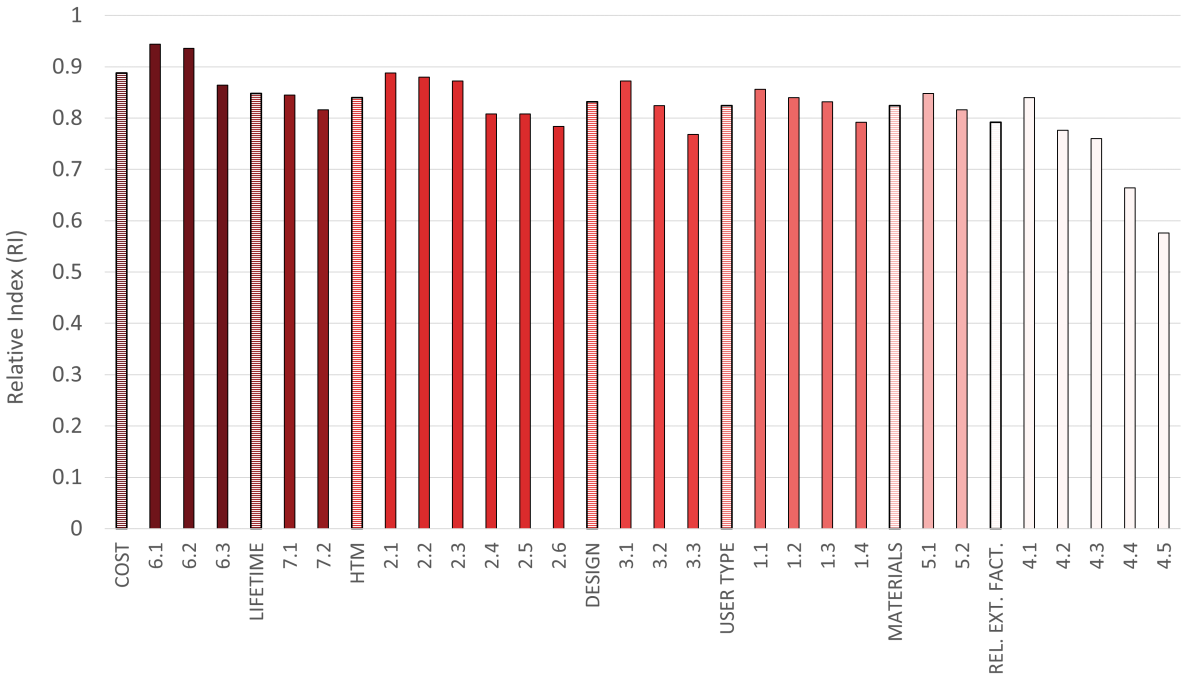


Figure 3.20: The relative indexes are reported for each criterion, grouped by domain. The first column of each group is the relative index of the domain itself. The full name of the criteria could not be reported for brevity. The legend is presented in Table 3.9

Reliance on external factors. Reliance on power sources (4.1) comes first in this domain, followed by the reliance on water distribution (4.2), the reliance on location air (4.3) and the need for sample preparation (4.4), with which it is correlated. All these are essential to the efficient and effective use of certain MDs. As regards understanding and stating the dependence of the MD from the medical location characteristics (4.5), its RI is as low as 0.576, and the Delphi study showed a consensus regarding a "Medium" importance of the criterion. Hence the authors decided to discard it. Three additional criteria were added a posteriori of our field studies, i.e., resilience to dusty environments (4.6), resilience to high-temperature environments (4.7), and resilience to high-humidity environments (4.8).

3.2.4.6 Validation and use of the framework

The protocol (see Appendix C) to test the framework includes an information table with the qualitative scoring of the MDs. The criteria selected only as informative and not discriminatory of a technology are the ones belonging to the cost and lifetime domain. This further division was introduced because the comparison for such domains could be made only if there were references to use. For example, if someone were trying to compare two MDs with similar

functions, he/she would need a MD of reference in order to consider the cost and life domains discriminatory. In that scenario, it would then be possible to compare the costs and the lifetime of one of the MDs compared to the one of reference and consequently assign them values such as "low", "medium", or "high". The 3 criteria added a posteriori are Resilience to dusty environments, Resilience to high-temperature environments and Resilience to high-humidity environments. According to the traffic light rating system adopted, poor performances were marked as red, medium ones as yellow, and good ones as green. For example, as regards the "End users' background", red would denote the fact that the technology could only be used by medical doctors, yellow by any health care professional and green by lay users. Or as regards "Reliance on power sources", red would denote the fact that the technology relies only on the power supply, yellow on the power supply and batteries, and green on the latter and solar panels. Applying this process to one of the selected MDs, i.e., the pulse oximeter, to make further examples, we can notice how it scores yellow for 'End-users' background', as lay users are not enlisted among possible end-users. Such a device also scores green for "Training needs", as no further training is required, and scores red (also the missing data are classed as red) for resilience to dusty, high temperature and humidity environments, as the manufacturer did not give any information about this. The selected MDs were namely: low-cost computed tomography scanner, pulse oximeter, anesthesia delivery for LRSs, mobile-enabled non-invasive measure-through motion and low perfusion pulse oximeter, electrocardiogram handheld digital, phototherapy for jaundice, external fixation for bone fracture and white blood cell counting system. Only 9 out of the 21 discriminatory criteria performed generally well (predominantly green cells) and they belonged to different domains: installation requirements, maintenance frequency and complexity, portability, compactness and robustness, limiting the number of components/spare parts, reusability, reliance on water distribution, reliance on medical location air and need for sample preparation. The 3 MDs that resulted efficient are the two pulse oximeters and the external fixation for bone fracture; the 4 whose efficiency resulted medium are the electrocardiogram, the phototherapy device and the white blood cell counting system; finally, the computed tomography scanner and the anesthesia machine resulted not very efficient.

3.2.5 Discussion

This study aimed to respond to the urgent need for a comprehensive framework for the design of MDs resilient to low-resource settings and to propose a possible solution. To date (April 2021), MD design frameworks have been proven ineffective when using the MDs outside of 'their bubble', i.e. settings

that have more resources and some guaranteed standards that are not readily available in LRSs [3]. The results of this study show the timeliness and importance of such a topic. In fact, the international experts' views were elicited through MCDA, which was proven to aid decision making processes, and knowledge production and consumption [142], being able to capture all the various dimensions of the evaluation problem [143], enhancing the quality of decisions, allowing them to be more rational and efficient and transparent [142, 144, 145], also in the relevant emerging technology and biomedical fields [146]. From the results, it emerged that the experts in different fields shared their opinions and agreed on most of the criteria. A particular criterion had a slightly lower response rate 20/25, with 5 panellists who replied, 'Do not know'. The authors think that this criterion, i.e., Understanding/stating the dependence of the MD from the medical location characteristics (e.g., Group 0,1,2), was underestimated probably because of a general non-expertise in such a specific topic. Correlations are essential to understand how criteria are interrelated. In fact, they give an understanding of the trends that characterise the set of criteria. Positive correlation between criteria A and B means that the higher the importance of criterion A is also followed by higher importance for criterion B. The opposite is true in the case of negative correlation. This type of information is useful to inform the design of the MDs, since the criteria with positive correlations need to be jointly taken into account to guarantee the successful design and development of a MD. For example, the domain of cost, running costs are positively correlated with maintenance costs, but not to the initial costs. This confirms that the respondents consider these two kinds of costs interrelated. Hence, they need to be jointly considered when designing a MD. From the results, it is clear that even if all the domains share a similar relative index of importance, the resulting priorities are a comprehensive representation of the current state of the art (as of 2021) regarding the design of MDs for LRSs. In particular, the domain of cost comes first, and the domain of the reliance on external factors comes last. However, within the domain of cost, the operating and maintenance costs resulted to be slightly prioritised in respect to the initial cost. Although capital costs can be high for some equipment, the operating or maintenance costs are often underestimated. Malkin [95] had concluded that for a MD to be effective and economical at point of purchase is not sufficient for a technology to help LRSs, highlighting common misconceptions, such as the belief that the capital cost of a technology is always the primary barrier. Indeed, the cost is crucial, but the underestimation of the reliance on external factors or of the user type (i.e., the last but two) is dangerous. These factors are the ones that may severely influence the functional operation of MDs, as it has also been reported in the literature, and that leads to the so-called 'contextualised design'. For this reason, as mentioned before,

after their latest field studies in Benin and Uganda, the authors of this paper decided to include three new criteria that underline critical challenges for LRSs, i.e., the presence of dusty environments, high temperatures and humidity. Once again, this stresses, even more, the importance of these factors that are often overlooked. In the authors' opinion, the results from this study are the relevant representation of the current (2021) approach of MD designers; it is clear that there is a need to change the way of approaching MD design if one wants to support global health without differences across the countries. This study is the first of its kind to use a triangulation of qualitative and quantitative methods to obtain a comprehensive and effective framework for the design of MDs resilient to LRSs. This framework is further proof of the need for a change and adaptation both of the existing international standards and the MD design criteria. The authors believe that an approach like the one presented by Adler [72] and currently utilized by the IT industry, i.e., the use of the IP code standard and military standards (MIL-STD-810H), is the future of MD design. The harsh conditions typical of LRSs, in fact, could be simulated through apposite tests for humidity, temperature, pressure et cetera adapted from the military world. Moreover, any researcher involved in the design of MDs or any MD designer could potentially use this framework either to check whether their design is compliant or to start a design from scratch. The validation of this framework proved that the protocol to follow for assessing a MD is quite simple and does not require external expert inputs. Any person with a biomedical engineering background should be able to complete it and straightforwardly assess the technology. The validation also confirmed that the domain of reliance on external factors is often underestimated, as it resulted to be one of those obtaining a majority of yellow and red scores.

3.2.5.1 Limitations of the study

As already mentioned, some of the criteria were classified as informative, because to use such domains for comparisons, there is a need for extra references, which can be investigated in case someone wanted to compare different options of the same kind of technology. In addition, some of the scales are only available as qualitative, as semi-quantitative scales would need to be investigated further with ad-hoc studies, and there are several "-", meaning that no information is available to score some MDs. The latter are data gaps that should be filled to get a more realistic understanding of the performances. Currently, these missing data are assigned the worst-case colour (i.e., red), using a precautionary approach. Finally, the validation that has been carried out is a valid internal validation of the framework, but an external validation/testing could preferably be performed as well.

3.2.6 Conclusions

The aim of this study was not only to highlight the current challenges and gaps in the design process of MDs, but also to show its timeliness and to create a framework for a contextual and user-driven design that can be used for the design of MDs, which will be operating correctly and efficiently in any country of the world, irrespective of the income or the resources. Although Aranda et al. [117] proposed a frugal framework, differently from theirs, ours only focuses on the aspects on which the designer has a potential influence. The advantage of the framework presented in this paper is not only due to the fact that it emphasizes the urgency of taking into consideration particular realities, but also to the technical tool it represents. Such a tool, in fact, can be one of the first steps towards this inclusive approach. Nonetheless, it is pivotal to underline that the authors' invitation to take contextual realities into account should not be misinterpreted as "relativism", which, trying to defend and safeguard differences, ends up failing to see any common prospect. Rather, this framework fosters glocalization, as per Bauman's definition [147]: i.e., the preservation of individual identities within a complex system. In fact, far from dividing the world into its different parts, each characterized by the richness of its peculiarities (none being superior to the others), Augé's theory of the "Non-place", i.e., an effectively inclusive space where each context finds its citizenship [148], could be reaffirmed. To conclude, this framework could encourage and inform the creation of novel contextualised international standards, which would empower LMICs by enforcing import restrictions according to the WTO-TRIPS, by fostering the local production of medical equipment and by obliging MD manufacturers to comply with this new consensus standard if they wanted to market their products in LMICs. Starting from this paper, further international political actions should follow to bring forward design frameworks based on the best available evidence and real users' needs elicited by experts, in order to drive the real change of the existing norms, regulations and standards.

Chapter 4

Use cases

This chapter introduces several use cases, i.e., MDs that were designed and prototyped according to the frugal engineering paradigm presented throughout this thesis. These use cases were divided into three main groups according to their field of application, namely screening, treatment, and clinical engineering, and into two subgroups, namely primary and secondary. As the reader will make out from the the text, these technologies are at a different level of maturity in terms of development. Further conclusive comments regarding this are presented in Chapter 5. All these works are aimed towards the UN's SDGs. In particular, SDG3 - Good health and wellbeing, but also SDG 9 – industry, innovation and infrastructure; SDG 10 – Reduced inequalities; SDG 12 – Responsible consumption and production; SDG 15 – Life on land. The work presented in this chapter is already published [5–7] or currently under review [8, 9].

4.1 Pupillometry via smartphone for LRSs

This first use case belongs to the group of screening.

4.1.1 Introduction

The photopupillary reflex regulates the pupil dilation and constriction according to the intensity of the light that hits the retina and is controlled by the sympathetic and parasympathetic nervous systems. Therefore, this reflex is used as an indirect measure of the central and autonomic nervous system [149]. The key medical applications of the photopupillary reflex measurements include the detection of brain trauma and the assessment of its severity [150, 151], the assessment of the level of anesthesia and pain [152, 153], an aid to the certification of death [154], the evaluation of alcohol [155] and drug intoxication [156, 157], and the study of ophthalmological diseases such as

diabetic retinopathy and Horner's syndrome [149, 158]. A quick evaluation of brain trauma via pupillometry, i.e., the measurement of pupil size, symmetry and reactivity, can make the difference on the patient's health and future life and is an essential part of the supportive care provided in this case [159, 160]. The early management of traumatic brain injury, in fact, minimizes the progression of the injury and improves recovery and clinical outcomes [160, 161]. Accordingly, in many HICs, technologies for photopupillary reflex analysis have been proposed [162–165], also using smartphones [166–169]. Recently, an app for tracking the photopupillary reflex using trained object-detectors was introduced [170]. As regards the pupil and iris detection algorithms, there are various technical solutions available including edge detection and Hough transform [171], Starburst transform [172], blob detection algorithms [1], watershed segmentation [173], gradient vector flow snake-based method [174], and deep learning [175]. However, very little has been proposed for LMICs, where traumatic brain injury is becoming one of the main causes of morbidity and mortality. In fact, Africa owns less than 5% of the motor vehicles in the world and accounts for 10% of global deaths caused by vehicular injuries [176]. In LMICs, and in particular in LRSs, there is a lack of expertise and diagnostics to assess brain trauma [177]. Accordingly, the UN aims to "halve the number of global deaths and injuries from road traffic accidents". The photopupillary reflex can be measured with a simple penlight. Despite the simplicity of the device, accurate and reliable assessments of the photopupillary reflex require an experienced user: Couret et al. [178] demonstrated that the penlight photopupillary reflex observation in neurocritical care is prone to human error, limited reproducibility and low precision. In many LMICs, diagnosis and healthcare delivery is hindered by the lack of specialized clinicians, alongside the lack of resources and poor supply chain [63]. An alternative is the digital pupillometer, i.e., a MD performing automated pupillometry using infrared cameras, which are expensive and not designed (i.e., not resilient) to operate in the harsh environments (i.e., dusty, warm, humid, with unstable power supply etc.) typical of SSA. This article presents the early results of our study aimed at designing, prototyping and validating a mobile app, based on relevant international and military standards, for testing the photopupillary reflex via Android in LRSs. The aim of this app is to act as a screening tool that can be used by nurses (or also lay-users) to test the direct pupillary reflex in order to screen the incoming patients' conditions (e.g., suspected presence of brain injuries) and plan further investigations. This is crucial in LRSs. Specifically, this paper describes the acquisition of videos, the signal processing and their technical validation. The results from eight field studies

[1] https://it.mathworks.com/matlabcentral/fileexchange/49599-tracking-pupil-using-image-processing

in SSA have informed the contextualized and user-driven design, and can also be relevant for informing the design of other devices for LMICs. In fact, additional design criteria were added, due to the challenges typical of SSA, which included the lack of specialized clinicians, the scarcity of funds, of spare parts and consumables, poor maintenance, which hinder the safe and efficient operationalization of MDs. This paper demonstrates how these peculiar contextual characteristics can be cascaded into the design of a mobile app and redesign of a MD. This work was inspired and informed by existent regulations and standards. In particular, those related to existing pupillometers were taken into consideration, because of their similarity to our solution. Further punctual analysis of standards and requirements will be needed in the later stages to pass from prototype to product.

4.1.2 Methods

4.1.2.1 Ethnography-driven User-need and Contextual Analysis in LMICs

Designing MDs for LRSs requires the synergy of different but complementary methodologies, comprising of not only engineering, scientific and quantitative techniques, but also qualitative approaches such as ethnography research [179]. Ethnography applied to the design is, in fact, one of the keys to further develop the current technological progress, by allowing designers and researchers to understand the design challenges more deeply, with a focus on a particular kind of end-users and their surrounding contexts. For this reason, the need and context analyses were conducted with a mix of methodologies (see Figure 4.1).

They were structured in three steps, which were iterated twice: general formalization, contextualization in SSA countries, and field studies in Benin and Uganda. The first requirements were identified by reviewing the literature on MDs and their related standards (i.e., ISO 14971 – Medical devices – Application of risk management to medical devices, IEC 62366 - Medical devices — Part 1: Application of usability engineering to medical devices, IEC 62304 - Medical device software — Software life cycle processes, ISO 15004 - Ophthalmic instruments — Fundamental requirements and test methods), and performing focus groups with international experts of MD design and management, and hospital engineering. Five focus groups were held with world leading experts of biomedical and clinical engineering during international conferences [11, 57, 180] and the Third and Fourth WHO Global Fora on MDs (2017, 2019). The contextualization in SSA was performed by administering surveys to African Scholars, and holding focus groups with biomedical and clinical engineers in SSA countries (in accordance with the ethical approval REGO-2018-2283). Five

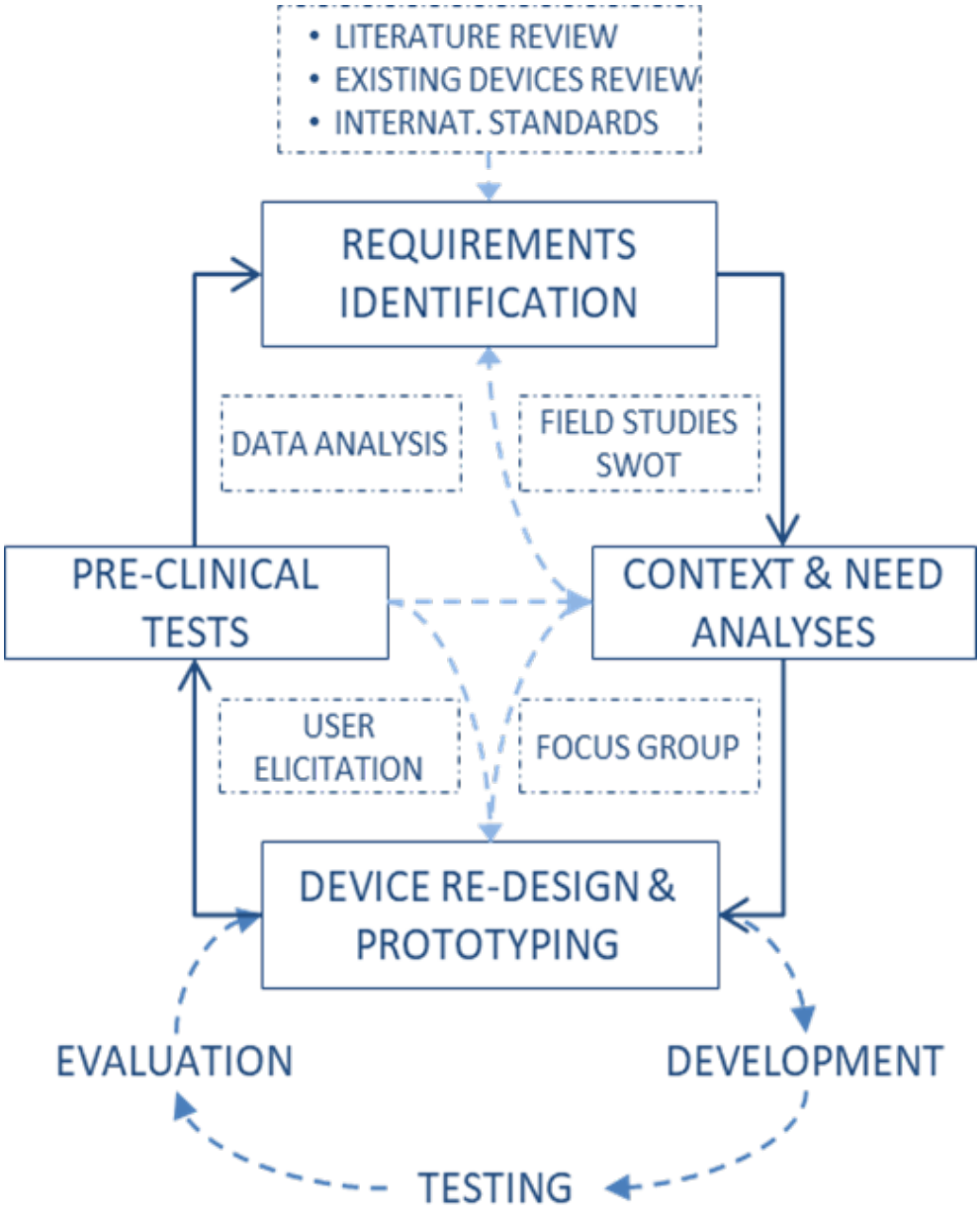


Figure 4.1: Context-driven design: the methodologies used for the design and evaluation of the proposed pupillometer.

focus groups were held in SSA and were attended by delegates from more than 12 SSA countries (two during the AfricaHealth conferences, two in Benin at the Ecole Polytechnique d'Abomey-Calavi, and one in Ethiopia) [35]. Three field studies were conducted in Benin in April 2017, January 2018 and November 2019 and one in Uganda in October 2019. During these studies, several aspects of MDs and MLs were analyzed. This included electric measurements, examinations of MDs, inspections of MLs in 6 African hospitals and semi-structured interviews with the available staff, including biomedical engineers, technicians, nurses, doctors and hospital directors [1, 2]. In collaboration with the International Federation of Medical and Biological Engineering African Working Group, focus groups were organized. The ethnographic analysis was conducted in accordance with the ethical approval REGO-2018-2283, obtained from the Biomedical and Scientific Research Ethics Committee. For quality insurance, the prescriptions of the European regulations on MDs, which equate medical apps to MDs, were considered. Moreover, this work was based on the 5As principles of the WHO, i.e., affordability, availability, adequacy, accessibility, and appropriateness, in line with the solutions proposed in the WHO compendium of innovative health technologies for LRSs.

4.1.2.2 Development of the Smartphone-based Pupillometer

The development of the smartphone-based pupillometer followed 5 stages, namely the smartphone pupil stimulation and video acquisition, the preprocessing, the image processing, the system integration and the technical validation, which will be described thoroughly in the following subsections. These stages were developed and validated with videos acquired from 11 healthy subjects in accordance with the ethical approval obtained from the Ethical Committee of University of Campania Luigi Vanvitelli[2] . Further details about the dataset can be found elsewhere [162].

- **Smartphone pupil stimulation and video acquisition.** During the first feasibility study, the pupil of a subject with light brown eyes was stimulated with the flash embedded in a smartphone (i.e., ZTE Blade C341), with the illuminance set at 480 lux and the duration at 500ms. The photopupillary reflex was captured with a second smartphone, namely a Samsung Galaxy a7 (2016) with a 13-megapixel camera, although the final app integrates both functions and only one smartphone without tripod support is needed for future use (see Figure 4.2). In fact, in the final app the video recording and the flash are synchronized as follows: the flash starts 2s after the recording has started, lasts for 500ms and

[2]Registration number 500, approval title "Studio pilota sull'utilizzo della pupillometria cromatica per la diagnosi e il monitoraggio delle degenerazioni retiniche ereditarie")

the recording is stopped when 9s in total are reached. This allows a recording of about 6-7 seconds of the pupil reaction, in line with the typical duration of the event [181]. Both smartphones were selected depending on their availability at the times of the experiments and were placed on a tripod at a distance of 8 cm from the subject's face. In literature, distances in the range of 8-15 cm were used [168, 182, 183]. As the luminance will vary according to the distance from the light source following an inverse-square law [184], the luminance at various distances (i.e., 5 to 20 cm, with a 1-cm step) was also evaluated to check whether small differences in distance could significantly affect it. It resulted that in the above-mentioned range, i.e., 11.5 ± 3.5 cm, the luminance had an average percentage change of 10.7%. Furthermore, it was investigated whether the flashes at 8 cm and at 15 cm would trigger a pupil reaction, and whether the minimum reached by the pupil would be similar. This was tested with two smartphone models available at the time of writing (i.e., a Doogee S60 Lite and an iPhone 7). The pupil minimum, expressed as the normalized pupil/iris ratio, resulted to be varying in the range $71.2 \pm 2.7\%$ (percentage variation of 3.8%) with the Doogee S60 Lite flash, and in the range $50.7 \pm 0.4\%$ (percentage variation of 0.8%) with the iPhone 7. This difference is probably due to the more powerful flash embedded in the second smartphone model. Therefore, assuming the test will be run with the same device, the pupil contraction will remain substantially the same in the recommended distance range. The height at which the two smartphones were placed was so that the eye resulted to be at the center of the frame. The opposite eye was neither stimulated by the flash, nor covered. Throughout these experiments the ambient light was measured using a luxometer (Dr. Meter, LX1010B), in order to ensure a approximately constant baseline light intensity. The videos were then fed to a dedicated algorithm as detailed below. At this prototyping stage all the signal elaborations are performed on Matlab. In the future, the definitive algorithm will either run on a dedicated server application that will include a Matlab compiled dynamic link library (DLL) to foster the accessibility of older models of smartphones, or will be embedded in the mobile device itself, for the most performing models.

- **Preprocessing.**

  The images contained in the frames of the video are preprocessed by turning them into gray-scale (see Figure 4.3, IIa), binarizing them according to a certain threshold, and going through morphological opening (i.e., erosion followed by dilation) and closing (i.e., dilation followed by erosion) to remove any dark unrelated pixel or particularly small objects

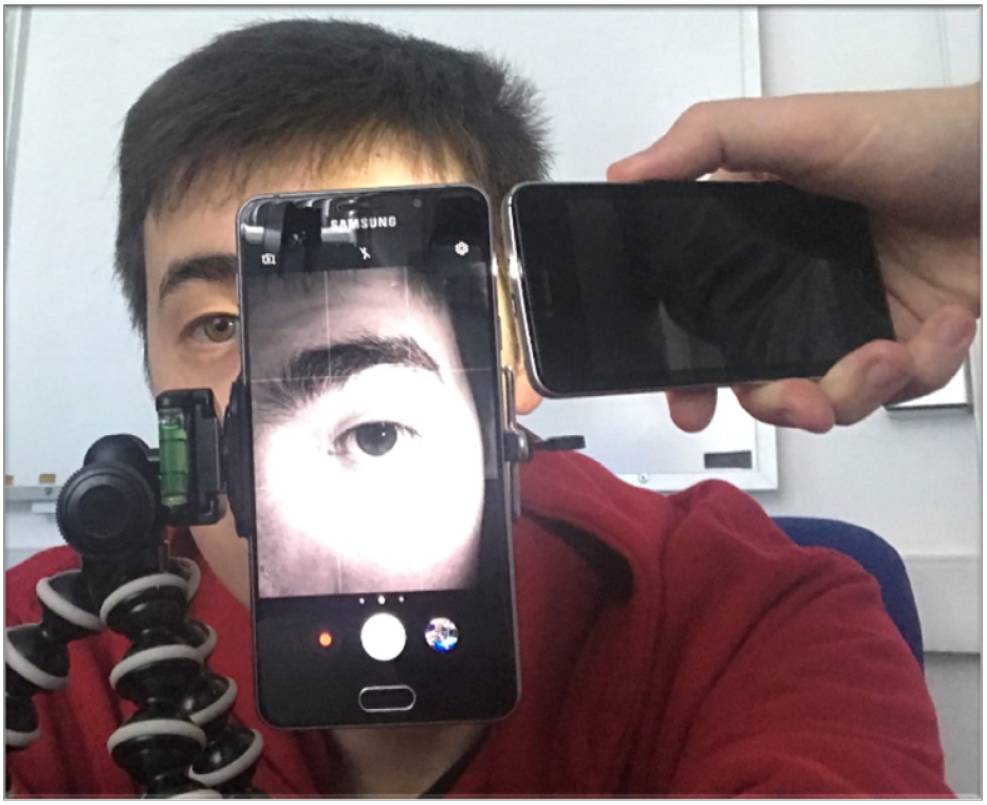


Figure 4.2: The layout of the first feasibility study.

(see Figure 4.3 2, IIb). The binarization phase is a pivotal pre-step and can be influenced by the overall light intensity of the frames: if the intensity changes over the frames, the results may not be ideal. In case the acquisition is performed with high intensity of light (e.g., flash light on), a higher threshold is selected, by assessing the mean intensity of the first 3 frames (i.e., baseline) and setting the highest threshold if the mean intensity of a frame results 5% greater than the baseline. The values of the two thresholds were determined empirically. The final app records 9-s H.264 encoded-videos with a 30-fps frame rate and an average size of 11.5 MB.

- **Image Processing.** The image recognition algorithm consists of two main parts: the pupil and the iris recognition. The reason behind the choice of including the iris part is due to the contextualization of the design and will be further explained in the results subsection 4.1.4.1 A.

  1. *Pupil recognition algorithm.*

     The algorithm (see Figure 4.3) starts by prompting a user input, i.e., the framing of the part of interest (i.e., the eye). The user can draw a rectangular box, superimposing it on the first frame of the video, and the coordinates of such polygon will be utilized to

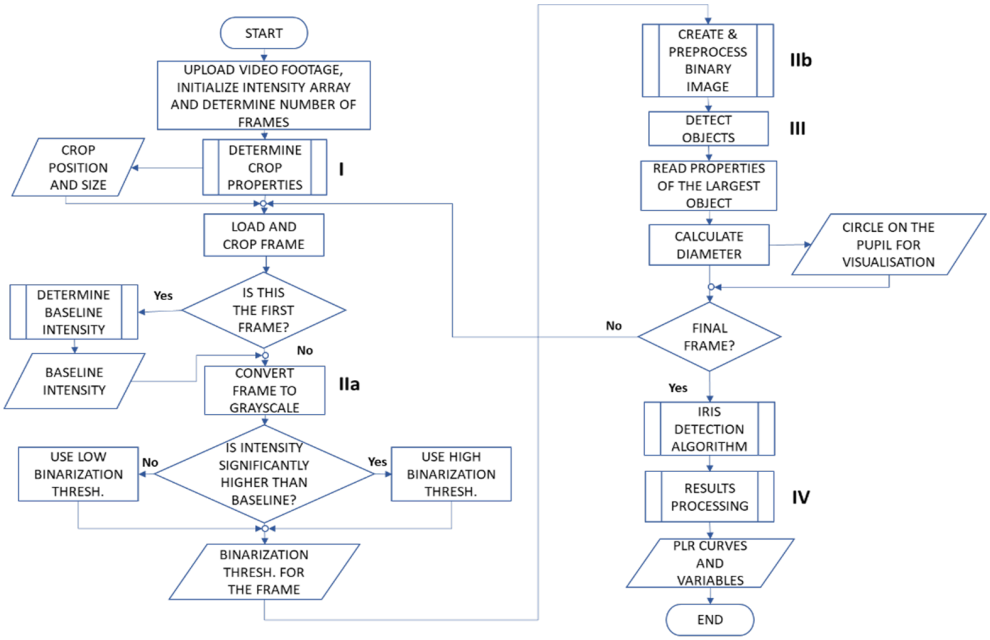


Figure 4.3: The flowchart illustrates the various steps of the preprocessing and image processing, with a specific focus on the recognition of the pupil.

crop the frames used during the tuning step of the algorithm (see Figure 4.3, I) (more information can be found in Appendix D). The latter consists in running the commands for preparing the images (as described above) and for finding the pupil and its center, only over the first three frames of the video. As regards the pupil recognition, three different approaches were tested, namely blob-detection algorithm, circular Hough transform, and watershed transform. These methods were assessed computing the mean absolute error (MAE) and the correlation with the manual measurement (Pearson's r). In particular, the blob-detection algorithm used in the comparison was a variation of the original that consisted in removing the spikes and substituting them with the average value of the points preceding and following the spike. The blob-detection algorithm was inspired by Barragan's algorithm[3], which detects the blob with the greatest area contained in the picture, circles it, and finds its center. The diameter output of the tuning stage is called baseline diameter, because it is then utilized to automatically calculate the cropping frame dimensions for the main part of the algorithm, by creating a framing square with a side equal to four times the baseline diameter, centered on the pupil. The same pupil recognition algorithm is then called again upon all the newly-cropped frames and an array

[3]https://it.mathworks.com/matlabcentral/fileexchange/49599-tracking-pupil-using-image-processing

containing the unprocessed diameter is saved (see Figure 4.3, III).

2. *Iris recognition algorithm.*

   The algorithm (see Figure 4.4) starts by prompting a user input, i.e., the framing of the part of interest (i.e., the iris). A circle is superimposed over the first frame and the user can resize it according to the iris boundary in the frame. Given the position of three points of such circle, its equation is derived as well as the baseline radius of the iris, which is then used as a parameter for the circular Hough transform algorithm (see Figure 4.4, II, and Figure 4.5). In this case, the same three algorithms tried out for the pupil recognition were tested as well. Before being fed to this algorithm, the frames are preprocessed as described above (see Figure 4.4, I, IIIa, IIIb). Moreover, as the outcome of the application of the circular Hough transform algorithm depends on the sensitivity, an extra precaution is taken in this direction. In fact, although the initial sensitivity is set to 0.88, if no circle is found during the first run, the sensitivity is increased by 0.02 until a circle is found. An array containing the unprocessed diameter is saved.

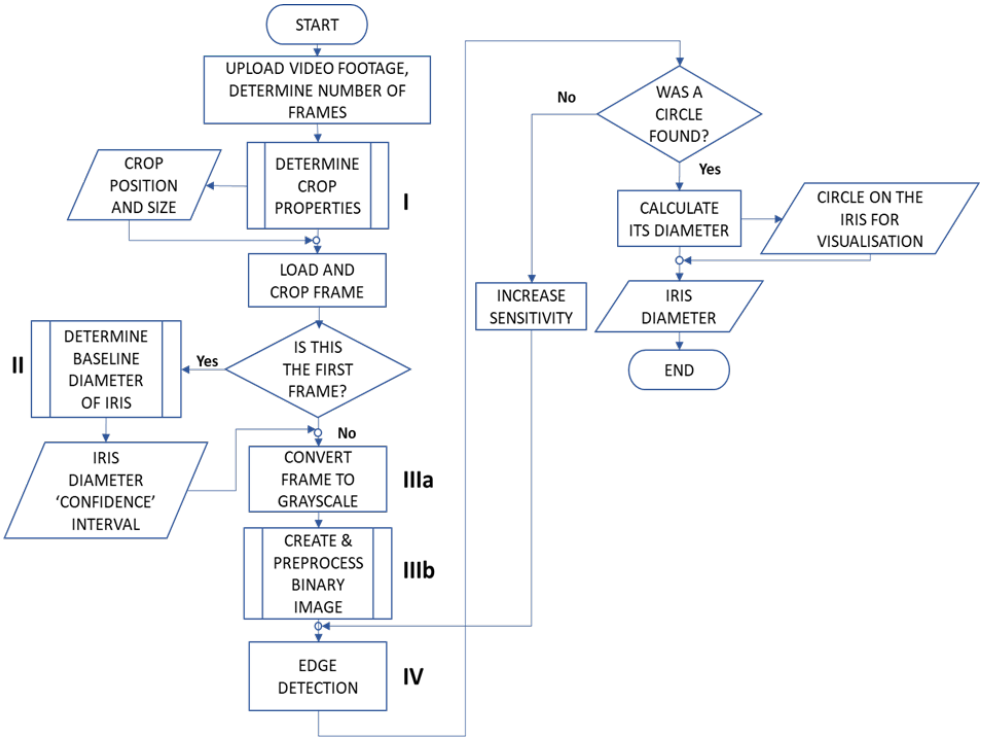


Figure 4.4: The flowchart illustrates the various steps of the image processing, with a specific focus on the recognition of the iris.

3. *Postprocessing.* The acquired pupil measurements were often subject to artifacts such as blinking and image overexposure due to flash.

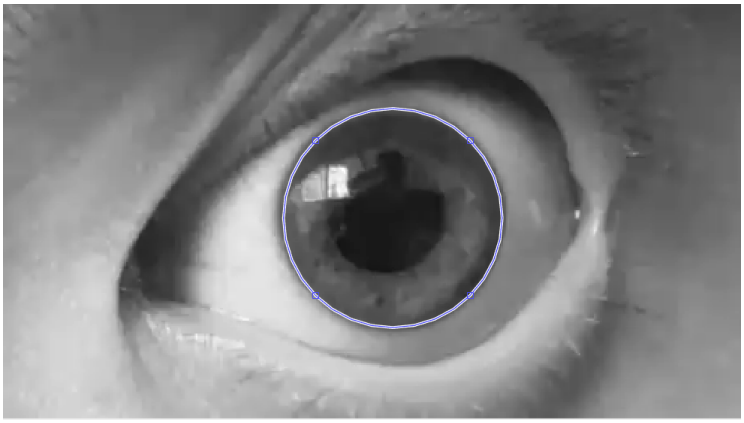


Figure 4.5: The manually superimposed circle over the iris used to calculate one of the parameters of the Hough transform, i.e., the iris radius.

For this reason, a series of functions were applied in order to smooth spikes and filter out noise. In particular, the affected data were identified, removed from the dataset and the gaps were filled using an interpolation. As regards the flash, the above-mentioned threshold for the binarization was designed to tackle this problem. However, the method is not completely robust and can fail to switch to the correct threshold in the first and final frames of the flash, when it is not at full brightness. Consequently, the flash-related frames were removed and substituted with a linear interpolation. This would not affect the overall performance as the first part of the constriction phase of the photopupillary reaction is steep and approximately linear. As regards the blinking artifact, it partially or completely obstructs the pupil, making the algorithm track nothing or a larger area (e.g., a shadow under the eyelid). Such sudden change of the detected area is a good indicator of when the pupil detection fails. Detrending and differentiation were used to identify these sudden changes: the data points affected by blinking are flagged when the local derivative exceeds a threshold in magnitude. Also in this case, the flagged points are removed and linear interpolation is used to fill the gaps (more information can be found in Appendix D).

Finally, the ratio between the diameter of the pupil and that of the iris is calculated and normalized to the initial value. The values related to the frames preceding the pupil reaction are individuated and substituted with 100% values. The part of the array related to the pupil reaction is fitted with a Gamma function, as suggested by Knapen et al. [185] (see Figure 4.3, IV). The algorithm also calculates some variables relevant to pupillometry:

– Pupil minimum, the minimum size reached by the pupil at

the end of the constriction phase; the constriction phase was considered to start when the pupil/iris normalized ratio fell under 98% of its original value;
- Latency, the delay in the pupil response calculated as the time between the start of the flash and the start of the constriction phase;
- Max constriction velocity, the maximum rate of change in the pupil diameter during the constriction phase;
- Mean constriction velocity, the average rate of change of the pupil diameter during the constriction phase;
- Mean dilation velocity, the average rate of change of the pupil during the dilation phase, which is contiguous to the constriction phase and was considered to end when the pupil/iris normalized ratio overtook 98% of its original value;
- T75, the time implied by the pupil to recover 75% of the amplitude of the constriction starting from the peak of the constriction;

4.1.2.3 System Integration

The resulting pupillometry system has been designed as a three-tier application:

- Presentation layer: the Android app will be used for acquiring the video samples and firing the flash.
- Logic layer: a connection with the server code performing the analyses will be developed. The app will act as client. In case of high performance devices, both the client and the server software will be running on the mobile device.
- Data layer: our system will be linked to the database and web application described in [163–165] through RESTful dialog and dedicated APIs.

4.1.2.4 App Design

The app was developed in Android Studio, using Java for the implementation of functions and XML for the design of the user interface, targeting Android-based smartphones with an API level of at least 21 (i.e., Android 5.0 Lollipop), because of the use of the 'camera2' package. This choice allows 94.1% of Android users to use our app, as only 5.9% of the Android-based smartphones have an API level lower than 21 worldwide (and similar trends can be found in Africa)(from Android Platform/API version distribution – Android Studio) [186]. The logo, representing an eye-shaped logarithmic spiral, was hand-drawn and digitized using GIMP (GNU Image Manipulation Program).

4.1.3 Technical Validation

4.1.3.1 Video Acquisition Procedure and Image Processing

All the frames of one of the acquired videos were analyzed both with the Matlab algorithm and manual measurements. In particular, the frames were analyzed manually by one two independent authors that were blinded to the output of the pupillometer, in order to reduce the risk of bias of the authors: for each frame the diameters of the pupil and of the iris were measured twice and averaged in order to reduce the measurement error. Also in this case, the values related to the frames preceding the flash were individuated and substituted with 100% values. Consequently, Pearson's r and the associated p-value, the root mean square error (RMSE) and the MAE were calculated for the Gamma-fitted signal and the raw automated signal, compared to the manual measurements. Moreover, the error rate was estimated by calculating the percent error and counting how frequently it would go over a 10%-threshold.

4.1.3.2 Benchmarking

Our pupil tracking algorithm was also validated against the output of an IR Pupillometer (DP-2000 - NeurOptics). The gamma fit in this case was not needed because of the non-interaction between the flash and the IR recording. The technical validation was done based on the output variables, specified above. In particular, the variables outputted by the IR pupillometer were normalized in respect to the initially measured pupil size in order to make them comparable with those resulting from our algorithm. The RMSE and MAE were calculated for each variable and for both the algorithms, comparing them with those coming from the manual measurements, taken by two independent and blinded authors. Consequently, 3 Bland-Altman plots were generated for each of the 4 variables, after testing whether their residuals were normally distributed with a Shapiro-Wilk test [187] (normality being a necessary condition for such plots). The Bland-Altman plots compared the app Algorithm and the IR Algorithm, the app algorithm and the Manual measurements and the IR algorithm and the Manual measurements.

4.1.3.3 Testing the Safety of the Flash

An experiment was set up to test the safety of use of a smartphone flash on the human eye, although the safety of the procedure has been confirmed by preliminary research [182]. The smartphone was placed on a tripod and an operator held the sensor of a luxometer (Dr. Meter, LX1010B) in front of the camera at a distance of interest for pupillometry, i.e., 8.5 cm. Firstly, the illuminance in this condition (i.e., ambient light) was recorded; secondly

the flash was turned on and the illuminance in this condition was recorded. Hence, the illuminance could be easily calculated and compared against the ISO standards (ISO 15004-2, Ophthalmic instruments - Fundamental requirements and test methods, Part 2, Light hazard protection) after a conversion to W/cm^2.

4.1.4 Results

4.1.4.1 Ethnography-driven User-need and Contextual Analysis in LMICs

The contextual analysis highlighted that SSA countries have [1, 2]: extremely limited resources, an insufficient number of healthcare professionals and of specialized doctors; inadequate hospital infrastructures, highly unstable main power supply, poor transport infrastructure and supply-chain, and an uneven distribution of the resources that are concentrated in the capital to the detriment of remote areas. Nonetheless, SSA can count on a very young population, a wide diffusion of mobile phones, smartphones [188], and Information and Communication Technology literacy. There is a wide diffusion of one dominant smartphone operative system (i.e., 86.39% of smartphones based on Android) [189] and a good coverage of wireless telecommunication. Prospectively, the SSA market of MDs is fast growing (the compound annual growth rate is around 6%). The adoption of new technologies meets limited inertia and healthcare operators are resilient. In fact, working in challenging conditions pushes workers to practice with the unpredictable conditions and events, developing a great capability to react to, respond to and recover from emergencies. Nonetheless, this positive attitude comes with evident risks too. Often, non-specialized personnel respond to the MDs malfunctioning with creative shortcuts, which tend to become chronic solutions, prone to new risks, hindering the recovery of the initial level of effectiveness and safety [190]. Finally, a massive "brain drain" affects doctors and specialized doctors, who move to other countries for better opportunities, further depleting SSA health care systems [191]. The results of the contextual analysis have been discussed with African scholars and healthcare personnel in Benin, Ethiopia and South Africa, resulting in a series of specifications for the local manufacturing of a resilient pupillometer, with its consumables and spare parts. The design should be low-cost, based on free design and manufacturing processes, it should empower non-specialized healthcare personnel and providing clear guidance or affordances, possibly be battery-based and resilient to the unstable power supply, resilient to misuses, requiring no maintenance and easy to clean, and based on Android smartphones, possibly compatible with the high degrees of ingress protection (e.g., IP68) described in IEC 60529 and with rugged and military standards (e.g.,

MIL-STD-810G). None of the pupillometers reviewed resulted sufficiently resilient to LMICs. Existing smartphone solutions meet the cost-requirement, but as it emerged from our study, this is not the only criterion for being resilient in LMICs. For example, most of the proposed solutions widely utilized accessories and spare parts, including external LEDs, filters, and lenses, which will hinder the lifetime of the device in SSA. In fact, such parts would be difficult to retrieve, repair or replace in LRSs [1, 2]. Moreover, when deepening the design principles of a pupillometer, two technical requirements emerged: computational capability compatible with an old Android smartphone; use no accessories or only accessories that could be locally manufactured (e.g., 3D printed). This last criterion particularly influenced the design of the app. The majority of existing pupillometers utilize visible light to stimulate the pupil and infrared (IR) cameras to film its constriction, in order to avoid artefacts. Most smartphones do not contain IR cameras, therefore visible light was used both to stimulate the pupil, using the phone flash, and to film its reaction with the phone camera. As a consequence, the video frames coinciding with the flash resulted overexposed due to the sudden change of luminosity and the proximity of the subject, requiring the adoption of a fitting algorithm to recover the missing pupil diameter in those frames. Moreover, phone camera frame rates are lower than the one of many pupillometers. Thus, the proposed algorithm fitted the acquired diameter data first with a linear fitting, in order to recover missing data due to the flash, and then with a Gamma distribution for approximating missing frames, reconstructing the complete response of the pupil, as proposed in [185]. The interpolation also reduced the blinking artifacts, affecting also standard pupillometry. Moreover, the distance between the eye and the device created artifacts in the estimation of the pupil diameter. These artifacts could be limited with a recycled plastic 3D printed accessory clipped on the mobile phone, aiming at keeping the eye to phone distance constant. However, since a 3D printer could be not available, the proposed algorithm for the recognition of the pupil reflex was based on the ratio between the diameter of the pupil and that of the iris. In fact, while the pupil diameter reacts to light, the iris does not. The ratio was normalized with the value measured before the flash shooting to facilitate the reading of the pupil diameter. The adoption of these features required a specific technical validation of the final algorithm and app.

4.1.4.2 Development of the Smartphone-based Pupillometer

A total of 4 videos were recorded, in which the eye was stimulated 3 times in order to be sure to capture a good-quality response (i.e., absence or reduced number of blinks).

Preprocessing and Image Processing. Three methods were tested for the pupil and iris detection: a blob-detection algorithm, the circular Hough transform, and the watershed transform. The blob-detection algorithm outperformed the other methods with lower MAE (3.9% versus 4.55% of the Hough transform, and 21.25% of the Watershed transform) and higher correlation (Pearson's r of 0.95 and p-value <0.00001 versus 0.84 and p-value p-value <0.00001 of the Hough transform, and -0.03 and p-value of 0.83), being selected for the pupil tracking (see Figure 4.3, III, Figure 4.6). This choice also avoided the introduction of an extra user input, i.e., the pupil radius range, which is necessary for the Hough transform to work. The Hough transform outperformed the other methods in tracking the iris. Consequently, the Hough transform was performed for the iris tracking (see Figure 4.4, IV, Figure 4.6). Figure 4.7 shows the comparison of four signals, namely the gamma-fitted ratio, the algorithm measurement, the manual measurements, and the raw algorithm measurement. The removal of the flash and blink artifacts via post-processing are evident in Figure 4.7, by comparing the raw and the processed signal.

App Design. The app, named Oida (meaning "I have seen" and "I know", from Ancient Greek οραω), for tracking the photopupillary reflex is being finalized. As of now, the app comprises of a Main Activity, Instructions Activity and a Camera Activity (see Figure 4.8). It is available in two languages: English and French, both widespread languages in SSA.

4.1.4.3 Technical Validation

Video acquisition and image processing. During the manual validation (see Figure 4.7), the Gamma fitted ratio resulted significantly highly correlated with the manual measurement (Pearson's r = 0.963, p-value <0.0001 versus Pearson's r = 0.982 and p-value <0.0001 of the raw automated signal (app)), with a RMSE and a MAE of 3.20% and 2.24%, respectively (versus 3.96% and 3.09% of the raw signal). Moreover, the error rate for the Gamma fitted ratio resulted to be 7.14%.

Benchmarking. Ten videos acquired by clinical ophthalmologists with the IR-pupillometer on healthy subjects were analyzed with the IR-pupillometer software and with the app algorithms in Matlab. Figure 4.9 shows the pupil reaction over the frames, captured by the three different algorithms. Resulting measures were compared with those calculated by hand after annotating the diameter of the pupil manually for each video-frame. The MAE and RMSE demonstrated a significant improvement in comparison with the software provided with the commercial device, for all the variables, as reported in Table 4.1. The agreement among the measurement methods, namely app algorithms/IR

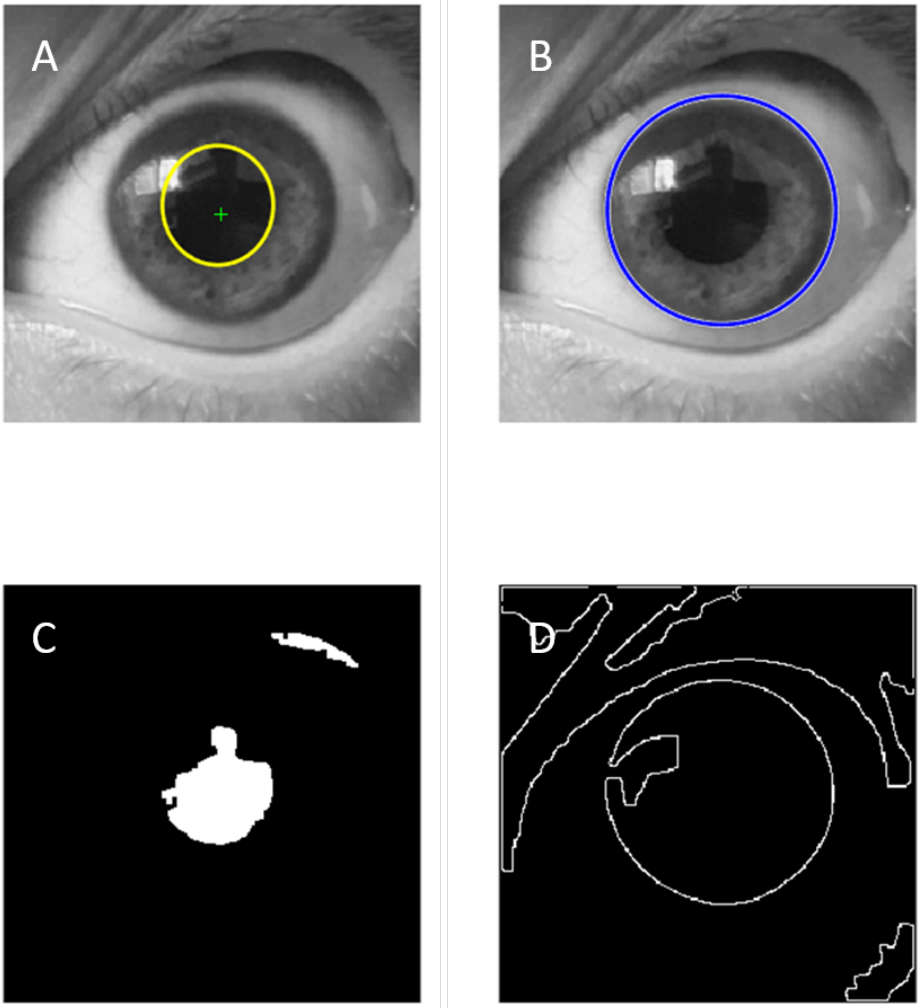


Figure 4.6: The pupil (A) and iris (B) tracking algorithms and the two different methodologies used (C, D).

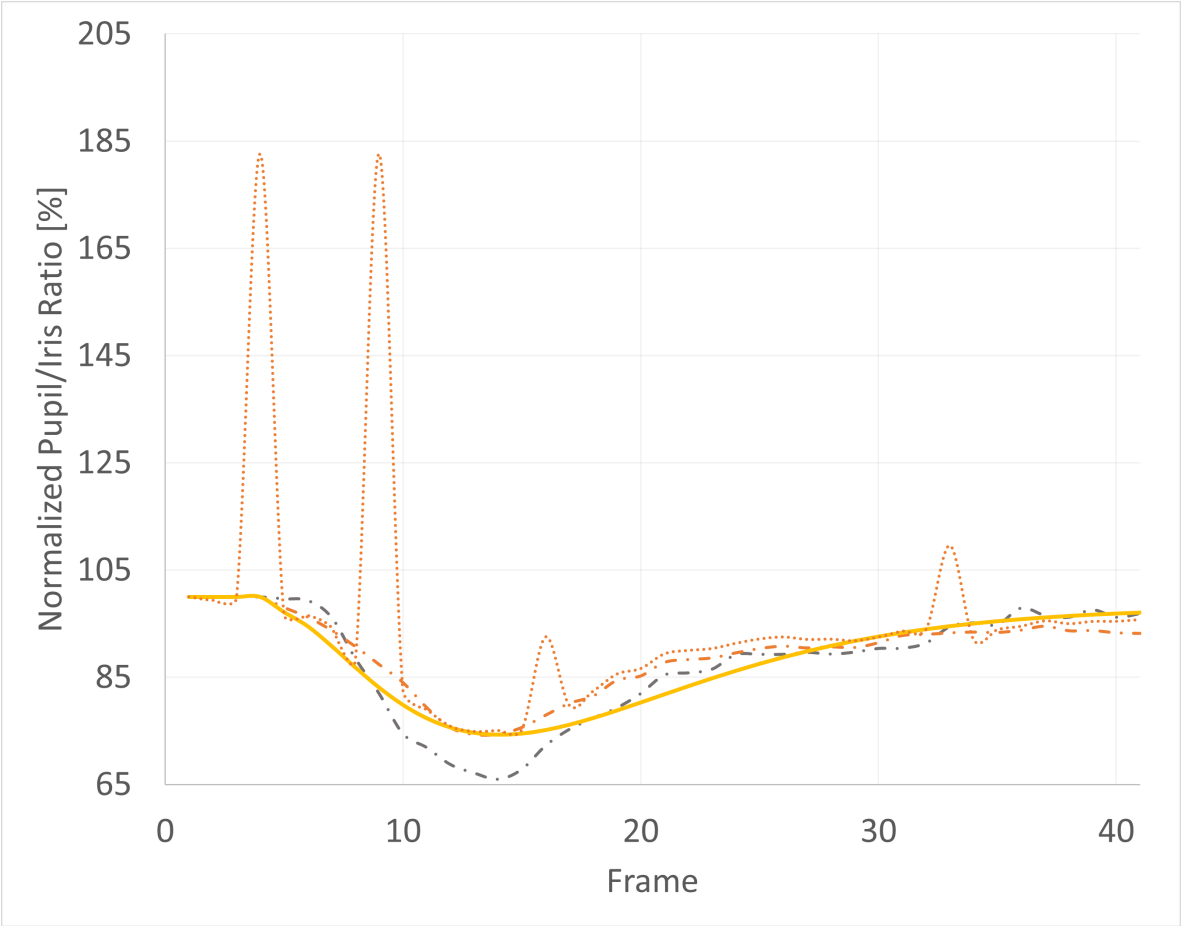


Figure 4.7: A comparison of the signals: the manual measurements (dashed gray line), the processed automated algorithm (dashed orange line), the raw automated algorithm (dotted orange line), and the Gamma-fitted ratio (yellow line).

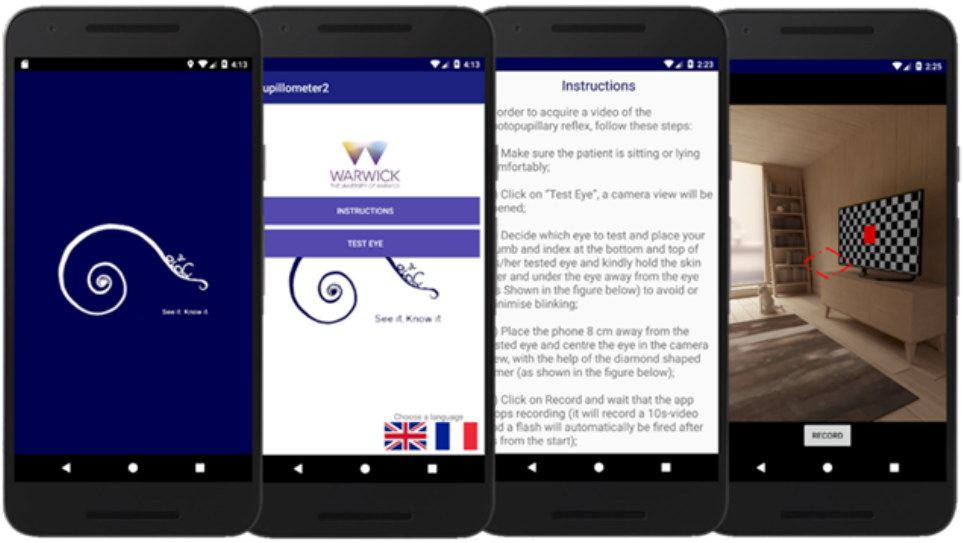


Figure 4.8: Screenshots of the App: Splashscreen, Main Activity, Instruction Activity and Camera Activity (emulated camera).

method, app Algorithms/Manual method and IR method/Manual method, was estimated with Bland-Altman plots [192–194], following the Shapiro-Wilk test for normality [187]. All the differences imputed to the Bland-Altman plot resulted normally distributed with a $0.842 < W < 1$ [187] at a 95% confidence level. The complete Bland-Altman plots are available in Appendix D. Table 4.2 reports the 95% limits of agreement for each variable (the lower the better). The agreement between the app and the manual method outperformed the other methods.

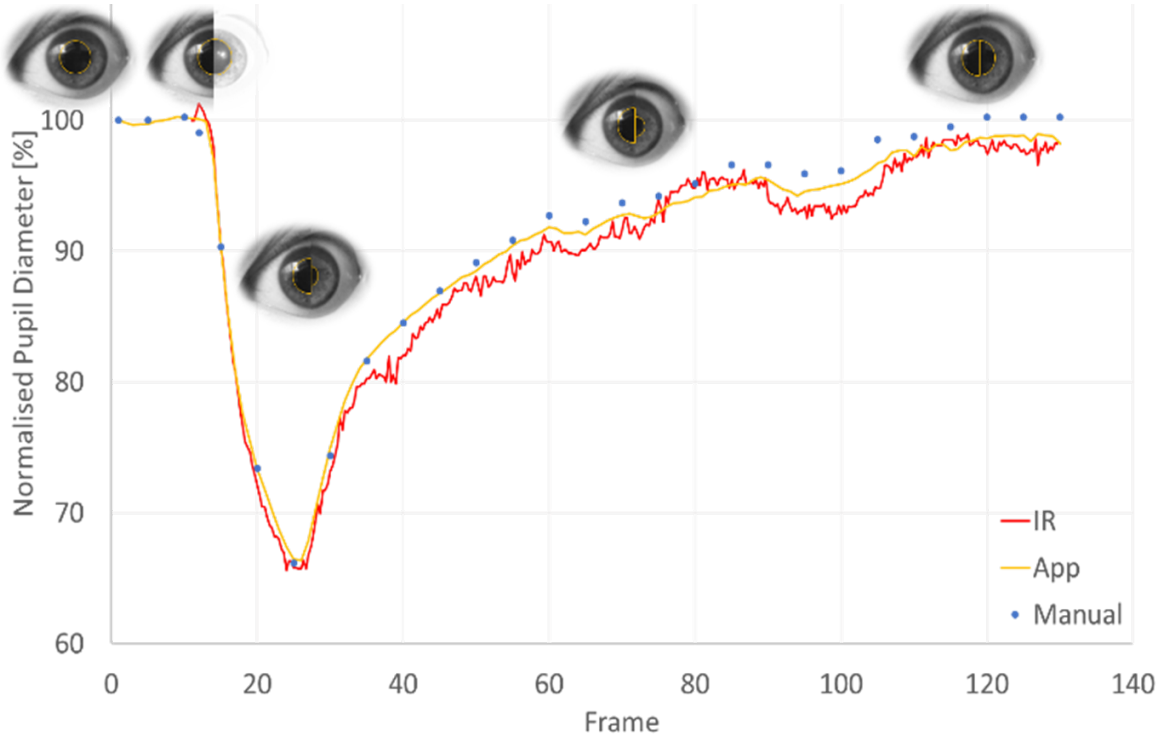


Figure 4.9: The normalized pupil diameter over the frames. Superimposed on the curve, 5 sample snapshots acquired during the app testing. Each snapshot comprises of two halves, highlighted by a yellow semi-circle: each left half represents the initial condition, and each right half represents the evolution of the response.

.

Testing the Safety of the Flash. The base illuminance (i.e., the one of the ambient) was measured at 200 lux; since the illuminance in the 'flash on'-state was 680 lux, the illuminance of the flash alone was 480 lux. The comparison of this value to the above-mentioned ISO standards ensured the safety of the procedure. In fact, 480 lux convert to $7.03 * 10^{-5} \frac{W}{cm^2}$ under the hypothesis of an average wavelength of 555 nm (the ISO standards set the max allowed value to $0.706 \frac{W}{cm^2}$).

Table 4.1: Values of the mean absolute error and root mean square error for the IR pupillometer and for our solution.

Parameter		**MAE**	**RMSE**
Pupil Minimum (%)	IR	1.11	1.55
	app	1.00	1.36
Max Constriction Velocity (%/s)	IR	6.76	8.07
	app	2.56	3.26
Mean Constriction Velocity (%/s)	IR	2.85	3.70
	app	0.47	0.70
Mean Dilation Velocity (%/s)	IR	6.84	7.35
	app	0.11	0.14

Table 4.2: Values of agreement between methods are shown for each of the four variables.

Variable		**Limits of Agreement**
Pupil minimum	app-IR	±2.74 %
	app-Man	±1.99 %
	IR – Man	±3.03 %
Max constriction velocity	app-IR	±9.48 %/s
	app-Man	±6.33 %/s
	IR – Man	±11.74 %/s
Mean constriction velocity	app-IR	±7.42 %/s
	app-Man	±1.23 %/s
	IR – Man	±7.52 %/s
Mean dilation velocity	app-IR	±5.61 %/s
	app-Man	±0.20 %/s
	IR – Man	±5.53 %/s

4.1.5 Discussion

This paper presented the design and technical validation of an app for the measurement of the pupillary reflex, intended to be used in LRSs. Given the absence of specific regulations or clear guidelines for the design of MDs for LRSs, the prescriptions of the European regulations on MDs, the relevant standards for designing smartphone applications, and the 5A principle of the WHO were adopted. The first part of this paper illustrated how the local needs and contextual analyses can be performed enriching engineering design with ethnographic methods. The second part presented and discussed the technical validation of the software, which was performed in two steps: validation of the acquisition and benchmarking of our app versus a commercial IR-pupilometer assuming as gold-standard the frame-to-frame manual annotation of pupillary video recordings from 10 subjects. The very low errors and high correlation resulting from the former validation confirmed that a smartphone-based pupillometry acquisition without accessories was viable. This concept was corroborated by the low errors and narrow limits of agreement for the variables resulting from the second validation. The latter proved that the proposed solution, despite being based on a simple app and a smartphone in order to be sustainable in resource-scarce settings, is able to perform just as well, and often better than the benchmark. These results were possible due to the interpolation algorithm and the normalization of the pupil diameter with the iris one, which minimised artefacts due to hand motions and the use of visible light for pupil stimulation via mobile phone flash and video acquisition. In fact, commercial pupilometers use IR for image acquisition, which is not available in the majority of smartphones. Indeed, the app described achieved better results than the commercial IR MD. Moreover, the comparison with existing literature suggested that the proposed solution is the only one designed for LMICs and rigorously validated. In 2013, Tae-hoon Kim et al. [166] proposed a smartphone-based pupilometer that works with an Android app and an add-on device, which contains two types of LEDs and an IR filter. Their results showed that their system could have been a good candidate for pupillometry, however it had not been validated against a CE-marked or FDA-cleared commercial pupilometer. Moreover, the required accessories would make its use in LMICs inconvenient. In 2017, Mariakakis et al. [167] proposed an iPhone-based pupilometer that works with a box similar to the one used for virtual reality headsets and makes use of convolutional neural networks. The box was used to eliminate ambient light and control the distance to the person's face. Nonetheless, the authors themselves claimed that such a box could be a hindrance in case of measuring the pupil light reaction with an unconscious patient and for tracking the whole reaction to the flash (i.e., the dilation phase cannot be captured because of

the lack of lighting). Their design, in fact, only allowed assessing the pupil constriction phase and seems to require a server connection in order to work. In 2018, McAnany et al. [168] performed a study proving that the iPhone camera could be used for this purpose, comparing it with an IR camera, which was not medical rated. In 2019, the start-up Brightlamp introduced an iPhone app for tracking the photopupillary reflex based on trained object detectors and on the use of no accessory. Such app was manually validated similarly to part two of our validation with no benchmarking, resulting in a higher MAE (2.9%) and wider limits of agreement for the pupil constriction (±14%, which improved to ±9% after bias correction). However, a recent study by McKay et al. [195] benchmarked Brightlamp with a portable IR pupillometer demonstrating that this particular iPhone app has poor repeatability and is not practical tool for supporting clinical decisions. Nonetheless, in general, iPhone-based pupillometry, relying on Hough transform, was proved to be possible and accurate enough by Neice et al. [196].

Moreover, the use of iPhones in SSA is quite uncommon due to their cost and because iPhone does not have any rugged model. In 2019, Vigàrio, et al. [169] proposed a system for the continuous monitoring of the pupil using a smartphone, the Virtoba support for mobile-phones and two LEDs. However, the system does not provide the typical pupillometry stimulus (i.e., flash in the eye) and its validation was limited to physiological data found in literature (i.e., the reaction of the pupils to a cold stress test). None of the designs above were conceived for LRSs. As it emerged from our contextual analysis, in fact, basing part of the design on extra add-on parts can turn out to be counterproductive either in a possible early health technology assessment phase or when already on the market. Adding extra add-on devices will increase the need for spare parts that will probably not be available in LRSs. For this reason, the authors of this paper suggest that the 'less is more' philosophy should be adopted when starting considering additional parts of a device conceived for these settings. Although the study was focused on pupillometry, its findings on the design can be relevant for other applications. For instance, it emerged clearly that affordability is not the only criteria for a device to be suitable for LRSs. Many other issues should be considered during the design, including affordance, easiness of deployment and use, resilience to underlying infrastructures that could be not stable, availability of spare parts and consumables, and available underlying technologies. Another issue that emerged is the tendency to release apps with healthcare ambitions without proper technical validations (e.g., manual and/or benchmarking for apps). In the past years, both the FDA and the European Commission equated medical software (including app) to MDs, making validation essential to guarantee safety and adequate performance. For this reason, in this paper, it was decided to adopt the European perspective for

CE marking medical apps, in order to stress the importance of the technical validation phase in the design cycle.

4.1.6 Limitations

This study presents the preliminary results of the design and technical validation of a smartphone app. The results are valid and limited to one Android smartphone model; further testing could include more models. In these further tests the different flashes of different smartphone models should be checked for safety against the relevant standards. Although our algorithm already takes into account possible artefacts, a more ad-hoc failure rate detection algorithm could improve the performance evaluation of the app. The current design relies on a server connection, which may be a bottleneck, although currently many remote areas of LRSs (e.g., Africa) are served by good quality mobile phone services. To overcome these limitations, future versions of the app will also include the processing algorithms. To this regard, also artificial intelligence may be explored. While this solution may be difficult to run on very old smartphones, it should run smoothly on the other models. Furthermore, a possible bias in the feasibility study might have been introduced because the opposite eye was not covered and could have potentially been partially stimulated by the changes in the ambient light. However, the ambient light was measured and maintained as constant as possible throughout the experiment. To this regard, healthcare workers will need to be instructed and cover the opposite eye in order to avoid bias in the pupillary reactions. Moreover, as of now, the app is not giving any result in terms of millimetres; future versions may include this feature only for the pupil size, as it would be redundant for the pupil/iris ratio. Finally, the performance of the app is currently evaluated on light brown eyes, darker shades should be investigated, as they may be more challenging for pupillometers relying on visible light only. Future experiments could test the application on subjects with three types of iris colour (i.e., fair, medium, and dark). In this way, the efficiency of our application on different iris colours could be evaluated. This could also inform future upgrades of the app software to make it more efficient.

4.1.7 Conclusions

This paper presented the design and technical validation of a mobile app aimed to perform smartphone-based pupillometry, suitable for use in LMICs. The performance of the app algorithm is promising and, being able to compete with the performance of the algorithm of a commercial IR pupillometer MD, suggests furthering the study with more smartphone models and transitioning towards a dedicated server application and/or a completely standalone app.

The performance of the algorithms of the app, as confirmed by the technical validation, are sound: the proposed solution, by exploiting the pervasive presence of smartphones in LMICs and by not requiring expensive settings or complex procedures, represents a significant improvement towards an extensive screening of eye pathologies and brain trauma worldwide.

4.2 A smartphone-based tool for screening diabetic neuropathies: a mHealth and 3D printing approach

This second use case belongs to the group of screening.

4.2.1 Introduction

Diabetic neuropathies, the top cause of neuropathy in the world, are nerve damages associated with diabetes mellitus [197]. Although their etiology is multi-factorial, one of the main causes behind nerve damage is the direct effect of long-term hyperglycemia, which reduces nerve perfusion [198–200]. In fact, a recent editorial by Papanas [201] reported that diabetic peripheral neuropathy is the commonest form of diabetic neuropathy and the most frequent manifestation of diabetes mellitus in the nervous system. However, a distinction should be made between type 1 and type 2 diabetes, because in patients with type 2 diabetes, even with blood glucose levels under control, there is a high risk of developing neuropathy [202]. There are different kinds of diabetic neuropathies according to the organ systems involved. In particular, sensorimotor polyneuropathy is the one affecting nerve cells, fibers and coverings, affecting the transmission of nerve signals up to the complete interruption of a nerve's activity [203]. The symptoms span from burning pain to hyperesthesia (i.e., excessive physical sensitivity on the skin) and deep aching pain, starting in the toes and feet, and gradually ascending in the lower limbs. Normally, affected lower limbs will be characterised by a sensory loss of touch, vibration, pressure and temperature. For these reasons, this kind of diabetic neuropathy can be extremely dangerous [204]. As also claimed by [201], diabetic neuropathies need to be diagnosed early for several reasons. In fact, this reduced sensitivity can contribute to increasing the chances of the development of non-healing ulcers and infections, which can lead to amputations and eventually death of the patients [204–206].

Regarding diabetes, its prevalence has been increasing since the 1980s, reaching 422 million people in 2014 and approximately 463 millions in 2019, worldwide. A dire projection forecasts 700 million cases of diabetes in 2045. About 79% of the cases are from low- and middle-income countries (LMICs),

which are also those that experienced a faster surge. In fact, diabetes is among the most prevalent non-communicable diseases (NCDs) in Sub-Saharan African (SSA) and it has been accounting for an ever-growing number of disabilities, morbidity and mortality since 1990 [207, 208]. Specifically, diabetic neuropathy, which is one of the most recurrent diabetes-related health issue [209], is an increasing problem in SSA, where it affects up to 61% of the people with diabetes [210]. Moreover, the annual costs of diabetic peripheral neuropathies and their complications were estimated to be 4.6-13.7 billion US dollars in 2001 in the US only, representing a huge economic burden [211, 212].

Screening for diabetic peripheral neuropathies, which is crucial for their prevention and treatment, is highly recommended in most clinical guidelines (e.g., the American Diabetes Association) [213]. According to both the International Diabetes Federation and the American Diabetes Association, all diabetic patients should have their foot checked annually [214]. Notwithstdanding, it is often neglected, due to the lack of consensus on the screening methods, of quick and reliable screening methods, as well as of preventative pharmacological therapies that are neuropathy-specific [213, 214]. Both questionnaires [215], composite neurological scores, and quantitative sensory or nerve conduction testing are clinically validated methods for screening and assessing diabetic peripheral neuropathies [213]. A recent (2021) publication by the World Health Organization [216], reported the 128 Hz tuning fork, the reflex hammer, the 10 g monofilament, and diabetic foot ulcer risk scales in the list of specific priority medical devices for clinical assessment interventions for diabetes. A recent systematic review by Fernández-Torres et al. [217] identified the instruments of choice that are of the highest quality for the assessment and monitoring of diabetic foot disorders. Fernández-Torres et al. [217] identified several tools and instruments such as Neuropad, the 10 g monofilament, Neurotip, the 128 Hz tuning fork, Vibratip, NeurAppathy app, diabetic peripheral neuropathy (DPN) check, tactile circumferential discriminator (TDC), Sudoscan and the footboard (FB) system. Neuropad was the most sensitive and specific tool in this subgroup for the staging of peripheral neuropathy. However, research is still needed to provide more robust methods for this purpose. In particular, more equipment-heavy and time-consuming methods were discovered in the recent years (e.g., skin biopsies, corneal confocal microscopy, thermography-based on automatic segmentation of the foot sole) [218]. For example, Arteaga-Marrero et al. [218] presented the powerful and promising automatised thermography-based approach that relies on the automatic segmentation of the sole of the foot along with the measurement of six contralaterally-matched plantar locations daily. Plantar temperatures that are out of normal values, in fact, may be an early sign of diabetic foot disorders. As means to screen for diabetic neuropathies, Roikjer et al. [213] also enlisted nerve conduction studies, which

are the gold standard for detecting large fiber neuropathies, but require special equipment, skin biopsies, which are promising for small fiber neuropathies, but are invasive and require specialised laboratories, and corneal confocal microscopy. They also suggested further experimental methods, including electrochemical skin conductance, sweat gland activity, laser Doppler-examinations, and neuropathic itch. Also Yang at al. [219] presented several novel diagnostic techniques such as Neurometer, DPN-Check and Sudomotor Testing, which may supplement clinical assessment and aid the early detection of diabetic neuropathies. However, there is limited evidence that those technologies could be introduced in the clinical practice.
If the possibilities surrounding the monitoring and early detection of diabetic neuropathies are scarce, those related to preventative therapies are even scarcer. In fact, currently, there is no treatment that is approved by the Food&Drug Administration nor by the European Medicine Agency. A recent systematic review by Robison at al. [220] showed that there is very low-quality evidence that whole-body vibration has a slight positive effect on glycemic control in patients with diabetic peripheral neuropathy, improving neuropathic pain and balance. Moreover, another recent systematic review by Akbari et al. [221] presented the most recurrent physiotherapy interventions, i.e., exercise therapy (e.g., Tai-Chi, strengthening training, balance training, aerobics), electrotherapy (e.g., plantar electrical stimulation, percutaneous electrical nerve stimulation, electroacupuncture), and other methods (e.g., acupuncture, Thai foot massage). In particular, exercise therapy proved to be the most effective one.

Among traditional methods for assessing the sensory loss linked to diabetic neuropathies, there are vibration perception tests through tuning forks or biothesiometers, 2-point discrimination tests, and monofilaments [214, 222]. All these tools, supported by the American Diabetes Association, evaluate different somatosensory functions that are progressively affected during diabetes [223]. In particular, vibratory sensitivity has been proven to be highly sensitive [214], and Zwaferink et al. [224] demonstrated that mechanical noise generated by piezoelectric actuators can decrease the vibration perception threshold, increasing the sensitivity in the foot. Moreover, Lindholm et al. [222] demonstrated that low frequencies seem to be a better indicator of the risk of developing diabetic foot ulcers, gait or balance problems or weakness of the foot. Overall, combinations of more than one test were proved to improve the sensitivity in detecting diabetic peripheral neuropathies [214], with values reaching more than 87% [225, 226]. In regard to this, Chicharro-Luna et al. [214] assessed the variability of different methods for diagnosing diabetic neuropathies, and they proved that vibration non-perception was the most commonly affected sensory parameter in diabetic patients, along with the absence of the Achilles reflex. In their paper, they demonstrated that the type of test that had the highest

degree of agreement is that of the International Working Group of the Diabetic Foot Criteria, based on the use of a monofilament, cotton wisp and tuning fork. For these reasons, and for the reduced sensitivity to vibrations of the elderly, they also recommended the use of this specific test, compared to others. Simultaneously, in the field of blood glucose levels monitoring and of diabetic management, there has been a flourishing of several methods, in particular related to mHealth [227, 228]. Kap et al. [228], in fact, claimed that, by 2020, 222 Android and 123 iOS diabetes-related applications were released. Such applications can be divided into four main functionalities, i.e., management (for monitoring glucose levels and for unit conversions), supportive (for receiving the feedback and support from doctors), informative (for diet and nutrition advice), and multifunctional. Kap et al. [228], in particular, reported that the recent developments in smartphone cameras made it possible to develop highly accurate and selective smartphone-based colorimetric detection systems that work with bodily fluid samples, e.g., sweat, tears, urine, saliva, interstitial fluid) to monitor glucose levels and enable patient-specific insulin therapies. As regards sweat, it is usually collected via wearable patches or disposable strips relying on filter paper, and its concentration can be increased by air-drying and using quinone as colorant. Images of the strips can then acquired via smartphone and analysed. Kap et al. [228] claimed that tears may be a more reliable and easy to use analyte, as the tear glucose concentrations are more closely correlated with those in the blood. For collecting tear samples, contact lenses were engineered with microchannels that allowed the tear sample to react with ad-hoc reagents, which would beget a change in the color of the lense. Such color change could then be captured via a smartphone camera. Similar considerations apply to urine, for which tests strips enriched by polydimethylsiloxane pumps jointly used with smartphone cameras can be used to evaluate glucose levels, and to saliva, for which paper microfluidic devices and smartphones can be used. Finally, also the interstitial fluid can be monitored, although there is usually a delay between the blood glucose levels and those present in the interstitial fluid. Subcutaneous tattooing is one of the widely used colorimetric methods for this.

On the other hand, a great share of the diabetes-related app sector is populated by apps for self-management, lifestyle modification, and medication adherence motivation (e.g., Glucose Buddy, VoiceDiab). As with mHealth in general, these apps and technologies can facilitate timely referral of those who are at the edge of foot ulceration for timely intervention care [229]. Moreover, they can dramatically improve the quality of life of people with diabetes in particular those living in low-resource settings (LRSs) [227]. Doupis et al. [227] reported existing smartphone applications relevant in this field and supported by prospective randomized controlled trials. Among these, Intelligent Diabete

Management, University of Alberta, supports type 1 diabetes patients with a glucose and meal tracker, similarly to Glucose Buddy. In addition to these functionalities, Diabetes manager, VoiceDiab and Diabetes diary provide for an insuline dose calculator. Similarly, Dbees, Diabetes Interactive Diary, and D-partner are equipped with similar features and also can rely on telemedicine for further patient support. Similar apps with similar features exist for type 2 diabetes patients. Some of these apps will also allow for the manual or automated input of blood sugar levels, such as Diabeo, Diabetes Pal, BlueStar and Bant2. Moreover, in literature, there are wearables and digital health developments for improving daily monitoring of plantar temperature and potentially higher sensitivity and specificity to predict diabetic foot ulcer and extend ulcer-free days in remission [229]. A recent review by Najafi et al. [229] discussed how wearables and digital technologies may improve the management and optimize prevention of diabetic foot ulcer by identifying high-risk patients for triage and timely intervention and personalizing therapy.

However, mHealth apps or tools are not yet used to screen diabetic peripheral neuropathies and help for fast referral to a specialised doctor.

In fact, to the best of authors' knowledge, no previous smart tool based on 3D-printed accessories and a smartphone app was ever designed for screening diabetic neuropathies. There are few studies in the literature concerning similar solutions for this purpose, as confirmed by [230–232]. In 2017, May et al. [230] was the first to prove that the vibrations generated from mobile phones (Neurappathy app) could be used to detect diabetic peripheral neuropathy, by comparing the their accuracy with a 10-g Semmes-Weinstein monofilament and a 128-Hz tuning fork. It resulted that the vibrating mobile phone had the highest accuracy (i.e., 88%), compared to the other tools. In 2018, Jacobs et al. [232] described the PeriVib, a portable smartphone-based peripheral neuropathy test platform, which uses a smartphone-controlled external motor to generate vibrations and test the perception.

Differently from the world of diabetes management and blood glucose monitoring, which is characterised by numerous mHealth solutions, as presented above, the world of diabetic neuropathy screening still needs to go further evolving towards a more digital approach. Throughout this paper, I demonstrate how a frugal and contextualised engineering approach, leveraging circular economy, mHealth and the wide availability of smartphones in LRSs, can be applied when designing medical devices (as also described and proved elsewhere [4, 5]).

In particular, the aim of this project was to design, develop, and test a smartphone app complemented by 3D-printed accessories, which could dramatically improve the screening for diabetic neuropathies and inform decisions of healthcare operators, worldwide, fostering the shift towards Care 4.0 [233] and

circular economy. This could be of benefit not only to LRSs in high-income countries, but also (and perhaps foremost) to those in low-income countries. This paper follows the frugal design criteria that were pinpointed downstream of our field studies with a Delphi study technique, which are duly explained in [4]. The findings of our field studies on the challenges and opportunities of LRSs will not be reported hereby, as they are already described in Chapter 2. Shall the reader be interested, they could find more information either in that Chapter or in the published paper [4].

4.2.2 Methods

4.2.2.1 CAD design and 3D printing.

3D printing was used to create specific parts that would complement the app, i.e., two two-point discriminators for the two-point discrimination test, and one smartphone-add-on tip for the vibration perception test. Such 3D printed parts were designed on Autodesk Fusion360, sliced on Cura and printed with the available 3D printer (Creality Ender3), which has a maximum layer resolution of 0.1mm and a print precision of ±0.1mm, using RepRap black polylactic acid (PLA), as it is a very versatile and biocompatible material.

In particular, the two-point discriminators were designed to have an octagonal shape with a circular hole in the middle, to facilitate holding in one's hand. Each side of the octagon features two pins that are distanced at increasing distances (i.e., 1-8 mm and 25 mm for one, and 9-15 mm and 20 mm for the other one). The smartphone-add-on tip was designed to fit a Doogee S60 Lite, i.e., a rugged smartphone, but can potentially be adapted to any kind of smartphone, and is characterised by a conic pin that extends for 22 mm terminating in a spherical tip. All these items were printed with 0.16 mm layer height and 50% infill, 200°C nozzle temperature and 40°C bed temperature.

4.2.2.2 Smartphone application.

The app was developed in Android Studio, using Java for the implementation of functions and XML for the design of the user interface, targeting Android-based smartphones with an API level of at least 21 (i.e., Android 5.0 Lollipop). This choice allows 94.1% of Android users to use our app, as only 5.9% of the Android-based smartphones have an API level lower than 21 worldwide (and similar trends can be found in Africa)(from Android Platform/API version distribution – Android Studio) [186]. The logo, representing a foot with a blue circle in the background (i.e., the international symbol for diabetes) was hand-drawn and digitized using GIMP.

4.2.2.3 Neuropathy Total Symptom Score-6 (NTSS-6).

NTSS-6 is a validated neuropathy sensory symptom scale, evaluating individual neuropathy sensory symptoms in patients affected by diabetes mellitus and diabetic peripheral neuropathy. It was introduced by Bastyr et al. [215]. The questionnaire focuses on the frequency and intensity of 6 symptoms, namely numbness and/or insensitivity, prickling and/or tingling, burning sensation, aching pain and/or tightness, sharp, shooting, lancinating pain, and allodynia and/or hyperalgesia. The possible scores for the NTSS-6 range from 0 to 21.96, where a score greater than 6 indicates clinically significant symptoms.

4.2.2.4 The two-point discrimination test.

The two-point discrimination test evaluates whether a subject can identify two close points on a small area of skin, and how finely they can discriminate them [234]. Different areas of the body will feature different sensitivity levels with the hands and feet being among the most sensitive areas, and the lower back and thigh being among the least sensitive ones [235]. With this test, the minimal distance, at which the subject can distinguish if one or two points of a caliper are held against their skin, can be assessed [236]. For these reasons, it is a measure of agnosia and a proxy for the presence of diabetic neuropathy [234, 237]. Any instrument used for this kind of measurement, will feature millimeters readings to facilitate the examination.

4.2.2.5 Vibration perception test.

The vibration perception test assesses whether a subject can perceive vibration. The vibration perception threshold can be considered a valid indicator of proprioceptive capacity [238]. A diminished vibration perception can, in fact, be predictive of future foot ulceration [239]. Normally 128-Hz tuning forks or biothesiometers are used to perform this test [240] and evaluate the ability of a subject to perceive vibrations on specific bony parts in the lower limbs.

4.2.2.6 Testing for normal thresholds.

In order to test the first prototype of this smart tool, a study was designed aiming at evaluating normosubjects with the different tests allowed by the smart tool, i.e., the NTSS-6 questionnaire, the two-point discrimination test, and the vibration perception test (see Fig. 4.10 and 4.11). 11 subjects were included in the study, and their average age was 32.18 years (no subject older than 65 was involved) (see Fig. 4.12). Personal information regarding the

subject and their medical history was recorded using the first activity of the app. This was essential to only include normosubjects and exclude potential outliers due to other concomitant diseases or factors that could interfere with peripheral nerve conduction (e.g., hypothyroidism, kidney disorders, recent injuries to the lower limbs, rheumatoid arthritis, etc.). Moreover, only subjects under 65 years old were included to avoid increasing heterogeneity in the considered sample, as both two-point discrimination and vibration perception thresholds will diminish with age [222, 241, 242]. The full list of questions can be found in Appendix E.1. After this screening, the patients were first tested with the NTSS-6 questionnaire, then the two-point discrimination test, and, finally, with the vibration perception test. Moreover, to fine tune the vibration perception test, also a commercial tool for the same purpose (i.e., Vibratip [243]) was tried on the subjects as a last step, comparing the perceptions. In particular, the two-point discrimination test was performed on the sole of the hallux and the small toe for both feet in an antero-posterior direction, as the two branches of the planter nerve (medial and lateral), arising from the posterior branch of the tibial nerve, innervate these two parts [244]. Specifically, the examination started with larger thresholds alternating two-tip and one-tip touches, gradually using tips closer to each other, until the subject could not correctly distinguish anymore between one- or two-tip touches. The vibration perception test was performed on the bony part of the distal interphalangeal joint (followed by the lateral malleolus, the lateral femoral condyle, and the hip crest).

These experiments were done in concordance with ethical approval BSREC 05/20-21. The data were then pseudonymised and statistically analysed using Microsoft Excel. Data normality was investigated by Kolmogorov-Smirnov test. The data are presented as Average and Standard Deviation (SD). Outliers were individuated by applying a modified Thompson's τ test. The deviations for this test were calculated as per Equation 4.1, where δ is the deviation, x_i is the ith value and $\bar{x}$ is the average value:

$$\delta_i = |x_i - \bar{x}| \tag{4.1}$$

The maximum deviation was then compared with the thresholds that were calculated by applying equation 4.2, where t is the threshold, S is the sample standard deviation and τ is the modified Thompson's τ (tabled value):

$$t = S \cdot \tau \tag{4.2}$$

Paired t-test or Wilcox sum-rank test was used to investigate statistical differences between two groups (left vs right part of the body). A p-value lower than 0.05 was considered significant.

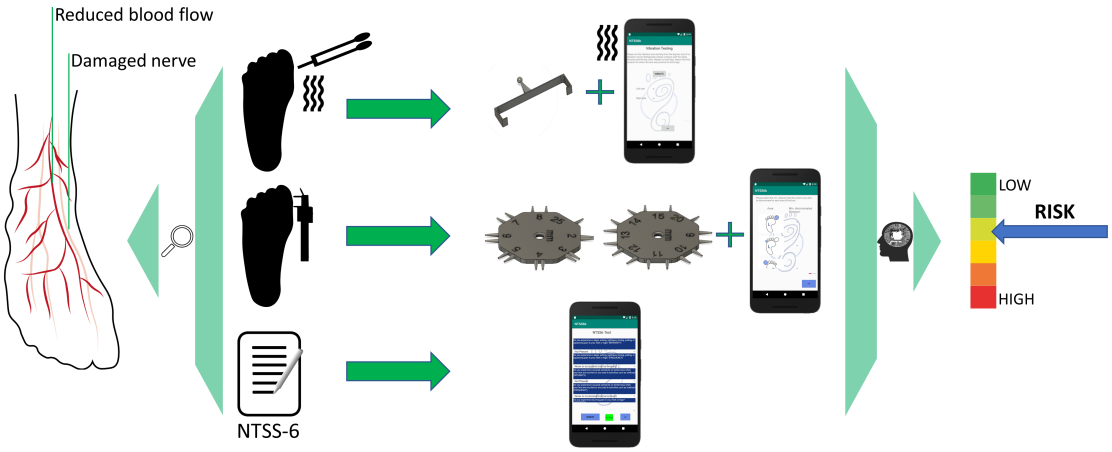


Figure 4.10: The testing diagram.

4.2.3 Results

4.2.3.1 CAD design and 3D printing.

After that the final CAD models were ready on Autodesk Fusion 360, and sliced with Cura based on the afore-mentioned values, they were sent for print to a Creality Ender 3 3D printer. The two two-point discriminators, with their octagonal shape and progressively-distanced tips, can be seen in Fig. 4.13. The print turned out defect-free and all the numerical inscriptions (i.e., those indicating the distance) resulted to be readable. Moreover, upon measurement with a ruler, all the tips turned out to be correctly distanced. Overall, the 3D-printed two-point discriminators resulted to be lightweight, quite sturdy, and easy to manoeuvre in an average adult's hand. Similarly, the smartphone add-on for vibration testing, comprising of a spherical tip attached to a truncated cone pin, can be seen in Fig. 4.14. Also in this case, the smartphone add-on resulted to be defect-free. Upon clipping on the smartphone (i.e., a Doogee S60 Lite), it fit satisfactorily. However, the fit could be further improved by remodelling the current design with a third side clip.

4.2.3.2 Smartphone application.

When first clicking on the icon, after showing the splash screen with the logo, the app guides the user through four main activities (see Fig. 4.15 and Fig. 4.16):

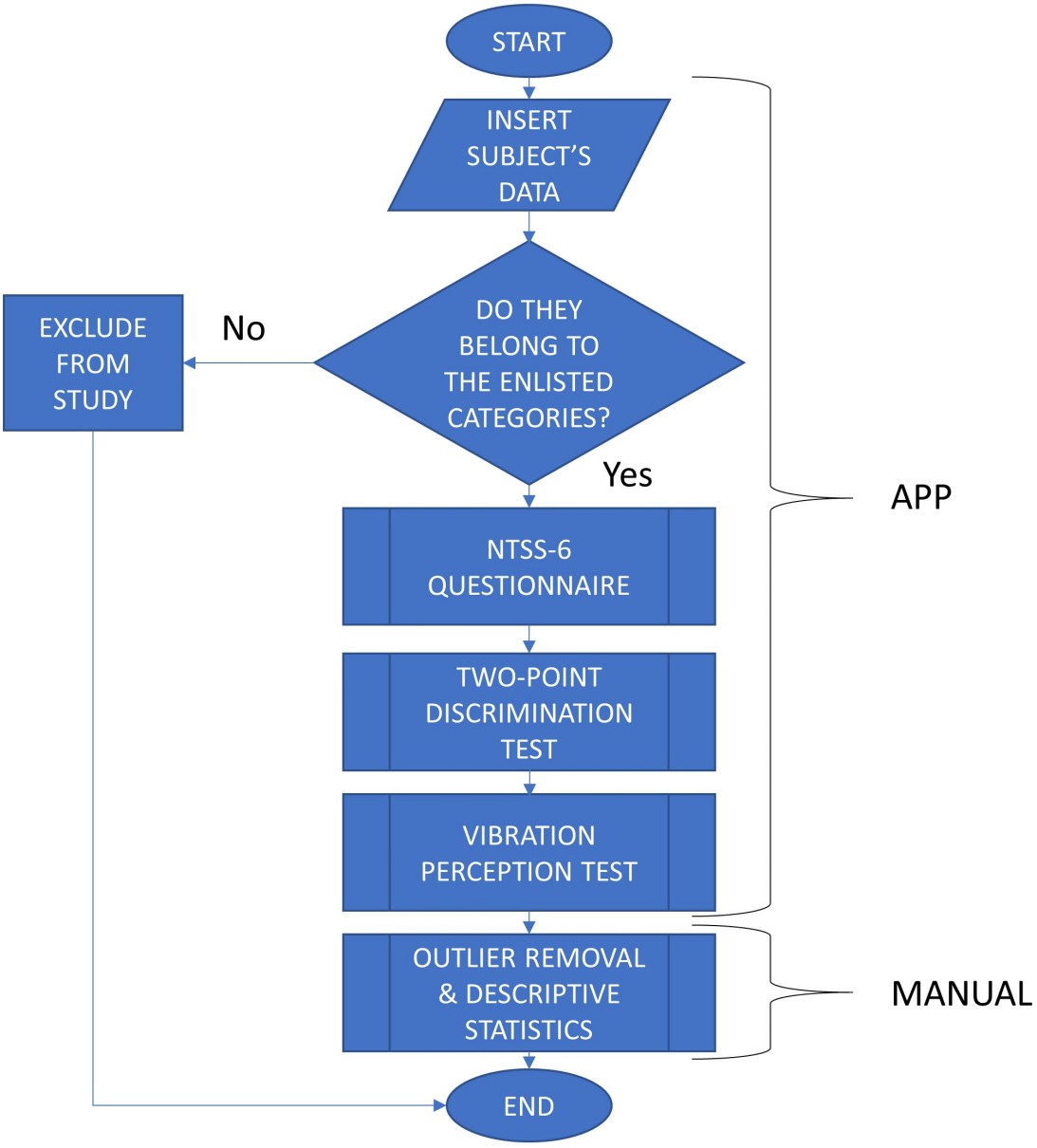


Figure 4.11: A flowchart describing the workflow of the test specifying the activities of the App and the manual activities.

Figure 4.12: The two-point discrimination test being performed on a subject.

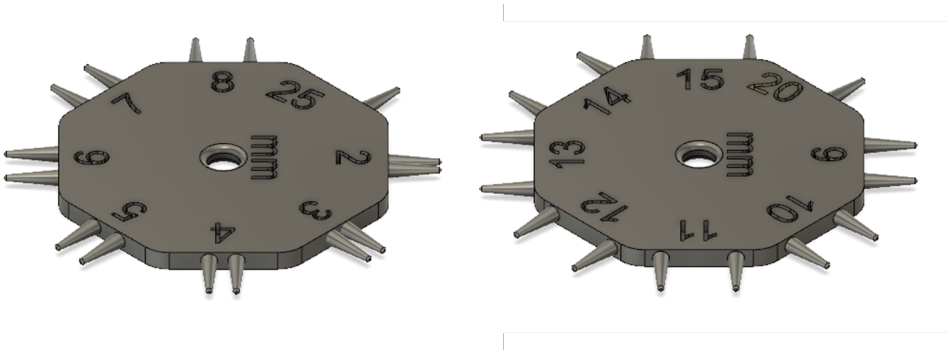


Figure 4.13: Two-point discriminators with different discriminator distances.

Figure 4.14: Smartphone add-on for vibration testing.

1. Screening form activity, which collects personal information about the subject (e.g., the relevant past medical history). This is useful to understand whether the subject is already suffering from diabetes or other conditions (e.g., hypothyroidism, Lyme disease, rheumatoid arthritis, etc.) that could alter their neurological pathways and perceptions;

2. The NTSS-6 questionnaire activity, which collects the answers related to the frequency and intensity of diabetic neuropathy specific symptoms (e.g., numb feeling in the hands, arms or legs, prickling or tickling feeling in the hands, arms or legs), and gives a final score as well as a recommendation, based on the interpretation given to the total score by Bastyr et al. presented [215]. Such recommendation is given through ad-hoc cardviews in the same activity;

3. The two-point discrimination activity, in which the user can input the minimum two-point discriminator thresholds that the subject perceived during the two-point discriminator test performed with the ad-hoc 3D printed tool;

4. The vibration perception activity, in which the user can decide whether activating the vibration mode or not by clicking on a button, before placing the spherical tip of the smartphone add-on tool in contact with the different bony parts of the subject. In the same activity, the user can then record the body region where the vibration/non-vibration was felt and correctly individuated.

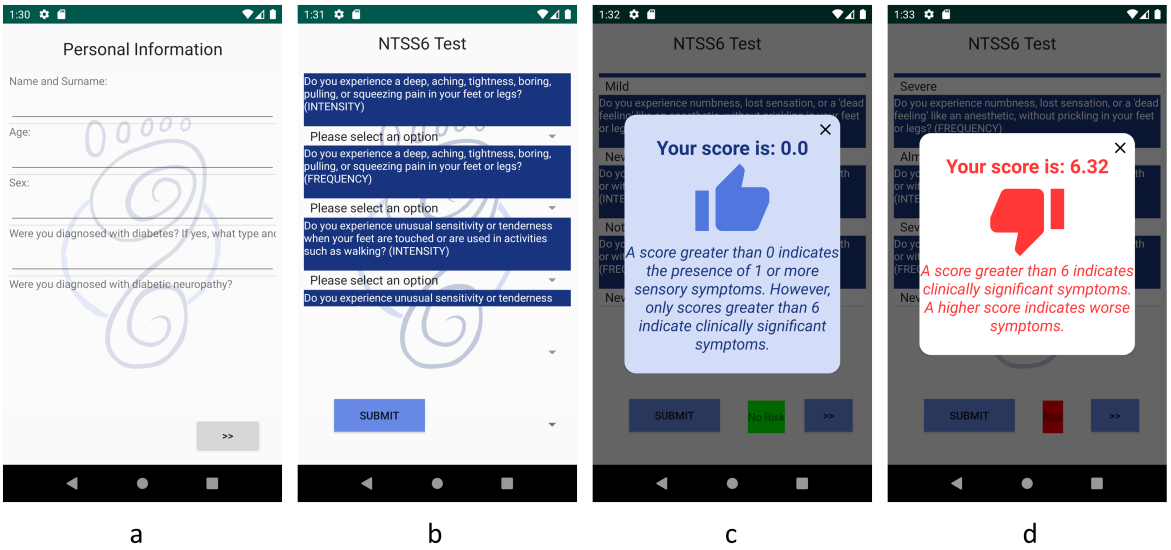


Figure 4.15: Screenshots of the app: a) the personal information activity; b) the NTSS6 questionnaire activity; c) and d) two cardviews representing the feedback of the questionnaire

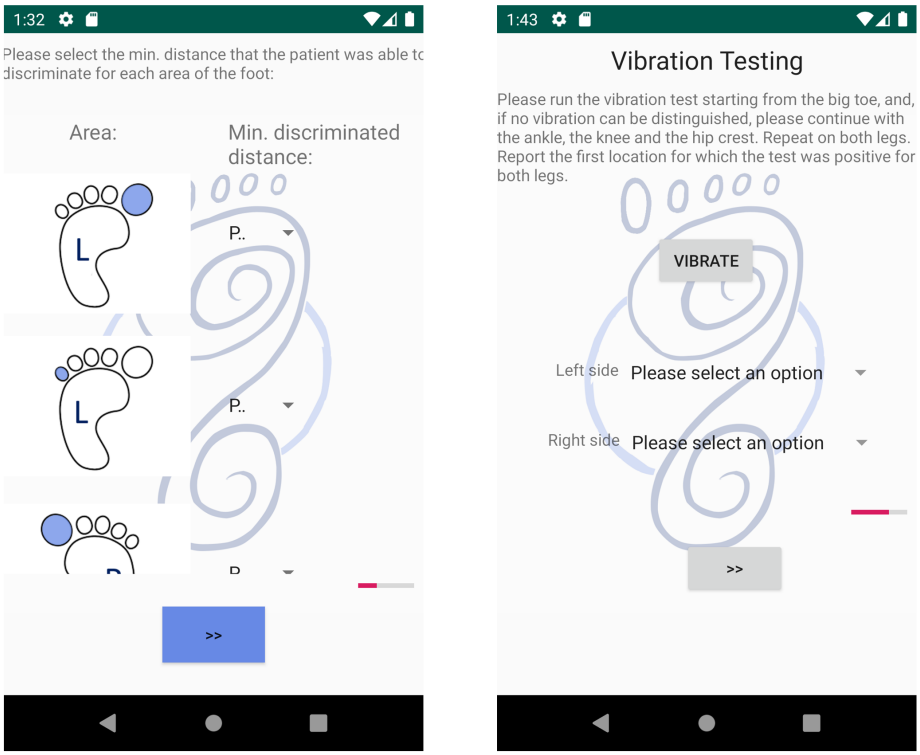


Figure 4.16: Screenshots of the app: a) the discrimination test activity; b) the vibration test activity

4.2.3.3 Testing for normal thresholds.

11 subjects (8 males, 3 females) volunteered to take part to the study, after reading the participant's information leaflet. No subject decided at any point to withdraw from the study, nor to withdraw their data within the cooling-off period.

Table 4.3 reports the data collected on the 11 normosubjects enrolled in this study. The collected data for each subject included age, sex, the NTSS-6 score, the two-point discrimination thresholds (in millimiters) and the body regions where the vibration was felt first. An additional column collects further comments that are related to the use of Vibratip as a benchmark for the vibration perception test.

Table 4.3: The collected data for each subject. 2PD stands for two-point discrimination; LH stands for left hallux; LLT stands for left little toe; RH stands for right hallux; RLT stands for right little toe; LAPV stands for left area perceived vibration; RAPV stands for right area perceived vibration; avg stands for average; std stands for standard deviation; *the averages and the standard deviations reported in the table are those calculated after the removal of the outlier (ID 4).

ID	Age	Sex	NTSS-6	2PD LH	2PD LLT	2PD RH	2PD RLT	LAPV	RAPV	Comments
1	22	M	2	9	11	9	9	Big Toe	Big Toe	
2	58	F	2	8	9	8	8	Knee	Knee	Vibratip felt on big toe
3	28	M	0	10	8	7	8	Big Toe	Big Toe	
4	62	M	0	10	14	13	15	Knee	Knee	Vibratip felt on big toe
5	27	F	0	8	8	8	7	Big Toe	Big Toe	
6	38	M	0	7	7	6	8	Knee	Knee	Vibratip felt on big toe
7	21	M	0	7	8	8	7	Big Toe	Big Toe	
8	31	F	0	10	9	10	9	Knee	Knee	Vibratip felt on big toe
9	21	M	0	4	8	7	7	Knee	Knee	Vibratip felt on big toe
10	27	M	0	8	8	8	10	Big Toe	Big Toe	
11	19	M	0	9	9	4	4	Big Toe	Big Toe	
Avg*				8	8.5	7.5	7.7			
Std*				1.76	1.08	1.65	1.64			

By observing Table 4.3 it is possible to notice that subject ID 4 scored values that are apparently distant from the rest of the group. In order to understand whether subject ID 4 is an outlier, modified Thompson's tau technique was used [245]. In particular, the deviations δfor 2PD LLT (two-point discrimination left little toe), 2PD RH (two-point discrimination right hallux), and 2PD RLT (two-point discrimination right little toe), resulted all to be greater than the

threshold value given by the multiplication of Thompson's tau and the standard deviation of the sample, as shown in Table 4.4. For these reasons, subject ID 4 was considered an outlier and removed from further analysis.

Table 4.4: The deviations and thresholds for the two-point discrimination variables. The * denotes values over the threshold.

	2PD LH	**2PD LLT**	**2PD RH**	**2PD RLT**
δ	1.82	5*	5*	6.64*
Threshold	3.23	3.54	4.14	4.89

After the removal of the outlier, the averages and standard deviations for all of the above-mentioned variables were calculated and reported in Table 4.3. The normality of the data was, then, investigated using a Kolmogorov-Smirnov test [246]. The four variables resulted to be normally distributed (for LH D=0.2 and p-value=0.749; for LLT D=0.29 and p-value=0.317; for RH D=0.23 and p-value=0.614; for RLT D=0.23 and p-value=0.61). As a consequence, in order to investigate statistical differences between the left and right part of the body, possibly linked to the subjects' handedness, a paired t-test was used (significance level of 0.05). The t-test results could not reject the null hypothesis that the paired samples came from populations with equal means (Hallux p-value=0.49; Little toe p-value=0.21) (see Fig. 4.17).

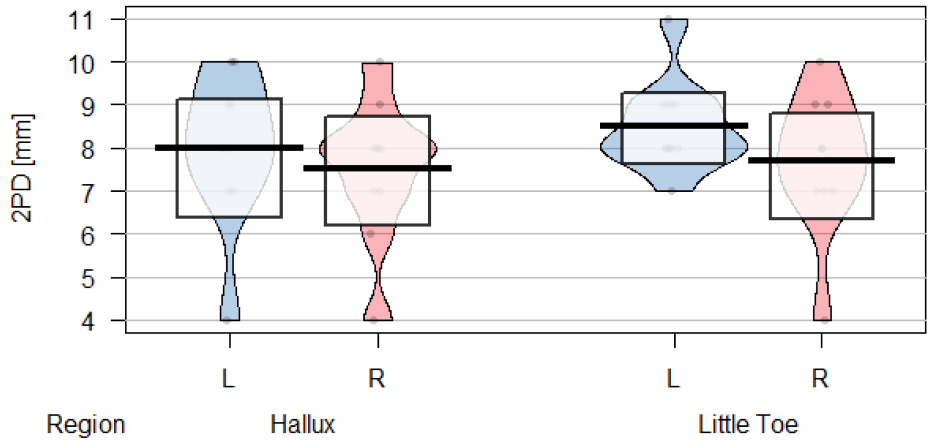


Figure 4.17: a) The pirateplots for the 2PD of both halluces (left VS right) and little toes (left VS right).

4.2.4 Discussions

An overview of the currently available technologies developed for diabetic patients brought to light the fact that, as opposed to the field of glycemia screening and lifestyle management, not much has been done in the field of mHealth for the screening of diabetic neuropathies, which are a major health burden, worldwide. In fact, as regards the former, as afore-mentioned in the introduction section, there are numerous mHealth solutions aimed at facilitating and improving the quality of life of diabetic patients, by allowing them to check and log their glycemia levels and blood pressure, record their daily food intake, medication, and physical activities, as well as access advice from a real health coach or communicate with healthcare professionals, as presented in the introduction [227, 228]. In particular, Kap et al. [228] reviewed several smartphone-based methods, relying on the collection of bodily fluids (e.g., saliva, sweat, etc.) samples through ad-hoc microfluidic devices to measure the amount of glucose levels. The latter can be manually or automatically recorded along with the daily diet and exercise on specific apps, as reported by Doupis et al. [227].

Conversely, as regards the screening of diabetic neuropathies, the currently available cutting-edge methods found in the existing literature, such as the automatic sole segmentation and thermography method reported by Arteaga-Marrero et al. [218], or the methods relying on nerve conduction studies, skin biopsies, corneal confocal microscopy, and electrochemical skin conductance as described by Roikjer et al. [213], or those additionally reported by Yang et al., [219] based on the assessment of the retinal nerve fiber layer thickness through optical coherence tomography, pupil responsiveness, or sudomotor testing, require more equipment and time, compared to traditional clinical practice. For this reason, I believe that our solution, which relies on the combination of different tests as suggested by Chicharro-Luna et al. [214], represents a more simple and frugal means to test for diabetic neuropathies, as reliably, in low-resource settings, as well as in high-resource ones, where it could empower less specialised healthcare personnel to perform such screening procedures, as well as foster telemedicine and Care 4.0.

Other technologies [243] relying on the vibration perception threshold measurement only, although proven reliable, do not warrant the same sensitivity and specificity of the combinations of different sensory tests [214, 225, 226]. Similarly, the solution proposed by Zwaferink et al. [224] only relies on vibrations and mechanical noise generated by piezoelectric actuators, and is not aimed at screening diabetic neuropathies, rather at developing some smart insoles that will increase the sensitivity of the feet and prevent damages linked to diabetic-neuropathy-induced decreased sensitivity in the lower limbs.

Moreover, to the authors' best knowledge, the only available smartphone-based solutions are solely reliant on vibration perception [230, 232] and, in particular, the tool developed by Jacobs et al. [232] makes use of a specific additional platform/motor that may not be accessible or so easy to reproduce in LRSs.

In light of this, this paper presented the design, prototyping, and feasibility study of a smart tool for screening diabetic neuropathies relying on a combination of methods, which can be a goad to a global healthcare evolution towards Care 4.0 as well as foster the socio-economic growth of LRSs, thanks to contextualised design and circular economy approaches.

In fact, during the design of this smart tool, a frugal engineering perspective was adopted, leveraging on contextual needs, 3D printing and protocycling, and mHealth. The results proved that this system can be easily manufactured and used by lay users to produce reliable results. This is of utter importance for a timely referral and screening, and also for those remote areas of both LMICs and high-income countries, which are often challenged by the lack of specialised personnel. In this regard, this smart tool would allow a more equitable access to the screening of diabetic neuropathies, globally.

In particular, as it can be observed from the results, the two-point discrimination threshold are in line with other results presented in literature [247]. As regards the vibration perception, 6 subjects could feel and distinguish vibrations on the hallux, while 5 of them could perceived it on the knee. Notwithstanding, the latter were able to distinguish the vibration coming from Vibratip on their halluces. This highlights the current limitations of the add-on system for applying the vibration. This is probably linked to the fact that an optimal vibration frequency for this test is 128 Hz [248] and due to further attenuation provided by the smartphone components. However, it is currently not possible to set the vibration frequency in smartphones. As a consequence, in order to tackle this, future designs might need to focus on optimising/enhancing the vibration transmission by considering the modal frequencies of the add-on device. Nonetheless, May et al. [230] previously proved that a smartphone without add-ons could be used for this purpose. In light of this, it is also possible that future releases will discard the add on and only use the mobile phone for vibration testing. Furthermore, while the current study is limited to healthy subjects, future investigations should include pathological subject, to allow the training of an artificial intelligence-based technology for the correct screening of diabetic neuropathies.

4.2.5 Conclusions

This smart tool seems novel in the way that it represents a frugally engineered device that makes use of 3D printed accessories and mHealth, which improves

its global accessibility and reproducibility. Moreover, compared to the existing state of the art in mHealth for screening diabetic neuropathies, this tool is less equipment-heavy, more sensible, easy to use, and reliable, thanks to the combination of different methods, namely, a scientifically-validated symptom-based questionnaire, a vibration perception test, and a two-point discrimination test. The future integration of artificial intelligence or a decision support system, which will process the results from the above-mentioned tests, will complement this smart tool further. Finally, having portability and compactness as other features, further increases its potential to improve the quality of care in terms of time and resource use, by streamlining and incentivizing the screening of diabetic neuropathies, worldwide.

4.3 A 3D-printed condom intrauterine balloon tamponade

This third use case belongs to the group of treatment.

4.3.1 Background

Although the number of women dying during pregnancy and childbirth has decreased by 43% since the 1990 [249], there is still a growing gap between LRSs and higher resource ones. In fact, women living in a LMIC have approximately a 33 times higher chance of dying from complications during pregnancy and childbirth in respect to those living in HICs [249]. The World Health Organisation (WHO) reported that in 2017 the maternal mortality ratio is 462 per 100000 live births for LMICs, compared to 11 per 100 000 in HIC [250]. The WHO also affirmed that LRSs accounted for 94% of mostly preventable deaths during pregnancy and childbirth in 2017 [251]. One of the most common causes of maternal death worldwide is postpartum haemorrhage [252], affecting 4% of all pregnancies and still accounts for 25% of maternal mortalities worldwide (a rate that has been unchanged since 1992) [253]. Postpartum haemorrhage is defined as heavy bleeding after birth and it can be classed as "primary" if there is a 500-ml blood loss (>2 litres in case of severe haemorrhage) within the first 24 hours after birth and as "secondary" if there is abnormal or heavy vaginal bleeding between 24 hours and 12 weeks after birth. The most common causes of postpartum haemorrhage, identifiable with the Four T's mnemonic, are uterine atony (Tone), and abnormal placentation as well as retained placenta (Tissue), genital tract lacerations and rupture (Trauma) and coagulopathy (Thrombin) [254, 255]. As per the WHO guidelines [256], first-line treatment of postpartum haemorrhage includes the use of uterotonics (e.g., oxytocin, or ergometrine or a prostaglandin drug, when the first one is not available), of

tranexamic acid, of uterine massage and intrauterine balloon tamponades. If all the above methods fail, the use of uterine artery embolization is recommended for treating postpartum haemorrhage due to uterine atony. Some measures are also recommended as temporary solutions, such as bimanual uterine compression, external aortic compression, and non-pneumatic anti-shock garments. Otherwise, also surgical intervention is one possible solution. Relative to this, the UN is aiming to "reduce the global maternal mortality ratio to less than 70 per 100,000 live births" by 2030 [257]. In light of this goal, with regards to intrauterine balloon tamponades, many solutions of different shapes, sizes and materials were released, including: the Bakri tamponade balloon catheter, the BT-Cath, the ebb tamponade system, the Every Second Matters uterine balloon tamponade, the Alves handmade intrauterine balloon [258], the Kyoto balloon system [252] a free-flow pressure controlled uterine balloon [259]. In addition to these, other devices designed for other purposes have been used for treating postpartum haemorrhage, including Sengstaken-Blakemore tube, Foley catheters, condom catheters and surgical gloves [249]. Although not initially conceived for this purpose, Condom catheter balloons prove to be a low-technology, non-invasive, safe, effective and easy-to-use solution for the treatment of postpartum haemorrhage. Above all in LRSs, where there is insufficient training, low numbers of experienced personnel and a lack of preassembled intrauterine balloon tamponades [254, 260, 261]. A recent metanalysis [262] and other contextual studies on the use of such solutions in African countries (e.g., Ghana, Kenya, Egypt etc.) confirmed a high success rate, ranging from 88.6% to 96% [253, 254, 261]. One study related to Sierra Leone and Kenya [263] also reported a significantly lower mean blood loss, lower occurrence of blood transfusions, lower intensive care unit admission rates and lower occurrence of infectious morbidities. The same authors reported lower success rates in cases of Caesarean sections and advanced maternal age. Nonetheless, Suarez et Al. [262] affirmed that further studies are required, as evidence on any uterine balloon tamponade efficacy and effectiveness from randomized and non-randomized studies is contrasting. Also Anger et Al. [264] claimed that intrauterine balloon tamponades increase the chances of postpartum haemorrhage related to surgery and death. This paper wreaked havoc in the scientific community and received commentaries by two specialists, S. Matsubara et Al. [265] and by Weeks [266]. Overall, the authors agreed regarding the fact that the sample size was too small, a new technology had been introduced without proper training, no techniques to mitigate the prolapse of the balloon were used, and that there were system issues at play (e.g., understaffing, referral systems, infrastructures, consumables, training, corruption etc.). Using these findings while also considering a circular economy approach, the authors of this paper conceived, designed, and validated with technical tests the first

3D-printed intrauterine balloon tamponade system ever. For this purpose, the relevant international standards (e.g., ISO 10993 - Biological evaluation of medical devices, ISO 62366 - Application of usability engineering to a medical device, ISO 4074 - Natural rubber latex male condoms), the European MDR 2017/745 and available guidance from the UK NHS were taken into account to ensure the safety and efficiency of this MD. According to the European MDR 2017/745, the final MD could belong to class IIa, based on the risk deriving from its use and according to the European Regulation. In fact, Rule 5 of Annex VIII of the medical device regulation 2017/745 reads that "*other than surgically invasive devices, which are not intended for connection to an active device or which are intended for connection to a class I active device are classified as [...] class IIa if they are intended for short-term use [i.e., from 60 minutes to 30 days, except if they are used in the oral cavity as far as the pharynx, in an ear canal up to the ear drum or in the nasal cavity, in which case they are classified as class I*".

4.3.2 Material and methods

4.3.2.1 Contextualised design

Several field studies were run over the past 3 years in 4 SSA countries, namely Benin, Ethiopia, Uganda and South Africa [267, 268], using a combination of quantitative engineering methods and qualitative ethnographic and bioethical ones. During these field-experiences, a SWOT analysis was performed, healthcare structures were inspected and assessed, healthcare personnel, biomedical engineers and technicians, and sociologists were interviewed to inform the design of different MDs, including this intrauterine balloon tamponade.

4.3.2.2 CAD design and 3D printing

The 3D printed parts were designed on Autodesk Fusion360, sliced on Cura and printed on a Creality Ender3 3D printer using black polylactic acid (PLA), as it is a very versatile material and is biocompatible. The parts were: 1) A valve 2) A flow-stopper 3) A modified bottle cap 4) A uterus model

Valve. Four different designs, namely two based on a snap-fit connection and two on a threaded connection, were created, printed, and tested. The valves were printed with 0.16 mm layer height and 15% infill, 200°C nozzle temperature and 40°C bed temperature. In particular, the threaded valves were printed so that their thread axes would be perpendicular to the print bed for best results. The selected threads were: M11x0.75 (finer) and M11x1.5 (coarser). In this case, a finite element method was applied to evaluate the mechanical behaviour of the different valve designs.

Flow stopper. The flow-stopper is a variety of globe valve which consists of two parts, one base through which a silicon tube passes and a screw that acts on such tube narrowing its lumen until there is no gap left for the water to flow back.

Modified bottle cap. The bottle cap was designed following the PCO1881 standard for threads compatible with common soda bottles. It was modified with a truncated cone-like additional structure to act as a channel for the silicon tube. Moreover, the cap was designed with 2 seals, namely a v-seal and a plug seal [269].

Uterus model. Following what Mollazadeh-Moghaddam et Al. [270] did, a post-pregnancy uterus model was designed and 3D printed with PLA, so that the internal volume would be of 400 ml and the cervix opening would have a diameter of 3 cm, resembling the conditions of uteri of post-labour women. This model, consisting of two threaded parts, was printed with 0.16 mm layer height and 10% infill.

4.3.2.3 Other parts and assembly of the system

Among the other parts, a common polyethylene terephthalate (PET) 500 mL bottle was used as a water reservoir, a standard latex condom was used as an inflatable balloon tamponade and a standard silicon tube (with an external diameter of 6 mm, 50 cm in length) was used for channelling water in the balloon. The assembly steps follow: 1) Insert the tube (6-mm outer diameter, 4-mm inner diameter) in both the bottle cap, the flow stopper and the valve; 2) Insert the condom on the male part of the valve and through the female part of the valve; 3) Screw the valve tight, paying attention not to excessively stretch the condom; 4) Fill the bottle with water; 5) Screw the bottle cap onto the bottle. 5.3 Technical Validation The system was assembled for each valve type and two validation procedures were performed, following the methods that Mollazadeh-Moghaddam et al. presented in [270]: i) water leak measurements open-air and in uterus model, ii) pressure measurements in uterus model. Figure 4.18 shows the inflation of the system and its technical validation.

Water leak. For the water leak experiments, the condom was tested with two fill volumes, i.e., 400-500 mL and/or 1500-2000 mL of water, repeating the filling 3 times with a 500 mL bottle. The water leaked out of the system was weighed with a digital scale and recorded hourly for up to 6 hours, as this is the suggested duration of treatment [271]. The test results were used to improve the designs (e.g., moving from a finer to a coarser thread) and to compare all the valve prototypes. Eventually, the water leak of the best-performing valve

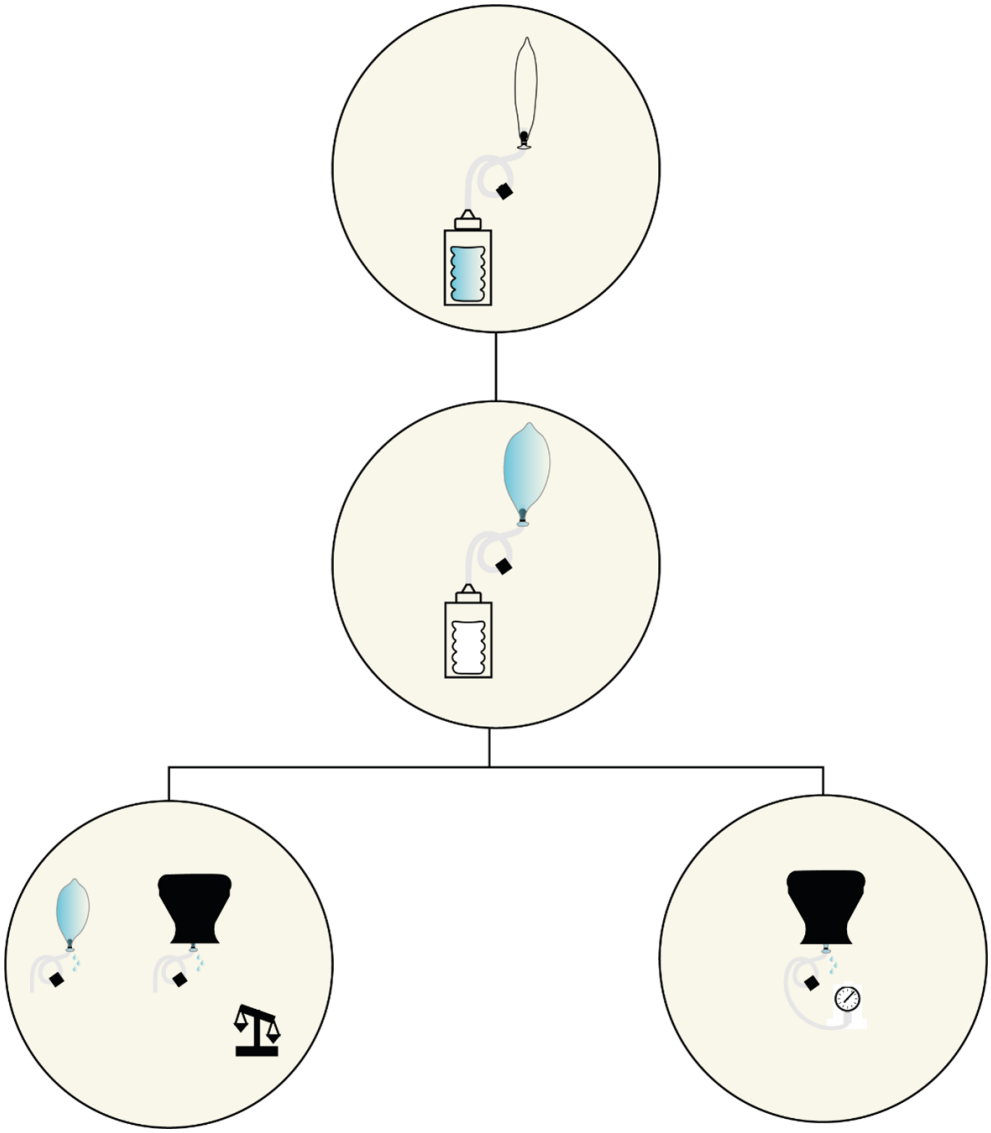


Figure 4.18: The inflation of the system and the two tests, i.e., Water Leak Tests and Pressure Drop Tests, carried out in two conditions, i.e., open air and simulated working conditions.

was tested on two different prints, twice, in order to test two filling volumes, i.e., 400 and 1500 mL (see Figure 4.19 for experiment setup).

Figure 4.19: The setup of the open-air experiments: the condom filled with water and the flow-stopper that prevents the water from flowing back through the tube.

Water leak in Uterus model. Only the system with the best valve was tested in the uterus model. Two copies of the same prototype were tested in this case. This kind of validation was tested in two positions, namely one in which the uterus model was suspended so that the "cervix" opening would point downwards, and gravity was acting on the balloon so that it pushed on the "cervix" (worst case scenario, 90°) (position 1), and one in which the uterus model was laid so that the longitudinal axis would be almost parallel to the ground (14.7° estimated from the CAD) (position 2) (see Figure 4.20). The water leaked out of the system was weighed with a digital scale and recorded hourly for up to 6 hours.

Pressure change in uterus model The same experiments for measuring water leaks with the system applied to the uterus model were then repeated for acquiring lumen pressures, hourly for up to 3 hours. The results from two experiments performed in the worst-case positioning of the uterus model (90°) were then collected and averaged. For this purpose, an ad-hoc water pressure circuit was assembled using an Arduino kit and a 26PCCFB6G water pressure

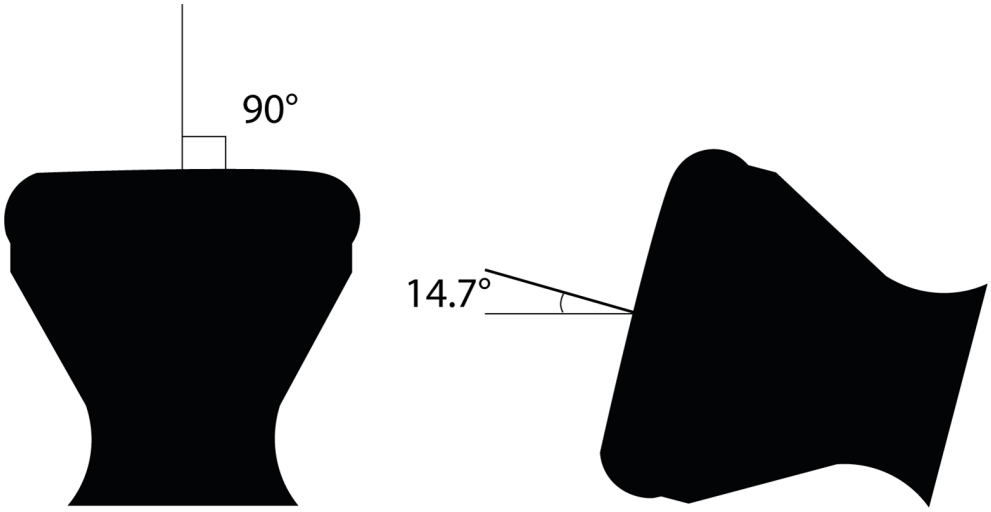


Figure 4.20: The two positions of the uterus model during the water leak and pressure test.

sensor by Honeywell. The water pressure circuit was validated using parts from a sphygmomanometer (i.e., the inflation bulb and the manometer) to increase the pressure in the tube and to compare the readings through a Bland-Altman plot, using the Matlab tool presented in [272].

4.3.3 Results

4.3.3.1 Contextualised design

The design of our intrauterine balloon tamponade was informed by quantitative engineering and qualitative ethnographic and bioethical methods field studies in sub-Saharan Africa (SSA), the full results of which are reported in chapter 3 and elsewhere [1, 2, 135]. In summary, the field studies highlighted the chronic challenges typical of LRSs, including: the lack of spare parts, consumables, expertise, functional health technology management and maintenance, funds, and the presence of harsh environmental conditions (i.e., high temperatures, sand, dust, and humidity). For these and other reason MDs, in general, lie idle in African hospitals and the commercial intrauterine balloon tamponade solutions may face more challenges than the frugal and self-assembled condom-based catheter balloons. Frugal engineering and design ethnography, can make the design of MDs more appropriate to LRSs working conditions [273]. Likewise, circular economy, with its 3 Rs (i.e., reduce, reuse and recycle) [274] can be one of the solution to many of the challenges faced by LRSs, in general and in the MD sector; in fact, it can help achieve a significant number of Sustainable Development Goals [275]. In light of this, I propose that a circular economy approach is feasible with our intrauterine balloon tamponade. Specifically, a

protocycler[4], i.e., an all-in-one recycling system for 3D printers, could be used to recycle, reuse and probably sterilise the 3D-printed parts of our intrauterine balloon tamponade.

4.3.3.2 CAD design and 3D printing

The principal function of the intrauterine balloon tamponade in treating postpartum haemorrhage is to inflate and provide pressure in the uterus, as is presented in Figure 4.21. The prototype and constituent parts are presented in Figure 4.22. Other than the condom balloon, common water bottle and standard silicon tube, the remaining parts (valve, flow-stopper, and modified bottle cap) were designed using computer aided design (CAD) and 3D printed. Four different valves were considered, all designed so that no overhang support would be needed. Finite element analysis (a computerised method for predicting behaviour against real-world forces) did not suggest any mechanical behaviour advantage of any one valve type, so all valves were tested during initial water leak experiments. In addition, a uterus model was designed to mimic the conditions of the uteri of post-labour women, Figure 4.25. This model was also 3D printed and used for validation testing of the prototype intrauterine balloon tamponade.

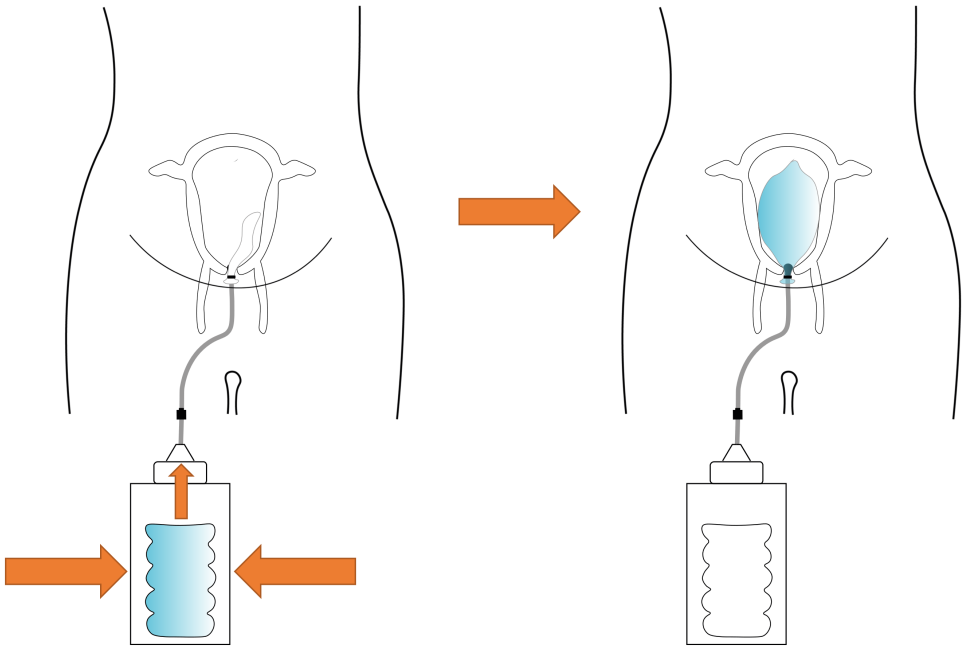


Figure 4.21: The proposed mechanism of the intrauterine balloon tamponade in treating postpartum haemorrhage. When the water reservoir is emptied into the condom balloon, the balloon becomes inflated, applying pressure inside the uterus.

[4]https://redetec.com/

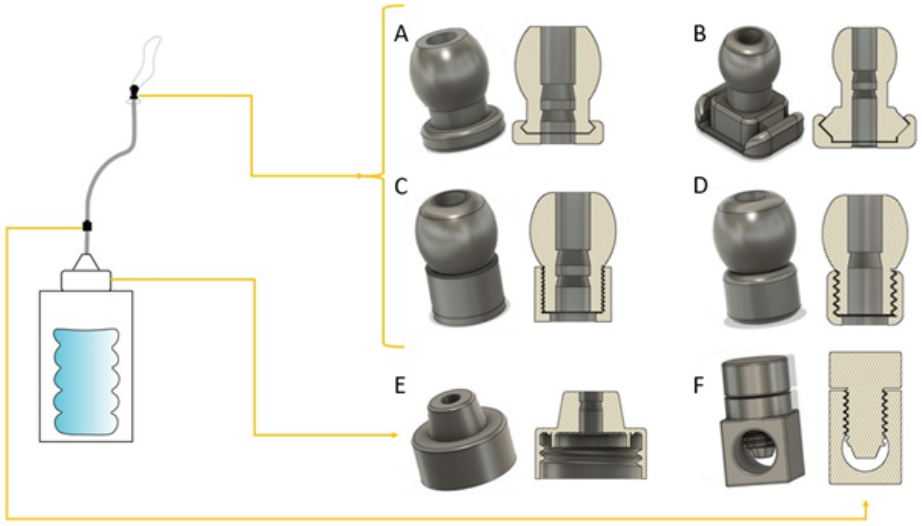


Figure 4.22: The prototype system, with CAD images of parts for 3D printing: A-D valves of different design: A, rounded snap-fit valve, B, square snap-fit valve, C, fine threaded valve, D, coarse-threaded valve; E modified bottle cap with plug and v seals, compatible with common soda bottles; F, flow stopper, a variety of globe valve preventing flow back of water down the tube.

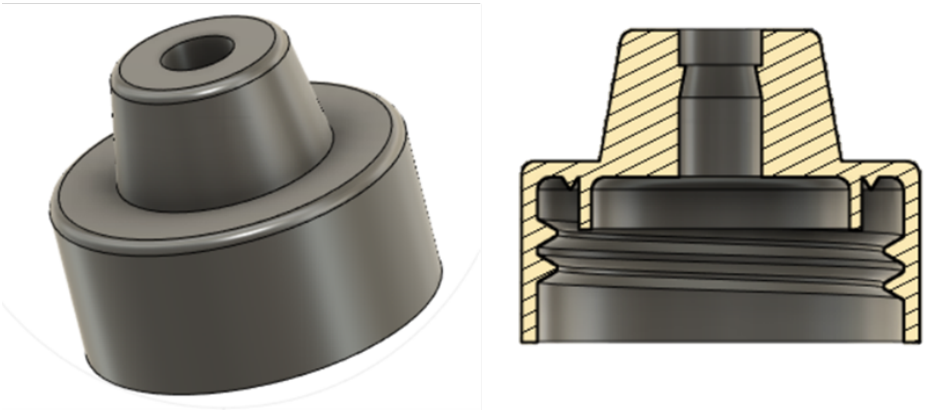


Figure 4.23: The modified bottle cap with the plug and v seals.

4.3.3.3 Technical Validation

Water leak. Valve A resulted in a mean water loss of 24.75 mL/hour (1.24%/h of the infill volume) and a mean total water loss of 148.5 mL (7.43% of the infill volume) over 6 hours. The performance of Valve B, C and D, resulted in a mean water loss respectively of 53.17 mL/hour (12.93%/h of the infill volume), 5.31 mL/hour (1.29%/h of the infill volume), and 0 mL/hour, and a mean total water loss of 319 mL (77.6% of the infill volume), 31.85 mL (7.75% of the infill volume), and 0 mL over 7 hours (see Figure 4.26). At this

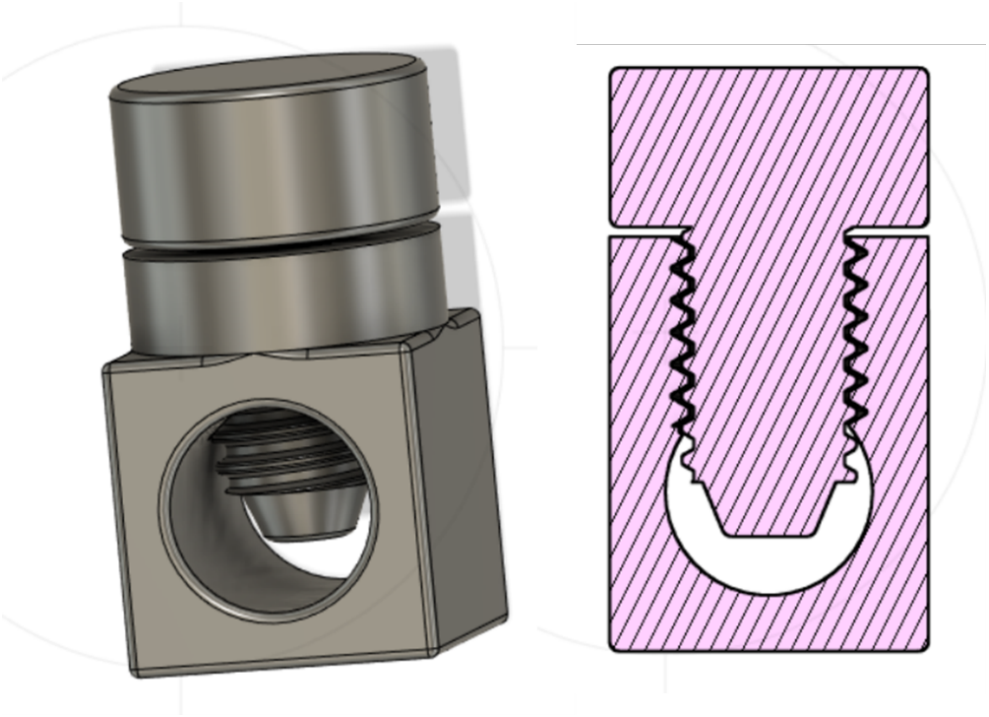


Figure 4.24: The flow stopper, a variety of globe valve.

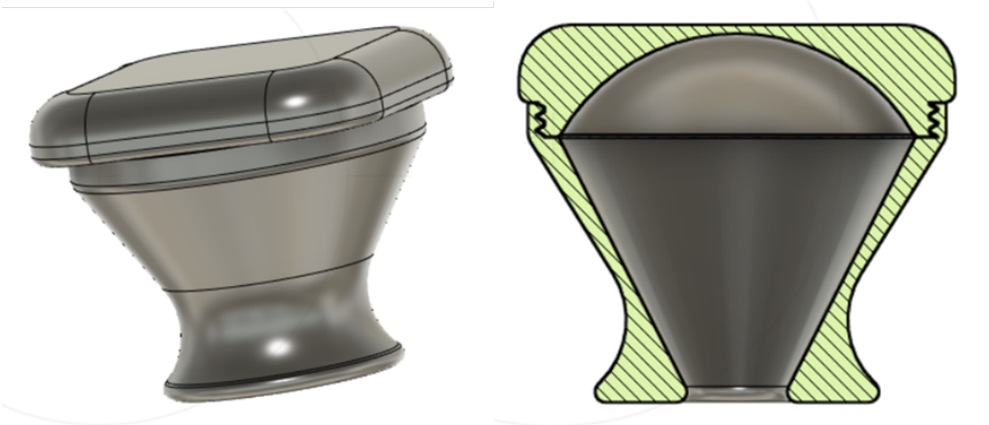


Figure 4.25: The uterus model.

point, valve D, the only valve, which did not lose water both when filled up with 400 mL or 1500 mL of water, was selected for further testing .

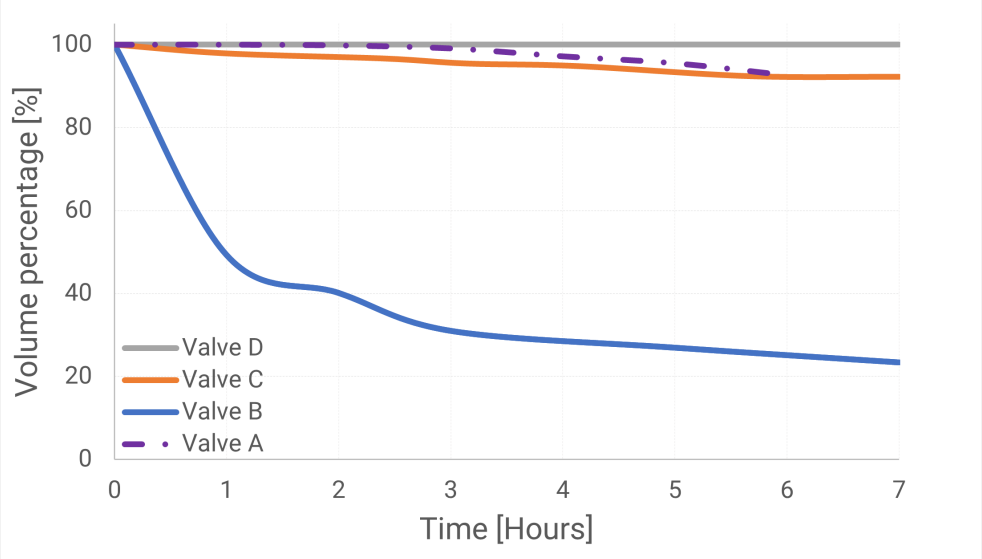


Figure 4.26: The hourly water leakage for the 4 different types of valves.

Water leak in uterus model. Two prototypes of Valve D were tested in the 3D-printed uterus model in two positions. In position 1, the uterus model was suspended so that the "cervix" opening was pointing downwards (worst case scenario), the average water loss per hour was 2.47 mL/hour (0.62%/hour of the infill volume) and the mean total water loss was 14 mL (3.51% of the infill volume). In position 2, the uterus model was laid sideways so that the longitudinal axis was almost parallel to the ground (simulating lying position), the average water loss per hour was 1.4 mL/h (0.35%/hour of the infill volume) and the mean total water loss was 7 mL (1.75% of the infill volume) over 5 hours.

Pressure. The water pressure circuit, constructed to monitor the pressure drop in the system resulting from the water loss, was validated against an analogic manometer (gold standard) and the resulting Bland Altman plots are shown in Figure 4.27. Our system had a very good percentage of agreement with the standard, apart from a 10.05-mmHg bias, which was accounted for in the measurement of pressures during the following tests. The average water pressure drop was 2.75 mmHg across the two performed experiments (0.92 mmHg per hour), and the average water leakage was 8.5 mL (2.83 mL per hour) (however, most of this leakage was due to the handling with the two sensors) over 3 hours. However, it is likely that most of this leakage was due to the experimenter's handling when swapping the connected sensors (this was

noticed by the experimenter, who did not see any water leakage on the tray below the system before the manual handling took place).

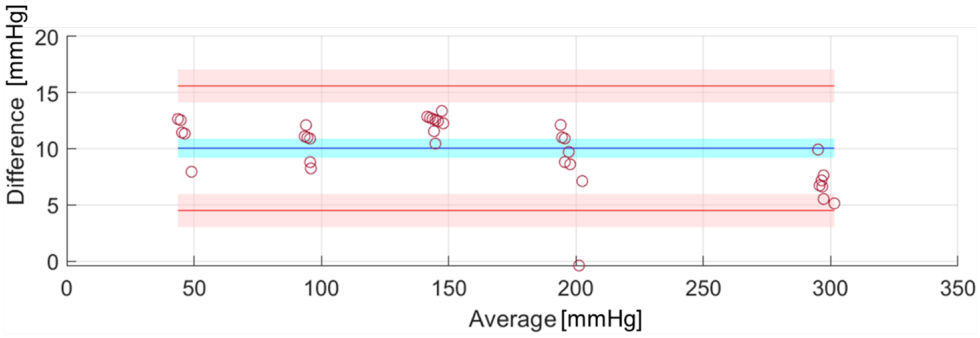


Figure 4.27: Bland-Altman plot showing the 95% limits of agreement (red lines) with the 95% confidence interval (red region) and the bias (blue) with its 95% confidence interval (blue region).

4.3.4 Discussions

This paper presented the design and the technical validation of a 3D-printed condom-based intrauterine balloon tamponade, intended to be manufactured and used in LRSs. A frugal engineering and design ethnography perspective was adopted, in conjunction with European international regulations and standards. This paper presented how contextual design principles can be taken into account and influence the final product and highlighted the results and importance of the technical validation, namely the water loss and pressures measurements within the balloon, for this particular application. From the results, it was clear that out of the four designed valves, Valve D, i.e., the one with a coarser thread, showed the best performance. In fact, it outperformed the other valves as there was no water loss (either when filled with 500 mL or 1500 mL) over 6 hours in open air. Moreover, when tested inside the uterus model, the mean total loss of water was negligible (i.e., 14 mL, 3.51% of the infill volume) in position 1 (the worst-case scenario) and even more negligible in position 2 (i.e., 7 mL, 1.75% of the infill volume). Nonetheless, to remedy this minimal water loss, the healthcare operator could potentially refill the balloon with an amount of water equal to the leaked one, if deemed necessary. With regards to the pressures at play, the average pressure measured at the start of the experiments (i.e., 40.75 mmHg) was lower than those reported in [270] for the condom-catheter balloon tamponade. However, the rate of pressure loss, a factor which is of higher importance, was much lower. In fact, different studies proved that an adequate tamponade does not require high intraluminal pressures nor excessive volumes, and that adequate haemostasis, in most cases, is reached with filling

volumes well below the recommended maximum [276, 277]. More specifically, Georgiou [278] demonstrated in vivo that a tamponade was efficient even when the intraluminal pressure was below the systolic blood pressure. In fact, as suggested by the author, that of exerting a pressure that is greater than the systemic arterial pressure is only one of the proposed mechanisms of this device. Other proposed mechanisms include endometrial contact, hydrostatic pressure effect on the uterine arteries, vascular compression and myometrial activity obtained through myometrial stretching. When compared to other existing solutions for postpartum haemorrhage, the proposed solution seems to be the most versatile and appropriate for LRSs. In fact, the other solutions, some of which may have a more physiological shape (e.g., the Bakri balloon or the Ebb tamponade system), rely on parts that are either proprietary or difficult to find in LRSs (e.g., syringes, catheters, nasogastric probes, surgical wires, latex segments). Consequently, as they are single use, the local populations have to rely on the continuous supply of spare parts and are not empowered nor supported to be independent. Our solution, conversely, comprises parts that are either widely available in this kind of settings (any kind of silicon tube, condoms, and plastic bottles) or that can be manufactured locally by universities or technical centres supplied with 3D printers and protocyclers, fostering a circular economy approach. Although our system may be simple, the technical validation demonstrated its efficacy. Moreover, as previously stated, the efficacy of condom-catheters intrauterine balloons was proven by different studies and the risk of prolapse due to the non-physiological shape can be mitigated with different techniques (using forceps, gauzes and/or sutures) [279–281]. Another advantage of our system is that the high temperatures used by the 3D printers and the protocycler (over 180°C) are enough to sterilize the instruments. Rankin et al. [282] demonstrated that the clean catch filament freshly extruded by a 3D printer was completely sterile. Thus, if the print takes place on a clean print bed and in a clean environment, the final product will most likely be sterile, as proved by Kondor et al. [283].

4.3.5 Conclusions

This paper presented the design and technical validation of a 3D-printed condom intrauterine balloon tamponade, suitable for use in LRSs. The performance of this device, as confirmed by the validation, is promising. The intrauterine balloon tamponade, in fact, proved to be able to hold large volumes of liquid and maintain the pressure stable for several hours, as per postpartum haemorrhage treatment guidelines. In addition, the system would be suitable to be manufactured and recycled locally, making it a promising option in combatting the devastating impact of postpartum haemorrhage in LRSs.

Overall, this research has also an important ethical substratum and fosters the enjoymentaims to the improvement of human rights, especially for women.

4.4 A vest for treating jaundice in LRSs

This fourth use case belongs to the group of treatment.

4.4.1 Introduction

Neonatal Jaundice is one of the most common conditions in newborns [284]. It is present in 60% of all births (and up to 80% of preterm births) worldwide, and the 10.5% of all neonates require prophylactic phototherapy treatment [285, 286]. Neonatal jaundice is usually due to the incapacity of neonatal livers to metabolize unconjugated bilirubin as they are still organically developing [287]. It results in yellow coloration of the skin and sclera because of the accumulation of conjugated or unconjugated bilirubin. The former being very rare (approximately 1 in every 2500 infants) and pathological and the latter being most common (with over 75% of cases being physiological) [288, 289]. Neonatal jaundice is indeed the seventh most common cause of neonatal mortality up to the age of 6 days, worldwide [290]. A systematic literature review and meta-analysis of studies related to the global prevalence of neonatal jaundice concluded that its rates are associated with a significant health burden in LMICs, further positing that the annual global morbidity and mortality rate due to neonatal jaundice (114000 and 63000 per annum, respectively), described by Bhutani et al., is likely to be significantly underestimated [291, 292]. Several studies underlined how, in LMICs, neonatal jaundice is not always accurately diagnosed, and treatment is not always effective [290, 293–297]. If left untreated, neonatal jaundice may lead to an array of kernicterus spectrum disorders (e.g., mild permanent brain damage, brain diseases, hearing loss, cerebral palsy and death) [284, 298]. Improving the healthcare of neonatal jaundice is of international relevance. As outlined in the NHS Long Term Plan, there are the relevant ambitions to provide extra support to premature births, expand support for perinatal mental health conditions and reduce child deaths during birth by 50% [299]. Additionally, there needs to be a greater push towards 'out-of-hospital' care, proliferating access to treatment for a greater share of the population. To this regard, this project aims at a shift from a hospital-based phototherapy to a home-based one, which has already been proven to be an effective solution to mitigate hospital patient load [300, 301].

In literature, there are selective studies from LRSs commonly identifying the need for more effective phototherapy by means of delivery [291, 293–297, 302]. In particular, the two field studies conducted in Nigeria and in India highlighted

the most common issues with treatment to be:

1. insufficient light irradiance (when compared to the American Association of Paediatrics [303] standards);
2. poor maintenance of burnt out/dysfunctional light sources;
3. poor operation and management of neonatal jaundice with phototherapy;
4. and inconsistent and unreliable electrical supply.

Although the devices currently used in LRSs for phototherapy have the capacity to deliver effective treatment, their real utility is limited due to poor management strategies. Furthermore, the need for "out of hospital" care emerged as international relevance across the socio-economic spectrum. As it has been stated by the NHS [299], it is widely accepted that accessible 'out-of-hospital' care has the potential to be more cost-effective, reasoning as to why it is manifested in popular literature [304]. There are selective studies from LRSs highlighting that neonatal jaundice is often inconsistently (and hence ineffectively) managed, identifying common failure modes such as insufficient training, poor setups with insufficient irradiance, poor maintenance and the idleness of the 70% of the donated MDs [1, 55, 119, 285, 294, 295, 305]. However, with locally sourced manufacturing (e.g., 3d printing and protocycling), increasing interest in resilient MD design, donations (although there are major concerns as to its long term benefit), and re-manufacturing, there are causes for optimism in improving global healthcare in an attempt to accommodate and improve MD management in LRSs [1, 306]. Although the developing phototherapy devices used in LRSs have proved to be effective, [307, 308], they are not able to totally meet the needs highlighted above. Contemporary phototherapy devices show a push towards using LEDs or surface mount LEDs with their advantageous high-irradiance-to-temperature output. However, although they are designed with portable power unit suitable for at-home therapy, not all the systems are independent from constant power supply, that is generally deemed to not be a commodity by definition of LRSs [309]. Moreover, the devices are designed as structures to wrap around the neonate for proximal emission while published research into garmented phototherapy is limited. One paper describes the design development of an 'automatic and portable phototherapy garment', featuring a transcutaneous blood bilirubin measurement device [310]. However, the main limits that emerged are related to the position of LEDs, directly on the garment itself, which affects the comfort and distribution of the light on the screen surface. Another current paper, implementing the plastic optical fibres in textiles to control light-output in neonatal jaundice phototherapy context [311], concluded a real viability in

using garmented treatment with sufficient irradiance [312]. For these reasons, domestic LRSs solutions for neonatal jaundice has been of growing World Health Organisation (WHO) interest, as an increasing number of device proposals in this domain have been published into the 'WHO compendium of innovative health technologies for LRSs' [110].
Overall, this project aims to address the issues and causes for insufficient neonatal jaundice phototherapy on a global scale by presenting the results of a needs assessment cascading into an innovative product design specification. This paper presents the envisioned ideal requirements of a vest embedded with plastic optical fibres and trans-cutaneous bilirubin (TcB) diagnostics integrated with the device for autonomous phototherapy treatment of newborn jaundice in LRSs. Moreover, it also presents the results of a feasibility study for some of the requirements conceived for our product, in particular those related to the use and efficacy of LED-powered fibre-optics in a newborn-sized vest.

4.4.2 Methods

4.4.2.1 Needs assessment and product design specification

The system V-model (see Figure 4.28), was holistically adopted throughout the project: from researching the clinical problem, defining the user requirements, formalizing the functional requirements, setting the design specifications and then continuing through with the design plan and implementation. Verification was then attempted at each stage and, beyond this project, prospective complete validation would occur through more iterations. The clinical problem was defined throughout a need assessment process focusing on intended patient population and setting of use. More specifically, seven field studies have been performed in Sub-Saharan Africa: one in South Africa (2016), three in Benin (2017, 2018 and 2019), one in Ethiopia (2018), and one in Uganda (2019). During some of these field studies, MLs were inspected and assessed and local biomedical engineers and technicians were interviewed and shadowed withing their workplaces, in order to evaluate the major challenges and opportunities [1, 2]. The review of the field notes and of the related publications, as well as the focus groups with relevant experts, and the literature review were essential to understand the intended population and setting of use as well as the requirements needed for our prototype. A literature review was then carried out in order to encompass the aspects of the clinical need that inform on the design criteria specification for the phototherapy vest and the solution scope, including the exploration of the viability of integrating transcutaneous bilirubin (TcB) diagnostics with the device. Results from literature review were compared and integrated with the relevant standards and regulations (e.g., the European MDR 2017/745). Once the general design requirements were

defined, a list of detailed user and functional requirements was set up. The way to measure them and their punctual definition were outlined throughout the integration between evidence from literature, and international experts' and stakeholders' opinions.

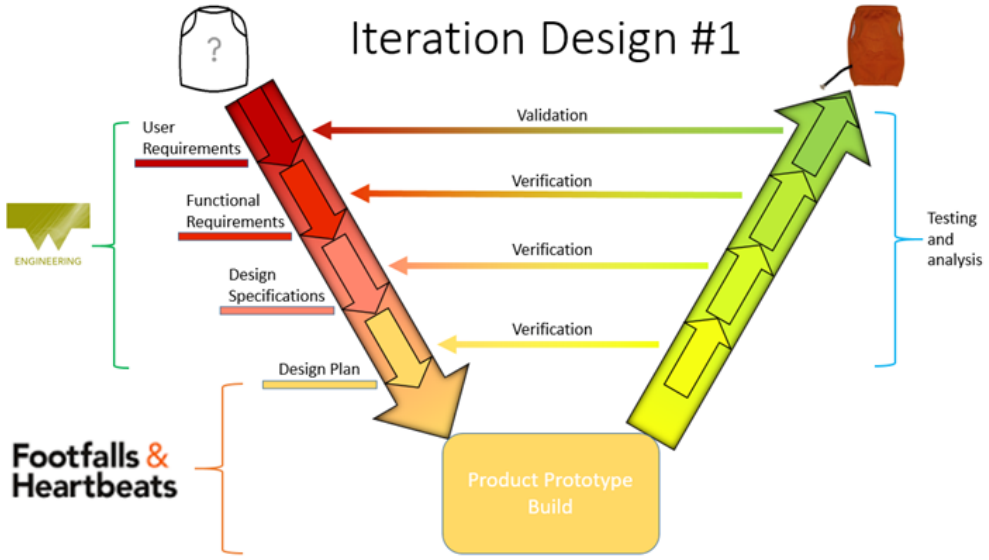


Figure 4.28: Diagram of the systematic design approach for the project, highlighting the different roles.

4.4.2.2 Feasibility study

The feasibility of some of the aforementioned requirements was evaluated during the prototyping and validation phases, in collaboration with a UK-based smart textiles company, Footfalls&Heartbeats[5]. The extent of Footfalls&Heartbeats' input into the project was in the practical design and implementation of the textile vest with optical fibres. In fact, the project's design specifications were taken by Footfalls&Heartbeats to produce the first iterations of the vest, which thereon have been subject to verification and validation testing.

4.4.2.3 Validation

Several tests were performed to evaluate:

1. the modelled absorption at an interpolated or extrapolated skin thickness, to assess the level of light penetration;
2. safe phototherapy emission bandwidth verification;
3. LED performance and efficacy comparison;

[5]https://www.footfallsandheartbeats.com/

4. fibre-optic loss prediction and required number of LEDs to achieve effective phototherapy.

The tests (see Figure 4.29) were performed taking into account the light power spectra specifications for efficient phototherapy, presented by the American Academy of Pediatrics [303]. The tests were performed using a spectroradiometer (EKO Spectroradiometer LS-100), different LEDs, the vest prototype, and 2mm-thick synthetic skin samples. Moreover, a power source with a voltage and current readout (VOLTCRAFT Power supply LSP-1403) was used, as well as a multimeter to verify current readout on power supply and take LED voltage (VOLTCRAFT Multimeter VC265), a laptop for data measurement and storage, a ruler for apparatus distance setting, and a thermometer and hygrometer (Anymeter Thermometer and Hygrometer TH101E). Further information regarding these tests can be found in Appendix F.

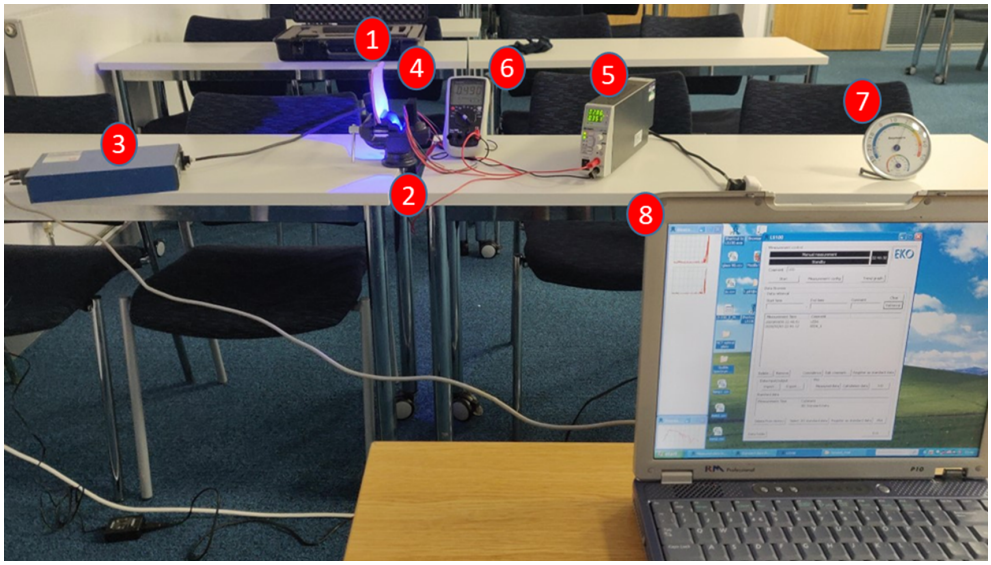


Figure 4.29: Experimental setup example for testing with synthetic skin: skin sample (1), bench clamp (2), calibrated absolute spectroradiometer (3), monochromatic light source (LED) (4), Power supply (5), multimeter (6), laptop (7), thermometer and hygrometer (8).

4.4.3 Results

4.4.3.1 Needs assessment and product design specification

The results from the needs assessment are summarised in the requirements shown in Figure 4.30. These have been taken from American and UK neonatal jaundice management standards as well as modern neonatal jaundice therapy devices, and have most significantly highlighted our prototype's need to increase its radiated intensity at skin surface.

The requirements were grouped into 7 domains, presented in decreasing order of importance:

1. Neonate Safety, comprising all the requirements related to the risks to which the newborn is exposed, linked to UV light and possible healthcare-acquired infections (HAIs)

2. Vest Fibre-optics and LEDs, comprising all the requirements related to the intensity and characteristics of the blue light for optimal skin radiation levels

3. Bilirubin Diagnostics, comprising all the requirements related to the bilirubin sensor for the closed-loop therapy

4. Operating Temperature, comprising all the requirements related to the monitoring of the room temperature and the temperature reached by the skin of the newborn

5. Electronics and Data Relay and User Interface, comprising all the requirements related to the power supply, the communication protocols, storage, and the ease of use

6. Cost, comprising all the requirements related to the costs of production and maintenance

7. Military standards, comprising all the requirements related to the resilience of the device to harsh environmental conditions (e.g., high temperatures).

4.4.3.2 Evolution of the concept

The initial prototype design for the vest included light emission at the end of the fibre-optic tips directly onto the skin. Textile samples of end-emitting fibres had already been produced by the company and so were already feasible. However, as prototype development went on, there were discussions with Footfalls&Heartbeats on using side illuminating fibres instead, as the end tips embedded in the fabric were relatively sharp and would give physical discomfort unsuitable for a neonate. The current prototype relies on side-illuminating plastic optical fibres inserted non-uniformly and set into the vest using thermosetting plastic (see Figures 4.31, 4.32) is 8.5x13.5 cm in size (complying with clothing sizes by Noppies), and weighs 100 g. The vest itself is stretchable, washable, foldable, and lightweight and has an inner layer of spun polyester, providing comfort to the neonate as they move around through treatment.

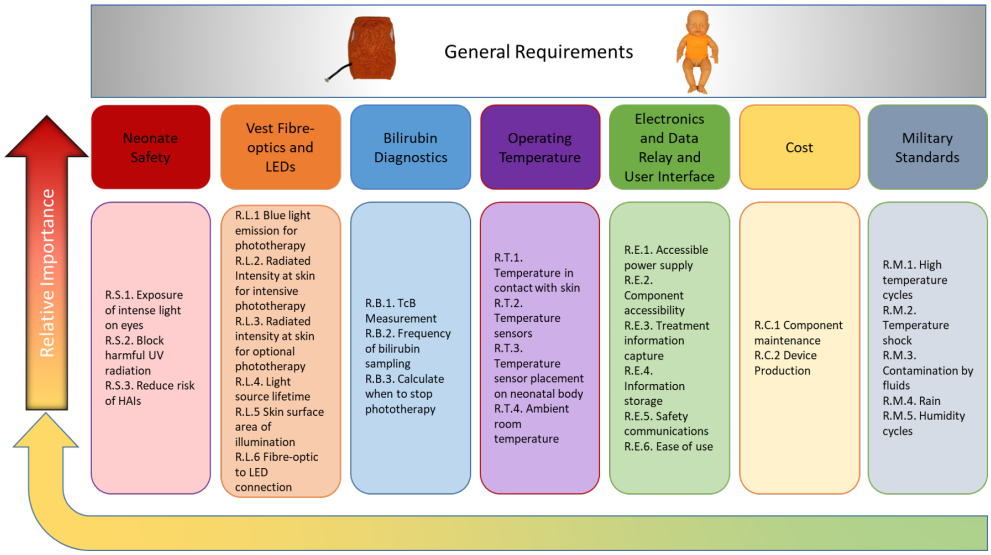


Figure 4.30: Conceptual device requirements, laid out first in terms of category and secondly in terms of importance. The relative importance (going right to left, upwards) between categories and then sub-category requirements is illustrated.

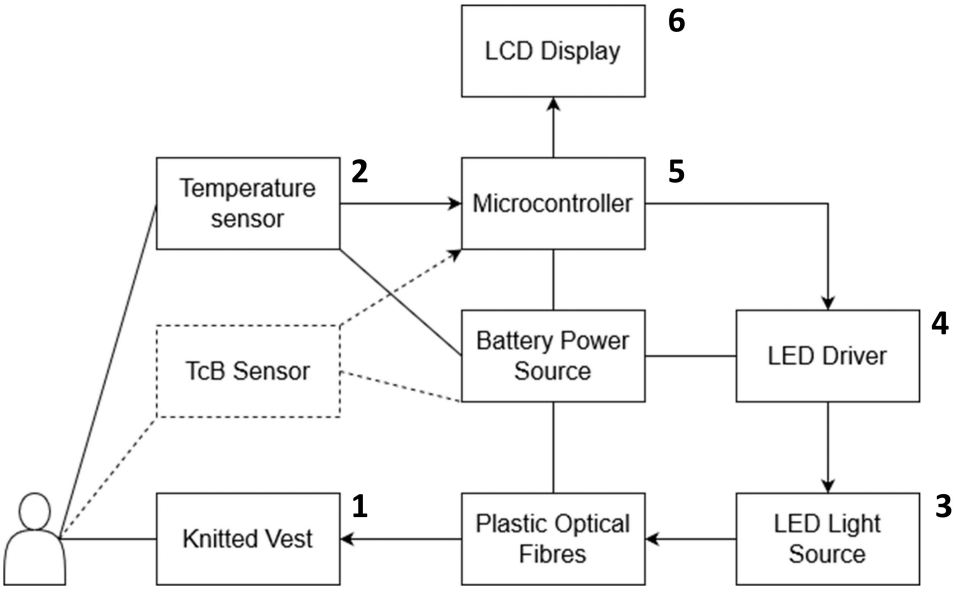


Figure 4.31: The block diagram of the newborn vest. The dashed box represents possible future developments of the enhancements of the prototype. The annotations refer to Figure 4.32

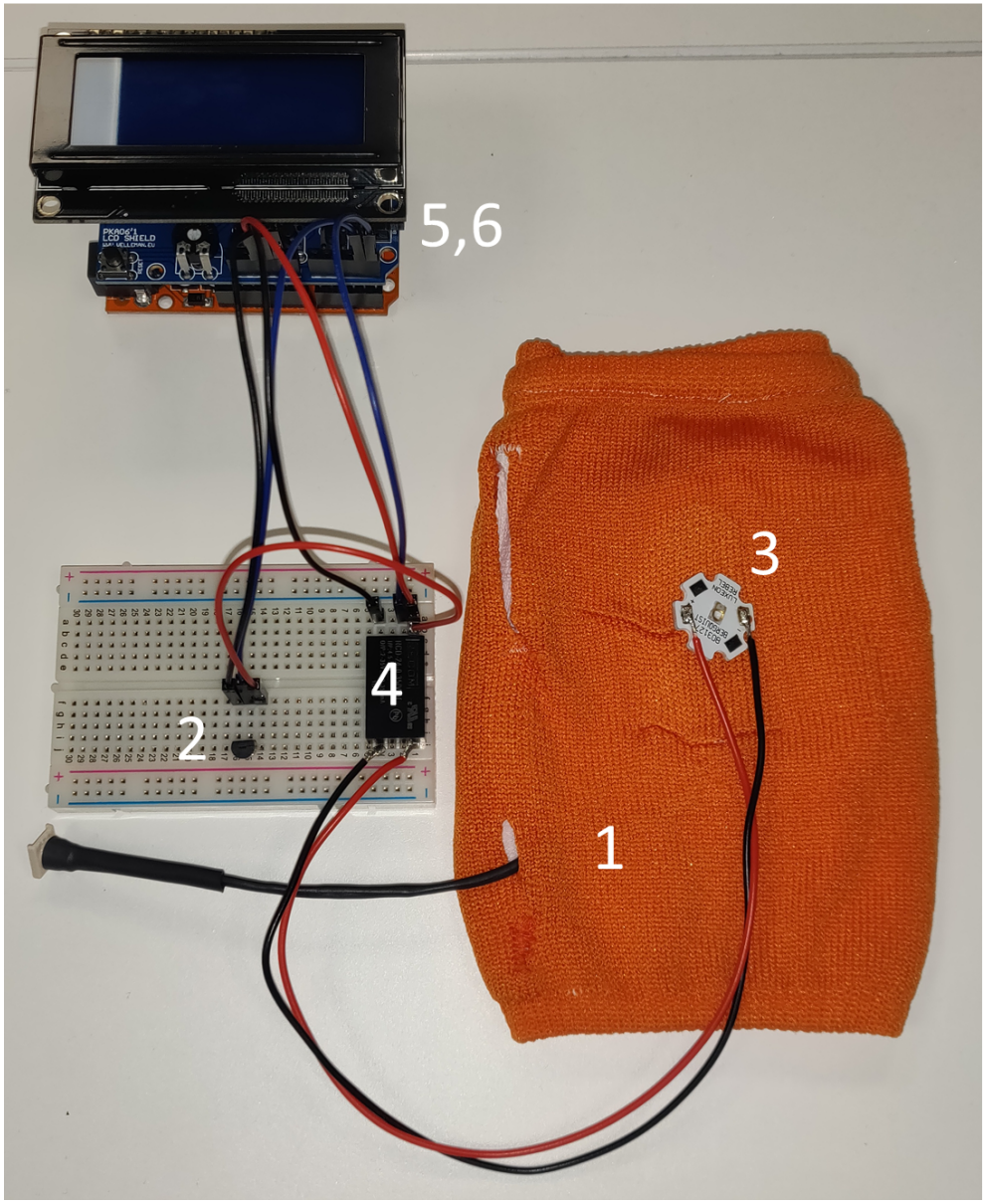


Figure 4.32: Prototype components layout with annotations referring to Figure 4.31

Furthermore, a prospective detachable light link means the neonate may also be taken out of phototherapy temporarily for post maternal care and bonding without a big hassle of deconstructing the setup for phototherapy. The current design concept also includes a battery to make the device less reliant on possibly unreliable power sources, a temperature sensor to ensure that the newborn is never exposed to harmful temperatures, and a trans-cutaneous bilirubin diagnostics unit to automatically evaluate the need for phototherapy and adjust the treatment settings, without the intervention of a doctor. In this way, the complete prototype would be easy to use for lay-users and could be a potential solution for at-home therapies.

4.4.3.3 Feasibility study

As of now, with the current prototype it was possible to fulfil the following requirements, either by light testing or by observation and analysis: R.L.1. (via observing the emission spectrum to have dominant wavelengths suitable for phototherapy), R.L.4. (via LED manufacturer stating average 50'000 operational hours), R.L.6. (via a 3D-printed pigtail, see Figure 4.33), R.S.2. (via observing negligible UV emission in spectra), R.T.1. (via comparison with other phototherapy devices), R.S.1.(via vest design with opaque outer layer), R.S.3. (via washable vest), R.C.1. (via modular design), R.C.2 (via components and vest manufacturing price). The primary focus now is the prototype's radiated intensity, which reaches around 1 mW/cm^2, inadequate for effective phototherapy (R.L.2, R.L.3).

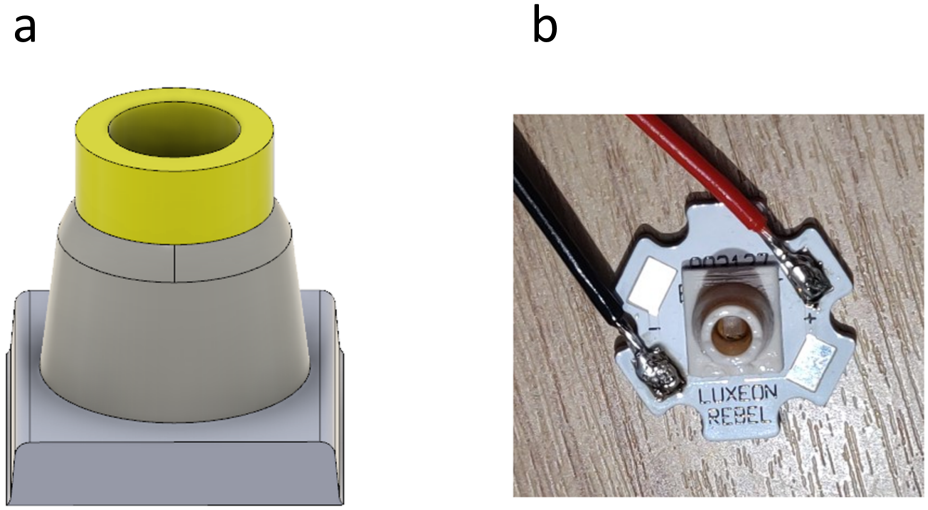


Figure 4.33: a) pigtail stl design model; b) 3D-printed pigtail placed on top of an surface mount LEDs

4.4.4 Discussions and conclusions

Results shows promise in the ability to emit an appropriate spectrum for neonatal jaundice phototherapy, but is yet to achieve sufficient skin irradiance through the means. It mainly provides testament to the potential of wearable health care, specifically under phototherapy treatment, as the vest is designed to be suitable for the dimensions of a neonate and can illuminate enough surface area for standard phototherapy. By design, this vest would be simple enough for lay users whilst improving ease of maintenance through being modular and leaving little leeway for delivering insufficient irradiance, given the light source is at skin surface level (provided the output irradiance improves to meet neonatal jaundice phototherapy standards). As of yet, there is no conceptual implementation for a TcB unit, but there is practical accommodation for it with the presence of a microcontroller and a light source control (see Appendix 6.6 for a the flowchart of an envisioned method of treatment outside of a health centre with the final prototype of such vest). Further into development, this device can expect to engage with a range of pressing stakeholders, as is typical of MDs. Because the prototype textiles manufacturing for this device uses a practically state-of-the-art machine (further details being trade secrets of Footfalls&Heartbeats), assessing the feasibility of regional textiles manufacturing in LRSs of this device will require further research. It is worth noting that the fabrics materials and plastic optical fibres for manufacturing the prototype vest alone (i.e., not including LEDs and electronics) can be priced at less than $3 per vest, as stated by Footfalls&Heartbeats, which raises optimism for the prospect.

4.4.5 Limitations and future work

The project presented in this paper is that undertaken by one of the authors in fulfillment of a BEng in Biomedical Engineering. The project was thus subject to time and resource constraints, and could be further extended with additional resources and workforce, in addition to further smart fabric industry collaboration. In particular, the ideal number of LEDs/plastic optical fibres to reach the required minimum illuminance for phototerapy remains unknown. As presented in the detailed tests in Appendix F, the tests would benefit from the use of another spectroradiometer with a smaller aperture, for more consistent and repeatable results. A future prototype may also benefit from a different design, shown in Figure 4.34, based on multiplexed LEDs coupled to different sets of fibre optics.

As regards the coupling design, it could be improved upon on two fronts: the safety and the quality of connection. Given the risk of being exposed to the intensive blue light, the base of the coupling could have a safety feature to

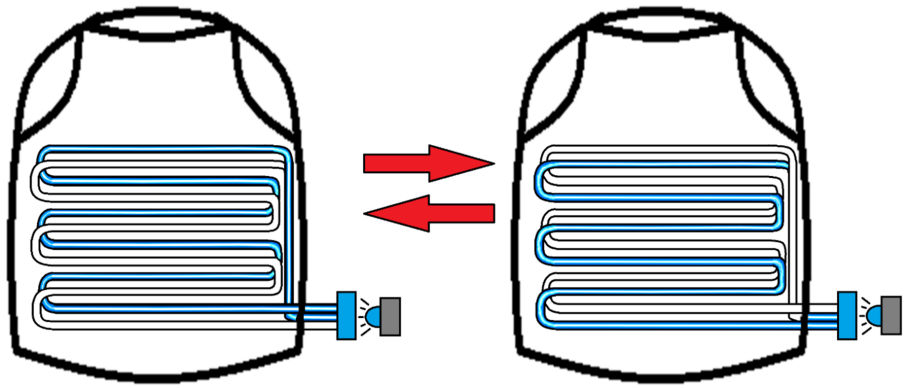


Figure 4.34: Schematic drawing of how multiplexed LEDs coupled with different fibre-optic cables could function.

restrict/deny the power to the light source when uncoupled. The conceptual design (see Figure 4.35a) could include a conductive lock base which acts as a switch, only allowing charge to the light source when attached. The light source type may also benefit from changing to a laser diode with the general marked benefits of higher directivity and power output. For example, the Osram Opto PL 450B laser diode (see Figure 4.35b) has similar radiometric power to LED4 but with 5 times less beam divergence. These aspects may reduce the error in alignment with the fibre-optic tips and increase the overall output irradiance. Given the similarity in structure, the next step would be the acquire a suitable array of laser diode candidates and assess their performance similarly using the light test protocol.

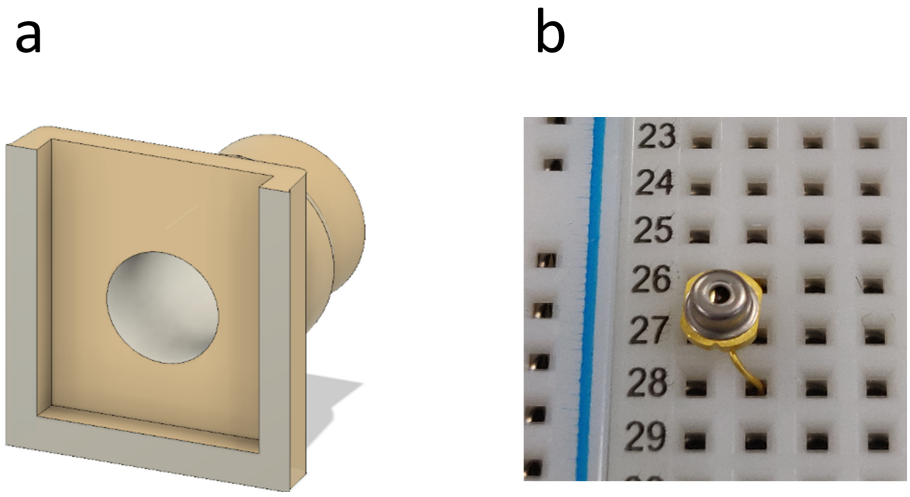


Figure 4.35: a) redesign of the pigtail connector with a conductive pad (coloured in silver) beneath; b) Osram Opto PL 450B blue laser diode mounted on a typical breadboard for scale.

As regards the measurement of bilirubin through TcB, as of now, there is diverging information about their reliability in literature. TcB, in fact, measurement devices tend to overestimate the total serum bilirubin levels, and are susceptible to false measurements if analysing phototherapy pre-treated skin [313]. Moreover, most of the studies assessing its efficacy are performed in controlled environments. However, there is a growing technological advance in TcB devices development, as highlighted in a literature review by Young et al. [314]. For these reasons, whilst there are design and conceptual accommodations for a TcB device in this prototype, further work on integration would only best suit if the technology becomes more reliable.

4.5 3D-printed activated charcoal inlet filters for oxygen concentrators: a circular economy approach

This fifth use case belongs to the group of clinical engineering.

4.5.1 Background

For brevity, this subsection is not reporting the whole text of the related publication. Shall the reader be interested, they could find more information, specifically about the background, the challenges and opportunities of LRSs in Chapter 2 and in the published paper [7].

Despite the WHO defined medical oxygen as an "essential medicine", the access to it remains critical in the healthcare systems of most LMICs [2, 315]. Currently, this situation is being exacerbated by the spread of COVID-19 pandemic. Over the last year, in fact, the demand for oxygen concentrators and ventilators by health facilities drastically increased, as they can play a vital role in the treatment of critical-condition patients infected with COVID-19 [316–318]. Currently, oxygen concentrators are enlisted in the WHO's priority MDs list for the COVID-19 response. Oxygen concentrators are MDs that deliver oxygen to patients with blood oxygen concentration levels below normal and that are used to treat individuals with breathing related disorders or conditions including but not limited to asthma attacks, pneumonia, and respiratory stress syndrome. Furthermore, oxygen concentrators are more suitable for LMICs than alternative such as oxygen canisters, as they concentrate oxygen from ambient air without requiring an artificial oxygen supply, significantly reducing costs and the problems related to the oxygen supply chain. Bradley et al. [319, 320] proved the cost-effectiveness of oxygen concentrators when compared to other oxygen systems (e.g., cylinders). In fact, they estimated that even when replaced every 5 years, the use of oxygen concentrators reduced the costs by 75%. Based on the field studies performed in Gambia, they also proved that, a good health technology management is at the base of a functioning oxygen concentrator service [320]. Moreover, they pinpointed how the most frequent issues affecting oxygen concentrators, i.e., those related to batteries and filters, are easy and cheap to fix. However, in [320] they also state the fact that the resources for and the access to spare parts are among the key elements of an oxygen concentrator support ecosystem. In the specific case of The Gambia unit, the access to such spare parts was guaranteed through a long-standing relationship with manufacturers. Nonetheless, this might not be the case for other LRSs. Mongolia and Malawi, for example, have difficulty in

retrieving spare parts, as well as Benin and Uganda [2].

Moreover, the constant power supply that they require to function could be a disadvantage because of the lack of/unreliability of the electrical power in LRSs. However, the amount of power they consume is relatively low (i.e., 280-600W depending on the model) [321] and this cost is much lower than the cost to refill and transport oxygen cylinders [322]. The WHO estimates, indeed, that the operating costs of an oxygen concentrator are between 2 and 8 US dollars equivalent for every 1000 liters of oxygen supplied, compared to oxygen cylinders that cost from 10 to 30 US dollars for the same amount of oxygen supplied [321].

Howie et al. [315] and Bradley et al. [323] presented oxygen concentrators systems relying on batteries and solar panels, that proved to be able to provide for a continuous supply of oxygen for two days, as well as to be more reliable and easier to use. When it comes to battery-based device, it is also essential to take into consideration the limitations of local contexts, such as the extreme environmental conditions. High temperatures challenge and reduce the battery life by 16% [324].

Despite the above-mentioned limitations and advantages, the presence of one to three filters within the oxygen concentrators (i.e., the gross particle filter, the inlet filter, and the micro disk filter) is one of the main issues. The filters, in fact, are designed to work a limited number of hours in ideal conditions (e.g., a surgical theatre where there is a 99.97% air filtration level). These ideal conditions cannot be found in LRSs, where these devices are bound to last much less, also because of the lack of a working supply chain for spare parts [1]. To the authors' best knowledge, there has been no attempt to design a replacement filter that can readily and rapidly be manufactured locally at a LRS medical facility. Due to its many advantages with regard to small scale local manufacturing, additive manufacturing appears to be an ideal process to tailor this aim towards. In fact, additive manufacturing is used to some extent in almost every major manufacturing industry and is widely used across a large array of disciplines, from the motor industry to medicine. Today, 3D printers are even accessible and affordable for members of the public in developed countries and are now also beginning to be adopted by organizations in low-income settings [325, 326]. For this reason, this project aims to present the redesign of the inlet filter of an oxygen concentrator, based on a reverse engineering approach, and on the use of 3D-printing along with activated charcoal, following the design paradigm presented in [4]. Moreover, this project aims to set out a sample process that, together with 3D printing and protocycling (i.e., the act of recycling used filament and prints to create new filament), can foster capacity building in local communities, especially in LRSs, empowering them to create a local supply chain for affordable and

environmental-friendly inlet filters for oxygen concentrators.

4.5.2 Methodology

This section presents the methods that were used for prototyping and validating our filter. The filter design was partially based on the existing inlet filter of EverFlo by Philips, which was selected because available in our laboratory.

4.5.2.1 3D data acquisition and post-processing

In order to have a casing compatible with the inlet of EverFlo, two methods of 3D data acquisition were used, i.e., handheld 3D scanning and microcomputed tomography scanning. The results from these two techniques were then compared and analysed, so that the superior method could be recommended for oxygen concentrator filters as well as other small-scale MDs future applications.

4.5.2.2 Handheld 3D scanning

Data acquisition The Nikon h120 handheld scanner, mounted on a MCAx25 scanning tripod setup was used for 3D handheld scanning. The Nikonh120 is still a highly accurate scanner, with a combined accuracy of 0.028mm. This process is important as it allows for the Computer-Aided Design that will be created to have as close dimensions as possible to the original filter, which will ensure that the new filters fit comfortably into the oxygen concentrator. Each filter was scanned twice, because, as the parts were scanned on a measuring table, a second scan of the underside was required to capture every surface. . The scanning software used was Nikon Focus. Each scan also captured part of the surface of the measuring table, so the scan data was all exported as an STL File into Geomagic Studio and the measuring table data was removed (as well as any other noise present).

Post-processing The two scans were then combined, by first carrying out a manual registration. Manual registration is when a number of common points (in this case 3) between two scan sets are selected. The software then uses these common points to align the two scans together, forming one combined item. A global registration was then carried out, which moves the two scan sets relative to each other until the highest overlap is located. The combined filter scans were then meshed. A side effect of conducting an alignment of two separate scans is that it will induce an additional nominal error into the model, meaning that the dimensions of the object will not be as accurate.

4.5.2.3 Micro-computed tomography scanning

Data acquisition The inlet filter was also scanned using a micro–computed tomography X-ray scanner. This method is able to capture internal data without having to move or damage any parts. The scan was carried out with specific scan parameters (see 4.5) in order to produce the cleanest data.

Table 4.5: The parameters used during micro-computed tomography scanning.

Parameter	**Value**
Voltage	40 Kilovolts
Exposure	50 milliseconds
Power	65 Kilowatts
Projections	2879
Resolution	150 microns

The filter data is initially presented as a set of 2879 2D projections. A voxel resolution of 150 microns was achieved, as this was the maximum possible resolution available that could also scan the filter in a single scan. A greater resolution could be achieved by dividing the filter into multiple scans and stitching them together in post processing, but this was not deemed as necessary in this application. From the 2D data projections the internal structures are visible, i.e., a pleated paper structure across the center of the internal area (see Figure 4.36).

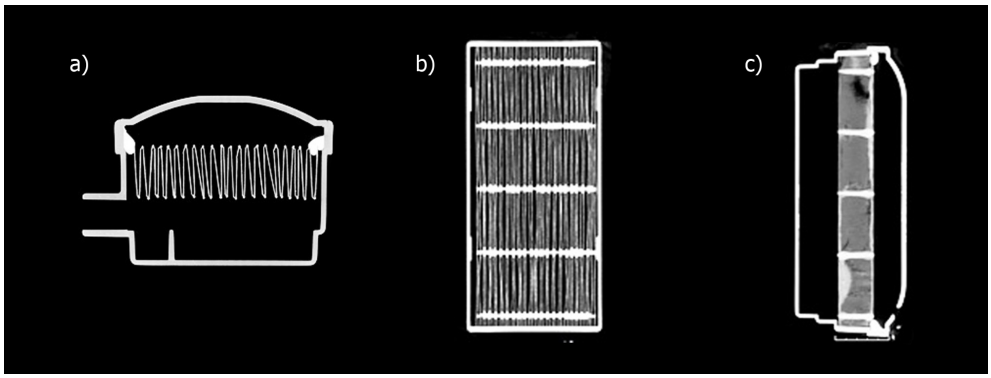


Figure 4.36: 2D projections of the inlet filters showing the internal structure: a) frontal, b) transverse, c) sagittal.

The post processing phase consists of stitching together the 2D stack into a 3D model which was then meshed via a reconstruction process. Similar to the handheld scanning technique, the 3D model was then converted into an .STL File. The .STL file type allows for easy analysis, measurement and editing of the model using CAD software. As well as providing an .STL File for future design like the handheld scanning method, the CT scan data also provided

important context as to the design of the original EverFlo filter, as it also shows the internal structure of the filter, something which handheld scanning is not able to achieve.

4.5.2.4 Filter material manufacture

From the micro-computed tomography scan data, it resulted that the internal structure of the inlet filter is a folded paper structure, which acts to trap gross particles in the air to prevent them getting into the oxygen concentrator and contaminating the air. Paper air filters are cheap and effective but require regular maintenance in order to clean out the residue that gets caught between folds. Failure to clean paper air inlet filters will reduce the effectiveness of the filter considerably, and in an oxygen concentrator may result in the oxygen delivered to the patient being contaminated with particulates. Before making changes to the reverse engineered data in order to produce an ideal CAD model for the new filter, a filter material must be selected, so that when the new model is designed it is done so with the specific material in mind. A number of different filter materials were considered, including cotton gauze, paper, sponge and activated carbon. Of these materials, activated carbon was selected due to the unique criteria presented by LRSs. In fact, charcoal is the main source of domestic fuel in several sub-Saharan African countries, which produce 65% of the world's charcoal[6]. Activated carbon filters are filters that use small pieces of powdered or granular carbon to filter air, have an extremely high surface area to volume ratio and are very porous (more so than regular carbon due to the activation process) [327]. The process to locally manufacture activated carbon, in fact, is easy to carry out, low cost and accessible. First wood is heated in a closed container until it forms a charcoal. After the charcoal is cleaned with water and left to dry, it is ground into a fine powder or pellets. To activate the charcoal, calcium chloride, either as a premixed solution or as flakes hydrated with water, is mixed with water in a 1:3 ratio. Alternatively, the citric acid contained in lemon juice can be used instead of calcium chloride. This mixed solution is then added to the charcoal, sealed for 24 hours, and then heated again to form the final activated carbon product [328].

4.5.2.5 Filter modelling

With the filter material selected and the 3D data of the pre-existing oxygen concentrator inlet filter obtained, a new version of the digital model was made. Due to the changing of the filter material from a paper structure to activated carbon, some changes to the 3D model were required. These changes were

[6] https://theconversation.com/why-efforts-to-clean-up-charcoal-production-in-sub-saharan-africa-arent-working-153462

also depending on the fact that the filter would be created using additive manufacturing, which implied that the filter material should be installed after manufacturing of the case is complete. The most simple and straightforward design solution that would allow filter material to be installed afterwards, was to simply split the filter casing into two distinct sections with a tight tolerance, namely a "base" and a "lid". Other designs were also considered including one with a hinge mechanism, keeping the base and lid of the filter casing connected. All CAD design work for this project was carried out using Solidworks Education Edition 2019 .

4.5.2.6 Finite element methods analysis

With the filter casing redesigned, a short simulation study was carried out using finite element methods analysis to ensure that there were no structural weaknesses, as it is important to confirm that the casing will not fail, excessively deform or otherwise be rendered ineffective during its life span. Consequently, Von Mises stress, strain and displacement values were measured against expected impacts, such as from the filter being accidently dropped, or the oxygen concentrator with the filter inside being knocked over. An additional safety factor of 10% was also implemented. Results are displayed as concentrations on the subject model, with a key that can be read to determine the regions of high and low stress, strain or deformation. Solidworks Education Edition 2019 was used to carry out this simulation.

4.5.2.7 Filter manufacturing

After the simulation testing process is completed, the inlet filter product can now proceed to the next stage, manufacture. Before printing, the right 3D printer should be selected to use, as there are many variations in model, with each being adapted for specific applications. This decision can be used both to manufacture the initial test model for this project but throughout the selection process it is important to take into consideration the suitability of the printer or similar model for a LRS facility. Among the 3D printers available at the UK facility, Warwick Manufacturing Group, there were the Fortus 360mc, the Stratasys J750, the Markforged Mark Two and the Connex Objet 260. The printer that was selected for this application was the Fortus 360mc. The Markforged Mark Two was discarded as it cannot print with ABS plastic, that is the material selected for the printer casing due to its durability and cost. The Stratasys J750 has the advantage of being able to print in colour but uses an 'in-house' version of ABS that is more expensive, and as the aesthetics of the filter are irrelevant this printer can be discarded. Between the Connex object 260 and the Fortus, the Fortus was selected due to its superior print

accuracy. The Fortus (or a similar model) would also be more useful to a LRS setting medical facility, as it is cheaper than the Connex, and swaps the ability to print in resin for other advantages more applicable to medical device manufacturing, such as interchangeable printing tips of various sizes, and a larger build area. After selecting and confirming the manufacturing method, the filter casing could be printed. The material of ABS plastic was used. This material was selected as it has excellent mechanical properties (e.g., good impact resistance and tensile strength) for its price (15-20 US Dollars per kg of ABS filament), which is an important consideration when designing MDs for LRS. ABS plastic is also extremely viable with 3D printing and is accepted by the majority of plastic using printers without complication, or loss of structural integrity. Using a more niche material would likely introduce complications in a LRS, including but not limited to increased costs, limited stock, and the risk of the material not being useable by the 3D printer at the LRS. The 3D printing software Insight was used to slice the model. The default build parameters and other settings were used, as the filter casing product does not require any special treatment such as thermal forming. The print time was approximately 3 hours. After the manufacturing of the filter casing is complete, the filter material (activated carbon) could then be manually installed. In this case, a piece of nylon tights was used as an extra container surrounded by a small layer of cotton wool, within the inlet filter casing.

4.5.2.8 Bench tests

The whole design and validation process followed the relevant standards for oxygen concentrators. In particular, once the final prototype was manufactured and assembled, bench tests were designed to validate our filter. These standards report the specifications and testing method for the so-called "micro-disk filter", which is the final component of the filtering system before oxygen is delivered. The testing requires the measurements of the number of particles within the oxygen-enriched gas sampled at the output of the oxygen concentrator. This testing should be performed by means of a light scattering particle counter and the number of particles should be within the limits of ISO5 (max 832 particles greater than 1 micron per cube meter). No testing procedure nor specific requirements were found in the literature, nor in the relevant standards, nor in the maintenance manuals of common oxygen concentrators. Further feedback was also sought after by contacting international experts of clinical engineering and ventilatory systems. As, to the best of our knowledge, no specific requirement exists for the inlet filters, it was decided to refer to the WHO's definition of inlet filter, i.e., a filter that "filters fine particles to protect compressor and/or valves" [329] and to estimate the filtering power of our 3D-

printed filter comparing it to the original one, as well as its pressure drop (airflow resistance). To this purpose, a light scattering airborne particle counter (Trotec PC200) was used to sample a volume of 2.83 litres in 60s, i.e., the maximum allowed by the device, by connecting it to the filter via a 3D-printed junction. The experiments were undertaken in a normal environment, subject to no air filtering nor air pollution control. The actual flow of air generated by the device was measured in different conditions, i.e., alone, with the original filter and with the Warwick filter in order to adjust the filtering power calculations according to the sampled volume. In fact, different filters will introduce different pressure drops, affecting the overall flow. In order to quantify the real flow and the pressure drop through each filter, a gas flow analyser (Fluke VT650) was used in series with the filter and the particle counter. Since the above-mentioned standards refer to the number of particles per cube meter, I estimated the number of particles in 1 cube meter by multiplying our values by 1000 (in fact 1 cube meter equals 1000 litres) and dividing by the respective volume sampled in 60 s (measured with the flowmeter). In order to make the measurements more reliable, 10 subsequent measurements were taken both using the original filter and our solution. Moreover, 10 measurements of the air of the room were taken similarly and dispersed through the filter experiments, i.e., a few at the start, a few in the middle and a few in the end, to have a reliable measurement of the background. Data were averaged and the filtering power was calculated with equation 4.3 (Fp stands for filtering power, Pa Particles in the ambient, Pf residual particles coming out of the filter):

$$F_p = \frac{P_a - P_f}{P_a} \cdot 100 \tag{4.3}$$

In the end, additionally, a similar procedure was performed to measure the gas outputted by the oxygen concentrator with either the original filter or our solution installed.

4.5.3 Results

4.5.3.1 Design and Manufacturing

The data from the micro-computed tomography scanner was selected to model the filter due to the data being less noisy, more accurate, and due to the additional compounded errors, that are introduced during the post processing stage of 3D handheld scanning, such as the global and manual data registrations. Figure 4.37 shows the 3D model of the final filter, devised as two separate parts, i.e., the base and the lid. Some simulations were run on this model using finite element methods analysis, the results of which can be found in Figures 4.38 and 4.39. From this analysis, it resulted that when impacted by

reasonable expected force, the filter casing performs adequately well, presenting around the point of impact acceptable stress and strain levels (note that ABS plastic has a yield strength of 29.6-48 Mpa). These low values imply that deformation levels will be minimal, meaning that the efficacy of the filter will not be unaffected by the impact, as the filter casing will still be able to fit into its assigned slot on the oxygen concentrator completely. The simulation also confirms the suitability of ABS plastic as the material for the prototype, as ABS material properties were applied to the model before applying the force. The simulation results (figures 5 and 6) highlight the most likely failure points by displaying the regions of greatest stress (shown in red), however, even at these points the stress values were well within acceptable limits. Finally, Figure 4.40 shows the 3D printed filter casing, filled with the filter material.

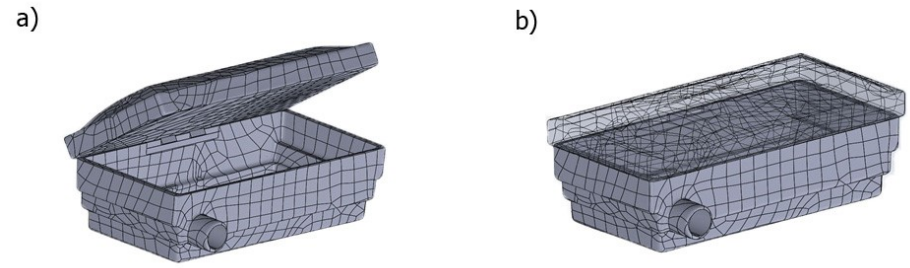


Figure 4.37: CAD model of the initial hinge-based prototype (a), later replaced with the "snap fit" model (b).

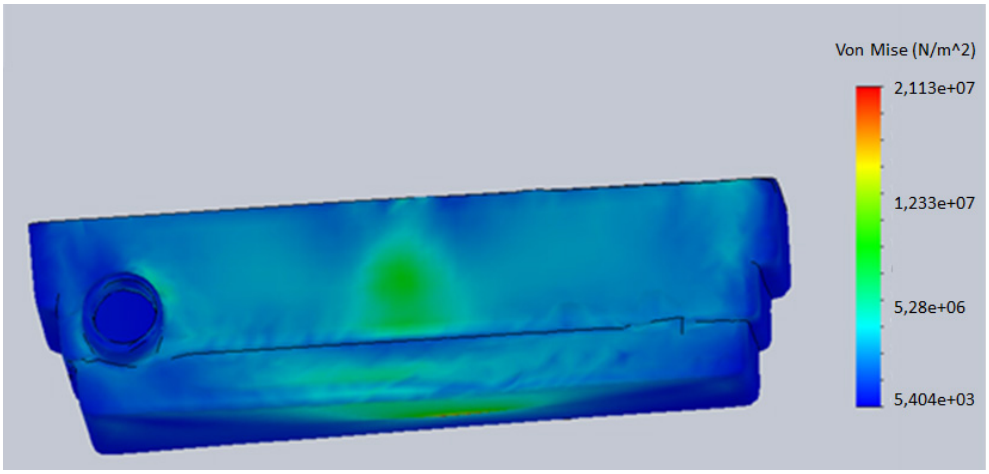


Figure 4.38: The results of the simulations, Von Mises stresses.

4.5.3.2 Bench tests

The results from the bench tests are summarised in Figure 4.41 and Table 4.6. Figure 4.41 reports the pirateplots for the distributions of the particles per particle size, comparing the different filters. It can be noted that, both filters

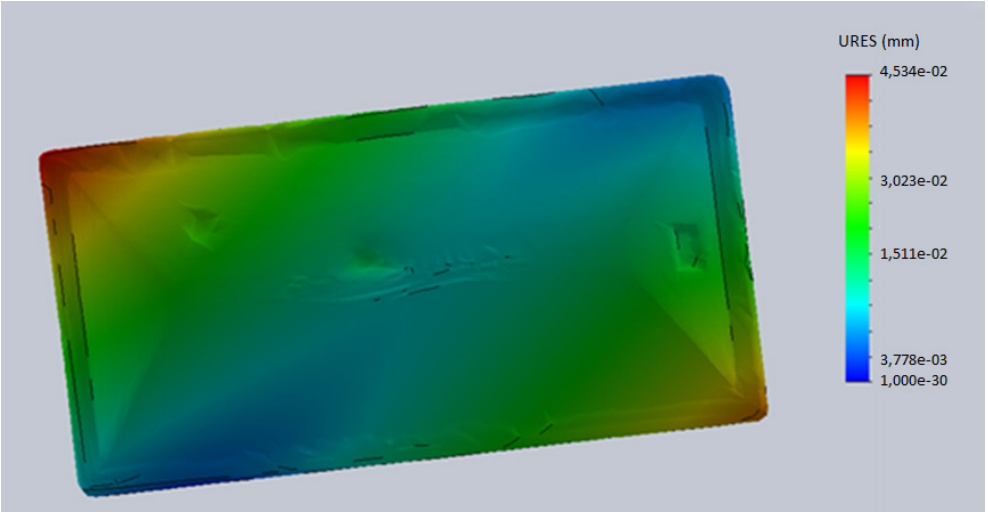


Figure 4.39: The results of the simulations, resulting displacement (URES).

Figure 4.40: The 3D printed filter with the filtering material inside.

effectively produced a significant reduction in the number of particles with respect to those naturally present in the test room. The detailed distribution of such particles is available in Table 4.6, which reports their average number per m3 per particle size, and the resulting filtration efficiency, adjusted according to the actual flow. In fact, from the measurements of the flow it resulted that the flows were: 2.83 litres per minute without any filter, 2.55 with the original filter and 1.85 with the Warwick filter, respectively. This was due to the airflow resistance linked to the presence of filtering material, which can be estimated by the pressure drop induced by each filter. In particular, the pressure drop related to the use of the Warwick filter was 0.035 mmHg, that linked to the use of the original filter was 0.011 mmHg. The relative pressure increase, due to the more resistance offered to the airflow by the activated charcoal granules, is 0.024 mmHg (0.0032 kPa). This small increase is negligible when compared to the capacity of oxygen concentrators of generating at least 55 kPa at all flows, to overcome pressure drops linked to long oxygen delivery tubing [321]. Table 4.6 also reports both the overall filtration efficiency and the filtration efficiency for particles greater than or equal to 1 micron. This is because, by observing the reduction of the particles induced by the Warwick filter, it can be noted that it is more effective for those particle sizes. Although the overall filtration efficiency is 38.8% (compared to the 96.3% of the original filter), in fact, the filtration efficiency for particles over 1 micron is almost double, i.e., 64.2% (96.9% for the original filter).

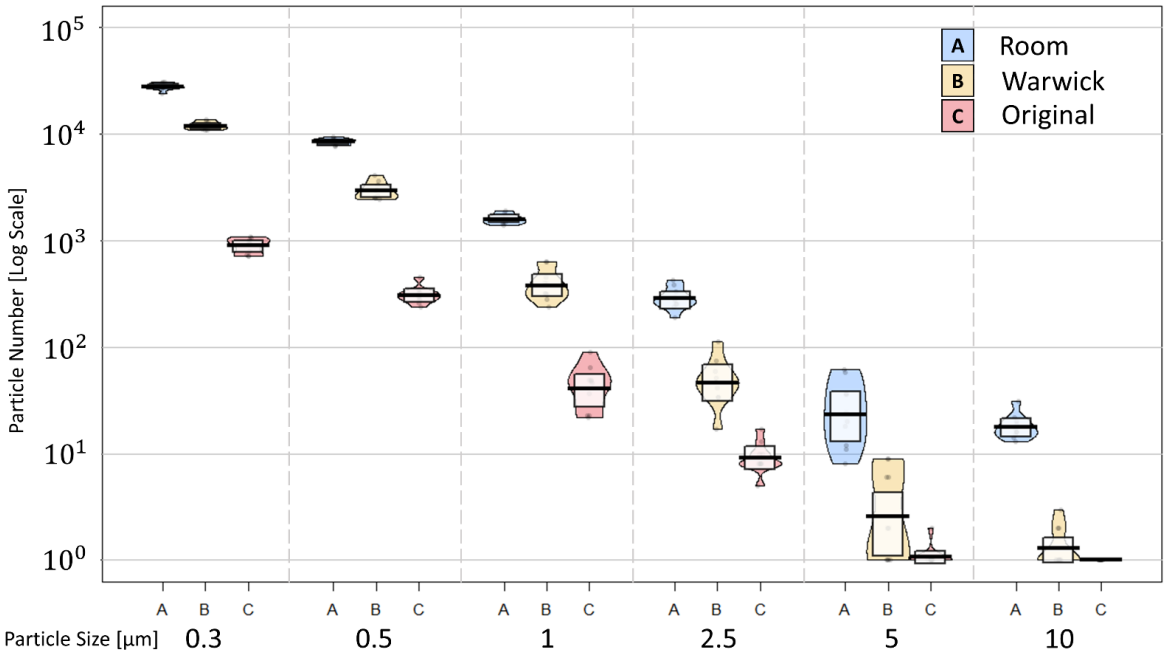


Figure 4.41: The pirateplots for the distribution of the particles per particle size for the Warwick filter (Yellow), the Original filter (Pink), and the room (Light blue).

Table 4.6: The table reports the average number of particles per cube meter per particle size as well as the total and the filtering power. The total filtering power is presented outside of the brackets; the filtering power on particles greater than or equal to 1 micron is between brackets.

Particle size (microns)	**Average particles per m3 - Room**	**Average particles per m3 - Original**	**Average particles per m3 – Warwick**
0.3	9935134	355019.6	6486000
0.5	2997740	122039.2	1609081
1	565678	17686.3	215081.1
2.5	103531.1	3725.5	28054.1
5	10098.9	78.4	1837.8
10	6461.9	117.6	594.6
Total	13618644.1	498666.7	8340649
Filtering power		96.3% (96.9%)	38.8% (64.2%)

4.5.4 Discussions and conclusions

This paper presented the design and technical validation of a 3D-printed activated charcoal filter for oxygen concentrators. One of the core aims of this project, was to set out a sample process that can be followed by others, particularly in LRSs. The design started with a reverse engineering phase through the use of both a 3D handheld scanner and micro-computed tomography scanning in order to obtain essential dimensional data for the specific housing within the selected oxygen concentrators (EverFlo). Ideally, Handheld scanners appear adequate for small scale MDs as the scanning object is small by definition, and the scan data does not need to be as detailed as the data obtained when using slower but more accurate scanners such as Computed Tomography (CT) scanners. Results showed, indeed, that the sets of data from both scanning techniques resulted highly accurate and more than suitable for this application. However, the latter gave less noisy and more detailed results and was selected for our application. The most important advantage that this method has over 3D handheld scanning is its ability to capture internal data, without having to move or damage any parts. Given the high costs of micro-computed tomography scanners and probably lower availability in LRSs, 3D scanning should be used instead. Although the CT data is less noisy and will contain less error, handheld scanning data is still more than acceptable for this application. It is only when dealing with MDs that require extreme levels of precision, for example medical stents, that the extremely minimal error of CT scanning becomes a determining factor. It is important to note that in most applications, handheld scanning still delivers highly accurate,

low error data, just not quite as good as CT scan data. Therefore, as both scanning techniques were more than adequate for this application, other factors (bearing in mind LRS applications) determined the final selection of handheld 3D scanning. These factors included cost, amount of training required to operate, ease of maintenance, portability and the size of the two scanners. While handheld scanning was recommended for LRS after comparing the data sets, validating the applicability of micro-computed tomography methods opens avenues for future MDs research, design and local manufacture, as it is able to obtain high resolution internal structure data through non-invasive means. 3D-printing, given its advantages and the wide availability of 3D printers, was selected to manufacture the prototypes of our filter casing. Nonetheless, despite being less accurate, the handheld scanning data would have been adequate for the external body data, and as the technique is cheaper, faster and more accessible, is to be considered for future real applications of this manufacturing method. Another essential step was to select and produce the filtering material. After careful considerations, activated charcoal resulted to be the best option, given its high impurity-absorbing capacities and its easy production. In fact, although primarily manufactured in large quantities, activated carbon can also be locally manufactured in small quantities, with a minimal cost and without the need of any expensive equipment, such as the large vats used by manufacturers when making activated carbon in bulk. This manufacturing method presented in method section allows producing activated charcoal in any kind of setting by using commonly available materials, such as wood and lemon juice. It is ideal for this project as only a small amount of activated carbon will be required for an oxygen concentrator inlet filter, and the same method can easily be carried out by facilities in LRS to due to the methods' low cost and accessibility. Furthermore, the wide availability and affordability of 3D printers make this design adapt for lower resource settings, keeping to the project aim to create a filter that is entirely locally manufacturable. Four 3D printers were compared to select the one that meet the essential requirement for our application. Overall, it would be unreasonable for a 3D printer to be obtained just to manufacture replacement filters for oxygen concentrators, but as already covered in this report 3D printers can be used in multiple different medical applications, particularly the manufacturing of small-scale medical devices. Finally, the 3D printer Fortus 360mc (or an equivalent model) was selected as it was considered more useful to a LRS setting medical facility. It resulted cheaper than the other options, and it swaps the ability to print in resin for other advantages more applicable to medical device manufacturing, such as interchangeable printing tips of various sizes, and a larger build area. Finally, another important step was to technically validate our device, by assessing its performance and comparing it against that of a commercial inlet filter for

oxygen concentrators. Overall, the results of this phase are satisfactory. In particular, it resulted that the Warwick filter has a mediocre overall filtering power and performs even better on all the particles over 1 micron. Although the performance is not comparable to the Original filter, it is still a satisfactory result, because the aim of the inlet filter is that of filtering out the gross particles to provide a cleaner airflow to the concentrating means of oxygen concentrator. It is then the second filter, i.e., the micro disk filter that further purifies the oxygen-enriched airflow. Currently, only this second filter is regulated by relevant standards. Currently, only the oxygen-enriched gas outputted by the oxygen concentrator, downstream of all the filters, is regulated by relevant standards. In fact, while output filters should be high-efficiency particulate arrestance filters, according to the WHO Technical Specifications for oxygen concentrators, there is no specification or no specific standard for inlet filters. This highlights the current inadequacy and/or incompleteness of some existing standards and regulatory frameworks, as reported and explained in another publication [3] concerning personal protective equipment. For these reasons, the filtration efficiency provided by this prototype, i.e., 38.8% overall, and 64.2% at particles equal to or greater than 1 micron, is a good result, as its use as well as its much easier supply and servicing would indefinitely extend the lifespan of the output filter, as well as of the oxygen concentrator, in respect to no inlet filter at all, or to an overused paper-based one. This envisioned specific clinical benefit can only be confirmed by an in-loco clinical evaluation, in which several prototypes could be trialled in existing oxygen concentrators working in typically harsh environments of LRSs. This could be potentially done in those healthcare locations of LRSs, which already receive (or could benefit from) the support of local universities/research centres. Such centres could be the local incubators for small enterprises that could provide the local health centres with the novel production of 3D-printed activated charcoal inlet filters. Before such clinical evaluations, the filter prototypes could also be challenge tested by measuring their performance and filtration efficiency in simulated harsher environments, i.e., labs with the possibility control cycles of high temperatures and humidity, as well as the amount of "pollution particles" present. However, such labs are not available at the University of Warwick and not trivial to reproduce. Thus, such "extreme" tests were not taken into consideration for this particular study. Should there be the opportunity to access such labs, further tests could be performed. As presented in a previous publication, in fact, the reliance on external factors, as well as other domains, should be taken into considerations when designing MDs for LRSs [4]. As the filtering material choice was limited to one, i.e., activated charcoal, due to its ease of production, other filtering materials, on the conditions that they are widely available in LRSs, could also be individuated and investigated in

further experiments. Possibly, in the current circumstances (i.e., COVID-19 pandemic) one could leverage the wide distribution of either surgical masks, cloth masks, or FFP2 respirators, to use them as filtering material. As regards different inlet filters of oxygen concentrators of different makes, the same exercise of scanning, remodelling, and 3D-printing could be performed on them, too. Ideally, there could be a shared database or open-source platform, where such scans and models could be uploaded, or where different experts from across the world could collaborate towards the creation of a novel inlet filter for a specific oxygen concentrator. One final consideration about the filter concerns the fluid dynamics within the filter, i.e., how and where the air will flow within the filter through and around the filtering media. This study did not investigate such matter, and, thus, did not look into the optimisation of the filter shape or filtering media shape/disposition. However, further studies could also investigate the enhancement of the design of a filter based on such considerations, relying on FEM simulations. Beyond presenting our activated charcoal filter, this paper wants to introduce a reproducible approach for designing, prototyping and manufacturing spare parts of medical devices, particularly feasible for LRSs. The empowerment of local realities with ad-hoc technological centres within universities, private companies or hospitals, equipped with 3D printers, protocyclers and skilled staff, can improve the quality of life and healthcare, by bypassing an often inexistent/poor supply chain. Such centres could also be supported by/cooperate with centres set in higher resource settings, which could rely on costly technologies, such as the CT scanner. In that case, the centre with such technologies available could be in charge of the scanning (and the CAD modelling, if needed) of the filter, which could then be shared through open-source platforms. Furthermore, the reliance of these local production centres on protocyclers would allow the introduction of resource recycling and reuse, and the reduction of the environmental impact, following a circular economy approach, which is suitable to the typical approach of LRSs of reutilising the few available resources. However, it is worth reminding that our envisioned solution, i.e., both the filter and its local production, should not be the first choice, in case the healthcare locations, in which they would be used, can rely on working agreements with manufacturers for the prompt delivery of spare parts and maintenance, as well as on non-harsh environmental conditions.

Chapter 5

Discussions

One of the aims of this thesis was that of evaluating, assessing, and highlighting the major challenges surrounding the world of MDs and MLs, also from a regulatory point of view, with a specific focus on LRSs. As presented in Chapter 2, the current regulations and standards related to MDs and MLs, are far from being definitive and universal. In particular, the global multifaceted regulatory situation, different from one country to another, and seriously limited in lower-income countries, was critically presented and discussed. This varied situation hinders the safe and efficient use of MDs in LRSs, jeopardizing the life of patients, and failing to accomplish an equitable access to healthcare, worldwide, as per the UN SDGs. As aforementioned in Chapter 2, this dire situation can be directly linked to the mismatch between who sets the regulatory frameworks and standards, usually HICs, and who has to try to adapt to and live by them, i.e., the often forgotten multitude of LMICs. As highlighted Locke's social contract theory, since these countries are excluded from the first stipulation of the social contract, they will need to adapt to a new community, which is often far from their needs and capabilities. This is taken to extremes with the so-called 'legal transplantation' phenomenon, which sees the transplantation and imposition of body of norms and regulatory frameworks, which are not contextualised and difficult to abide by and conform to. According to Legrand's view [39] legal transplants are not feasible, as laws need local and contextualised interpretations prior to being applied. This is debatable when applied to standards and minimum requirements, because the problem does not lie within their interpretation, rather within their glocal applicability. It, then, appears evident that a likely way forward could be the generation of political principles based on Nussbaum and Sen's capability approach, which focuses on human capabilities, fighting discrimination and unequal treatment.

After all, the problem of non-universality of norms and regulation is also affecting other worlds, such as that of PPE. As reported and demonstrated

in Section 2.4, the COVID-19 pandemic, causing a generalised condition of LRSs worldwide, highlighted the flaws of the current regulatory frameworks and pandemic preparedness plans, which hindered a fast and prompt response in the initial phase of the global emergency state. For these reasons, there is a clear need for a revolution of both the Substructure (current standards and regulations) and the Superstructure (the MDs and MLs design criteria).
In light of this, the second aim of this thesis, was to create, present and validate two frameworks, to assess the conditions of MLs in LRSs (see Section 3.1), and to design MDs resilient to LRSs (see Section 3.2). The former is useful to evaluate the healthcare locations, in which MDs will be utilised. A well-performed contextual analysis, highlighting the current challenges faced by such locations in LRSs, from a point of view of limited resources, healthcare personnel, a working health technology management program, and harsh environmental conditions, is pivotal and at the base of the design process of MDs resilient to LRSs conditions. Based on the information retrieved through the application of such framework and field studies, the second framework helps pinpointing the most important criteria to be taken into account, and can guide and inform such design process, like never before. Starting from these frameworks, further international political actions should follow to bring forward design frameworks based on the best available evidence and real users' needs elicited by experts, in order to drive the real change of the existing norms, regulations and standards.
The third aim of this thesis was to apply the acquired knowledge to design some MDs, leveraging on mHealth and 3D-printing, also fostering local self-sustained community production with a circular economy approach. The following case studies were presented: a smartphone-based pupillometer for detecting the presence and assessing the level of brain trauma (Section 4.1), a smartphone-based diabetic neuropathy screening tool (Section 4.2), a 3D-printed condom intrauterine balloon tamponade (Section 4.3), a newborn vest for treating jaundice in LRSs (Section 4.4), and a 3D-printed activated charcoal filter for oxygen concentrators (Section 4.5). These examples of contextualised and frugal design of MDs are proofs of the feasibility and applicability of the above-mentioned frameworks. Furthermore, as concluded by the use cases presented in Sections 4.2, 4.3, 4.5, 3D printing and protocycling can be used to manufacture simple medical devices at rather convenient costs, as well as to create and develop the local production of such devices, empowering local communities, fostering progress, and being environment friendly. On the other hand, also Care 4.0, i.e., the 4^{th} industrial revolution applied to healthcare, which leverages AI, novel technologies, eHealth and mHealth, is the way forward towards a more inclusive and equitable healthcare, globally. As concluded in Sections 4.1, 4.2, 4.4, in fact, the wide diffusion of smartphones in LRSs,

as well as the promising results of AI-based technologies, can be a feasibile solution for the lack of specialised personnel and the inefficient/inexisting local supply chains.
Nonetheless, it is worth reminding the reader that such proposed solutions, i.e., 3D printing, mHealth and AI-based technologies, as well as circular economy, are only solutions pro tempore. The envisioned long-term solution, actually, would be the reformulation of the current standards and regulatory frameworks surrounding MDs and MLs, to make them more universal, and aware of the variety of the particular of the single settings. However, the reader should be informed of the limitations of this thesis. Firstly, other than internal validations, further external validations could be performed on the two above-mentioned frameworks. This would mean for the framework to be utilised by other researchers either completely independently from the creators of such framework, or with a structured approach by being guided during workshops by the creators themselves. This would increase their overall reliability and applicability.

Specifically as regards the first framework, i.e., the one to assess MLs in LRSs, one big limitation is related to the fact that no other field studies were possible in the time-span of my PhD due to the onset of the COVID-19 pandemic. For this reason, I acknowledge the fact that the results reporting on the conditions of the visited hospitals in Benin and Uganda are indeed to be taken more as case studies rather than general reports on the conditions of hospitals in LRSs. Ideally, the number of hospitals and countries visited would have been expanded and that would have allowed for stronger results. In the future, this might be improved by planning more field studies or instructing local teams or other researcher on how to use the framework, so as more data, covering more hospitals and more regions of the world, could be collected.

Secondly, although most of the MDs presented in the use cases were either benchmarked or technically validated, a round of clinical validation, in which to test such devices on human subjects, is envisioned. As per MDR 2017/745, Clinical evaluations are, in fact, one of the essential steps for manufacturers to CE mark their MDs. A clinical evaluation, however, would require, among other things, ad-hoc approval by an ethics committee, which, for some of the use-cases, would be difficult to obtain, due to the risks associated with the use of such technology (e.g., the intrauterine balloon tamponade for treating PPE, the smartphone based pupillometer for assessing brain trauma in patients). Moreover, a thorough clinical evaluation is out of the scope of this thesis, as it requires time and resources that go beyond the expected amount of work for a PhD student.

Overall, it can be stated that some of the technologies presented in the use cases are at a rather mature stage of development, having gone through

technical verification and pre-clinical validation, i.e., the smartphone-based pupillometer, the 3D-printed activated charcoal filter for oxygen concentrators, the diabetic neuropathy screening smart tool. Ideally and hypothetically (had more time and money been there), these could have all been tested in loco. This would have helped to collect data from patients, which would have laid the basis for the development of artificial intelligence based algorithms that would complement the two apps, and to test the philosophy of small local production of 3D-printed filters for oxygen concentrators. As for the intrauterine balloon tamponade, this could have been pre-clinically validated using ad-hoc more realistic and uterus models equipped with sensors, either purchased or developed from scratch, before running an on-field study. As far as the vest for treating neonatal jaundice is concerned, it is the less mature project as it is only a proof of concepts. The next steps for this technology would have been to obtain a fully functional prototype (i.e., with the right amount of LEDs and optimal delivery of light), to then proceed with pre-clinical and clinical validation. Regarding further testing of the above-mentioned technologies in loco (i.e., in SSA), in my defence I can state that COVID-19 disrupted our original plans to have a second set of field studies during my third year (2020). A document detailing how COVID-19 affected my PhD project, directly or indirectly, was provided to the examiners and the School of Engineering as further proof. Nonetheless, I was able to re-address the remaining part of my work, dedicating it to wider reflections on the utter importance of the role ethics in science, especially in times of crisis. Ethics, in fact, should not be used only as an embellishment of one's work, rather it should be deeply interwoven with science, theoretically and methodologically. Besides, helping the evaluation of the arising issues, ethics could help scientists ponder on the risk-benefit balance of their publications, and also on the final purpose of their work, i.e., the progress of humanity.

Chapter 6

Conclusions

Overall, this thesis evolved from an initially theoretical approach to a practical one. In fact, it started from an analysis of the relevant and current regulatory frameworks and standards surrounding MDs and MLs, highlighting their fallacies and inadequacy to LRSs, and any kind of setting in times of crisis; it, then, focused on a thorough analysis of LRSs and their challenges, with a specific focus on MDs and MLs. Building upon the knowledge acquired through the field studies, two frameworks were created, validated, and presented, to assess MLs in LRSs, and to design MDs resilient to LRSs. Finally, in the last part, several use cases, presenting frugal designs of MDs or their parts, were showcased.

Appendix A

Excerpt of MIL-STD-810H

Downloaded from http://www.everyspec.com

METHOD 501.7
HIGH TEMPERATURE

CONTENTS

Downloaded from http://www.everyspec.com

CONTENTS - Continued

TABLES

Downloaded from http://www.everyspec.com

METHOD 501.7

HIGH TEMPERATURE

NOTE: Tailoring is essential. Select methods, procedures, and parameter levels based on the tailoring process described in Part One, paragraph 4.2.2, and Annex C. Apply the general guidelines for laboratory test methods described in Part One, paragraph 5 of this Standard.

1. SCOPE.

1.1 Purpose.

Use high temperature tests to obtain data to help evaluate effects of high temperature conditions on materiel safety, integrity, and performance.

1.2 Application.

Use this method to evaluate materiel likely to be deployed in areas where temperatures (ambient or induced) are higher than standard ambient.

1.3 Limitations.

Limit use of this Method to evaluating the effects of relatively short-term (months, as opposed to years), even, distributions of heat throughout the test item. This Method is not generally practical for:

a. Evaluating time-dependent performance degradation (aging) effects that occur during continuous long-term exposure to high temperatures (under storage or operational modes) where synergetic effects may be involved. For such high temperature aging effects, test in the natural environment.

b. Evaluating materiel in a high temperature environment where solar radiation produces significant thermal gradients in the materiel. For simulating direct solar impingement, use Method 505.7, Procedure I.

c. Evaluating actinic (photochemical) effects (use Method 505.7, Procedure II).

d. Evaluating the effects of aerodynamic heating without considerable tailoring.

2. TAILORING GUIDANCE.

2.1 Selecting This Method.

After examining requirements documents and applying the tailoring process in Part One of this standard to determine where high temperatures are foreseen in the life cycle of the materiel, use the following to confirm the need for this Method, and to place it in sequence with other Methods. It is preferable to conduct Method 505.6, Procedure I prior to Method 501.7, in order to obtain maximum response and stabilization temperatures for items exposed to direct solar radiation.

2.1.1 Effects of High Temperature Environments.

High temperatures may temporarily or permanently impair performance of materiel by changing physical properties or dimensions of the material(s) of which it is composed. The following are examples of problems that could result from high temperature exposure that may relate to the materiel being tested. Consider the following typical problems to help determine if this Method is appropriate for the materiel being tested. This list is not intended to be all-inclusive.

a. Parts bind from differential expansion of dissimilar materials.

b. Lubricants become less viscous; joints lose lubrication by outward flow of lubricants.

c. Materials change in dimension, either totally or selectively.

d. Packing, gaskets, seals, bearings and shafts become distorted, bind, and fail causing mechanical or integrity failures.

e. Gaskets display permanent set.

f. Closure and sealing strips deteriorate.

Downloaded from http://www.everyspec.com

g. Fixed-resistance resistors change in values.

h. Electronic circuit stability varies with differences in temperature gradients and differential expansion of dissimilar materials.

i. Transformers and electromechanical components overheat.

j. Operating/release margins of relays and magnetic or thermally activated devices alter.

k. Shortened operating lifetime.

l. Solid pellets or grains separate.

m. High pressures created within sealed cases (projectiles, bombs, etc.).

n. Accelerated burning of explosives or propellants.

o. Expansion of cast explosives within their cases.

p. Explosives melt and exude.

q. Discoloration, cracking, or crazing of organic materials.

r. Out-gassing of composite materials or coatings (i.e. VOCs, CO, and Phthalates).

s. Failure of adhesives.

2.1.2 Sequence Among Other Methods.

a. General. Use the anticipated life cycle sequence of events as a general sequence guide (see Part One, paragraph 5.5).

b. Unique to this Method. There are at least two philosophies related to test sequence. One approach is to conserve test item life by applying what are perceived to be the least damaging environments first. For this approach, generally apply the high temperature test early in the test sequence. Another approach is to apply environments to maximize the likelihood of disclosing synergetic effects. This test may be used in combination with shock and vibration tests to evaluate the effect of dynamic events (i.e., shipping, handling, and shock) on hot materials. Also, this test may contribute significantly to the results of low pressure testing of seals, e.g., see paragraphs 2.1.1d, e, and f.

2.2 Selecting Procedures.

This Method includes three test procedures, Procedure I (Storage), Procedure II (Operation), and Procedure III (Tactical-Standby to Operational). Determine the procedure(s) to be used.

> **NOTE:** The materiel's anticipated Life Cycle Environmental Profile (LCEP) may reveal other high temperature scenarios that are not specifically addressed in the procedures. Tailor the procedures as necessary to capture the LCEP variations, but do not reduce the basic test requirements reflected in the below procedures. (See paragraph 2.3 below.) **NOTE: Consider the potential synergistic effects of temperature, humidity and altitude, and the use of Method 520.5 in addition to this method. However, Method 520 is NOT a substitute for Method 501.**

2.2.1 Procedure Selection Considerations.

When selecting procedures, consider:

a. The operational purpose of the materiel.

b. The natural exposure circumstances (ambient or induced).

c. The test data required to determine whether the operational purpose of the materiel has been met.

d. Procedure sequence. If both the storage and operation procedures are to be applied, perform Procedure I before Procedure II. Consider using Procedure III in lieu of Procedure II for unique cases in which materiel in its operational configuration is non-operational (awaiting use) and is exposed to solar heating, e.g., aircraft cockpits, ground vehicle passenger compartments, etc.

Downloaded from http://www.everyspec.com

e. Other significant adjacent heat sources that could affect the materiel such as motors, engines, power supplies, other electronics, or exhaust air.

f. Combining of Procedures I and II when using constant temperature. When attempting to combine procedures it is preferable to conduct Procedure II followed by Procedure I and then a repeat of Procedure II. Testing should be conducted in series with no return to ambient conditions until test completion.

2.2.2 Difference Among Procedures.

While all three procedures involve temperature conditioning and performance testing, they differ on the basis of the temperature load prior to and during performance tests. The storage procedure assesses the effects of high temperature storage on subsequent materiel performance. The operation procedure assesses the effects of high temperatures during performance. The tactical-standby to operational procedure evaluates the ability of materiel (usually enclosed by transparent or translucent material) that has soaked in the sun in a high temperature environment to become operational in a relatively short period of time.

a. Procedure I - Storage. Use Procedure I to investigate how high temperatures during storage affect the materiel (integrity of materials, and safety/performance of the materiel). This test procedure includes exposing the test item to high temperatures (and low humidity where applicable) that may be encountered in the materiel's storage situation, followed by an operational test at ambient conditions. For materiel inside an enclosure that is, in turn, exposed to solar heating, consider using Method 505.7, Procedure I to determine the actual level of heating of the test materiel caused by solar loading.

b. Procedure II - Operation. Use Procedure II to investigate how high ambient temperatures may affect materiel performance while it is operating. There are two ways to perform Procedure II:

(1) Expose the test item to cyclic chamber conditions with the test item operating either continuously or during the period of maximum response (highest item temperature).

(2) Expose the test item to a constant temperature and operate the test item when its temperature stabilizes. (To be used only for items situated in close proximity to heat-producing equipment or when it is necessary to verify operation of an item at a specified constant temperature.)

c. Procedure III - Tactical-Standby to Operational. This procedure is not a substitute for solar radiation (Method 505.7). This procedure evaluates the materiel's performance at the operating temperatures after being presoaked at non-operational temperatures. Since actinic effects and directional heating are not applicable in this method, consider applying this procedure when materiel is in an enclosed environment, (e.g., aircraft and ground vehicles with closed transparent or translucent areas can develop high internal temperatures prior to equipment operation due to solar heating; enclosures such as communications shelters may require immediate operation after being exposed to solar heating). These are not items in storage or transit situation, but rather items in the operational configuration (ready-to-go as needed) that must be operational in a relatively short period of time. Usually, the "cooling" option refers to merely opening the enclosed areas and allowing the ambient air to begin cooling the interior areas so normal operation can begin.

> The term "tactical" is used here to identify materiel that is not in storage, but is in a standby operational configuration, and as such is subjected to extended non-operational conditions immediately prior to operation.

2.3 Determine Test Levels and Conditions.

Having selected this method and relevant procedures (based on the test item's requirements documents and the tailoring process), complete the tailoring process by identifying appropriate parameter levels and applicable test conditions and techniques for these procedures. Base these selections on the requirements documents and the Life Cycle Environmental Profile, and information provided with this procedure. Consider the following when selecting test levels.

Downloaded from http://www.everyspec.com

2.3.1 Climatic Conditions.

Identify the appropriate climatic conditions for the geographic areas in which the materiel will be operated and stored. There are two climatic categories where high temperatures are typically encountered: Hot Dry and Basic Hot (Part One, Annex C, Figure C-1). Data for these areas are shown in Tables 501.7-I, -II, and -III. Determine high temperature levels with respect to:

a. Climatic area of concern.

b. Exposure to solar radiation: Is this exposure directly on the materiel, shipping container, protective package shelter, etc.?

c. Analysis of the path of heat transfer from the ambient air and solar radiation to the materiel.

Table 501.7-I. Summary of high temperature diurnal cycle ranges.[1/]

Design Type	Location	Ambient Air °C (°F)	Induced [2/] °C (°F)
Basic Hot (A2)	Many parts of the world, extending outward from the hot dry category of the southwestern United States, northwestern Mexico, central and western Australia, Saharan Africa, South America, southern Spain, and southwest and south central Asia.	30 - 43 (86 - 110)	30 - 63 (86 - 145)
Hot Dry (A1)	Southwest and south central Asia, southwestern United States, Saharan Africa, central and western Australia, and northwestern Mexico.	32 - 49 (90 - 120)	33 - 71 (91 - 160)

[1/] The diurnal cycles for temperature and humidity are given in tables 501.7-II and -III.

[2/] Induced conditions are air temperature levels to which materiel may be exposed during extreme storage or transit situations, or non-operational but in the operational configuration without containerization.

Downloaded from http://www.everyspec.com

Table 501.7-II. High temperature cycles, climatic category A2 - Basic Hot.[1/]

Time of Day	Ambient Air Conditions		Induced (Storage and Transit) Conditions	
	Temperature[3/] °C (°F)	Humidity[2/] % RH	Temperature[3/] °C (°F)	Humidity[2/] % RH
0100	33 (91)	36	33 (91)	36
0200	32 (90)	38	32 (90)	38
0300	32 (90)	41	32 (90)	41
0400	31 (88)	44	31 (88)	44
0500	30 (86)	44	30 (86)	44
0600	30 (86)	44	31 (88)	43
0700	31 (88)	41	34 (93)	32
0800	34 (93)	34	38 (101)	30
0900	37 (99)	29	42 (107)	23
1000	39 (102)	24	45 (113)	17
1100	41 (106)	21	51 (124)	14
1200	42 (107)	18	57 (134)	8
1300	43 (109)	16	61 (142)	6
1400	43 (110)	15	63 (145)	6
1500	43 (110)	14	63 (145)	5
1600	43 (110)	14	62 (144)	6
1700	43 (109)	14	60 (140)	6
1800	42 (107)	15	57 (134)	6
1900	40 (104)	17	50 (122)	10
2000	38 (100)	20	44 (111)	14
2100	36 (97)	22	38 (101)	19
2200	35 (95)	25	35 (95)	25
2300	34 (93)	28	34 (93)	28
2400	33 (91)	33	33 (91)	33

[1/] These cycles were obtained from AR 70-38, 1 August 1979 (see paragraph 6.1, reference c), and essentially conform to those in MIL-HDBK-310 and NATO STANAG 4370, AECTP 230 (paragraph 6.1, references a and b). These values represent typical conditions throughout a typical day in this climatic category. "Induced Conditions" are air temperature levels to which materiel may be exposed during storage or transit situations that are aggravated by solar loading, or during non-operating situations but in an operational configuration and not containerized.

[2/] Humidity control during high temperature testing is generally not necessary. Use these values only in special cases where, for instance, it is known that high levels of temperature and low humidity may adversely affect your items.

[3/] Data were originally recorded in °F and converted to °C. Hence, table data conversion may not be consistent.

Downloaded from http://www.everyspec.com

Table 501.7-III. High temperature cycles, climatic category A1 – Hot Dry.[1/]

Time of Day	Ambient Air Conditions		Induced (Storage and Transit) Conditions	
	Temperature[3/] °C (°F)	Humidity[2/] % RH	Temperature[3/] °C (°F)	Humidity[2/] % RH
0100	35 (95)	6	35 (95)	6
0200	34 (94)	7	34 (94)	7
0300	34 (93)	7	34 (94)	7
0400	33 (92)	8	33 (92)	7
0500	33 (91)	8	33 (92)	7
0600	32 (90)	8	33 (91)	7
0700	33 (91)	8	36 (97)	5
0800	35 (95)	6	40 (104)	4
0900	38 (101)	6	44 (111)	4
1000	41 (106)	5	51 (124)	3
1100	43 (110)	4	56 (133)	2
1200	44 (112)	4	63 (145)	2
1300	47 (116)	3	69 (156)	1
1400	48 (118)	3	70 (158)	1
1500	48 (119)	3	71 (160)	1
1600	49 (120)	3	70 (158)	1
1700	48 (119)	3	67 (153)	1
1800	48 (118)	3	63 (145)	2
1900	46 (114)	3	55 (131)	2
2000	42 (108)	4	48 (118)	3
2100	41 (105)	5	41 (105)	5
2200	39 (102)	6	39 (103)	6
2300	38 (100)	6	37 (99)	6
2400	37 (98)	6	35 (95)	6

[1/] These cycles were obtained from AR 70-38, 1 August 1979 (see paragraph 6.1, reference c), and essentially conform to those in MIL-HDBK-310 and NATO STANAG 4370, AECTP 230 (paragraph 6.1, references a and b). These values represent typical conditions throughout a typical day in this climatic category. "Induced Conditions" are air temperature levels to which materiel may be exposed during storage or transit situations that are aggravated by solar loading, or during non-operating situations but in an operational configuration and not containerized.

[2/] Humidity control during high temperature testing is generally not necessary. Use these values only in special cases where, for instance, it is known that high levels of temperature and low humidity may adversely affect your item.

[3/] Data were originally recorded in °F and converted to °C. Hence, table data conversion may not be consistent.

2.3.2 Exposure Conditions.

Before determining the levels at which to set test temperatures, determine the way in which the materiel is exposed to heat in normal storage and operational circumstances. Review the Life Cycle Environmental Profile (LCEP) to help make this determination (see Part Three for additional guidance). Consider at least the following exposure conditions, and the possible alternative of using Method 505.7, Procedure I:

Downloaded from http://www.everyspec.com

a. Deployment configuration.

(1) Exposed. Of interest are the most severe conditions that materiel would experience when deployed in any climatic area of the world without the benefit of a protective cover or sheltering enclosure.

(2) Sheltered. Of interest are the most severe conditions that materiel would experience when deployed in any climatic area of the world when under cover or inside a sheltering enclosure. The amount of ventilation available and the presence of adjacent shade can significantly affect the temperature of the air surrounding sheltered materiel. Examples of these situations are provided below. (Note: If field data are not available, the conditions for this exposure may be approximated using Part Three of this document, MIL-HDBK-310 and/or NATO STANAG 4370, AECTP 230 (paragraph 6.1, references a and b)). The outdoor ambient air temperature and humidity conditions described in these references are those measured in standard meteorological shelters at a height of 1.2 to 1.8 m (4 to 6 ft) above the ground.

(a) Inside unventilated enclosures.

(b) Within enclosed vehicle bodies.

(c) Within aircraft sections having surfaces exposed to solar heating.

(d) Inside of tents.

(e) Under closed tarpaulins.

(f) Located above, on, or below the surface of the Earth.

b. Special conditions. Although high temperature testing is generally based on the average temperature of the air envelope surrounding the materiel, significant localized heating can occur because of special heating conditions. This localized heating can be well above the average surrounding air and therefore can significantly affect the evaluation of the materiel's thermal behavior and performance. When these conditions exist (as described below), include or simulate them in the high temperature test setup to the extent practical. These extreme conditions would be applied by extending the levels of the temperatures given in Tables 501.7-I and 501.7-II based on actual field measurements.

(1) Aggravated solar. These conditions are induced but involve temperatures as high as 71 to 85 ºC (160 to 185 ºF), making greater allowance for the effects of solar radiation. Applicable conditions for such testing include materiel that is employed in enclosed compartments having glazed or transparent panels (aircraft cockpits, vehicle compartments, etc.); consider applying Method 505.7.

(2) Man-made sources. Man-made heat-producing devices (motors, engines, power supplies, high-density electronic packages, etc.) may significantly raise the local air temperature near the materiel, either by radiation, convection, or impingement of exhaust air. This near constant temperature environment may negate the effects of the diurnal cycle.

2.3.3 Exposure Duration.

Determine the duration of exposure that the materiel will experience for each of the exposure conditions identified. Exposure may be constant or cyclic, in which case, also identify the number of times that the exposure occurs.

Caution: When temperature conditioning, ensure the total test time at the most severe temperature does not exceed the life expectancy of any material (see Part One, paragraph 5.19).

2.3.3.1 Constant Temperature Exposure.

For constant temperature exposure (used only for items situated in close proximity to heat-producing equipment or when it is necessary to verify operation of an item at a specified constant temperature), soak the test item until its temperature has stabilized, and maintain the test temperature at least two hours following test item stabilization.

NOTE: This is not a substitute for situations in which diurnal cycling is typical.

Downloaded from http://www.everyspec.com

2.3.3.2 Cyclic Temperature Exposure.

For cyclic exposure, determine the test duration based on an estimate of the number of cycles required to satisfy the design requirements and the guidance below. The duration of high temperature exposure may be as significant as the temperature itself. Because Procedures I and II could expose the test items to cyclic temperatures, the number of cycles is critical. (Cycles are 24-hour periods unless otherwise specified.)

a. Procedure I - Storage. The number of cycles for the storage test is set at a minimum of seven to coincide with the one percent frequency of occurrence of the hours of extreme temperatures during the most severe month in an average year at the most severe location. (The maximum temperature occurs for approximately one hour in each cycle.) When considering extended storage, critical materials, or materials determined to be very sensitive to high temperature, increase the number of cycles to assure the design requirements are met.

b. Procedure II - Operation. The minimum number of cycles for the operational exposure test is three. This number is normally sufficient for the test item to reach its maximum response temperature. A maximum of seven cycles is suggested when repeated temperature response is difficult to obtain.

2.3.4 Test Item Configuration.

Determine the test item configuration based on realistic configuration(s) of the materiel anticipated for storage and operation. As a minimum, consider the following configurations:

a. In a shipping/storage container or transit case.

b. Protected or unprotected (under canopy, enclosed, etc.).

c. In its normal operating configuration (realistic or with restraints, such as with openings that are normally covered).

d. Modified with kits for special applications.

e. Stacked or palletized configurations.

2.3.5 Humidity.

Generally, relative humidity (RH) control during high temperature tests is not necessary. In special cases, extremely low RH may have a significant effect on some materiel during high temperature testing. If the materiel has special characteristics that could be affected by extremely low RH, use the values for RH shown in Tables 501.7-II and -III.

2.4 Test Item Operation.

When it is necessary to operate the test item, use the following guidelines for establishing test operating procedures.

CAUTION: If the sheltered environment is intended to be occupied during exposure to high temperature, it is recommended that sensors are installed to detect VOCs, CO, and Phthalates due to potential out-gassing.

a. General. See Part One, paragraph 5.8.2.

b. Unique to this method.

(1) Include operating modes that consume the most power (generate the most heat).

(2) Include the required range of input voltage conditions if changes in voltage could affect the test item thermal dissipation or response (e.g., power generation or fan speed).

(3) Introduce the cooling media that normally would be applied during service use (e.g., forced air or liquid coolant). Consider using cooling medium inlet temperatures and flow rates that represent both typical and worst-case degraded temperature and flow conditions.

(4) For steady-state temperature testing, consider thermal stabilization to be achieved when the temperatures of critical internal operating components are relatively constant (as described in Part One, paragraph 5.4.1). (Because of test item duty cycling or the operating characteristics, a constant operating temperature may never be achieved.)

Downloaded from http://www.everyspec.com

(5) For cyclic temperature testing, and depending on the cycle and test item characteristics, the thermal responses of the test item will also be cyclic.

(6) Consider non-operational conditions similar to those of storage & transit, and the need for immediate operation without cooling - other than that of the surrounding ambient air.

2.5 Additional Guidelines.

Review the materiel specifications and requirements documents. Apply any additional guidelines necessary. Part Three of this document includes further information on the high temperature environment (e.g., paragraphs 2.1 and 4.1).

3. INFORMATION REQUIRED.

3.1 Pretest.

The following information is required to conduct high temperature tests adequately.

a. General. Information listed in Part One, paragraphs 5.7 and 5.9; and Annex A, Task 405 of this Standard.

b. Specific to this Method.

(1) Relative humidity control requirements (if necessary). (See paragraph 2.3.5 of this Method.)

(2) Thermocouple locations. The component/assembly/structure to be used for thermal response and temperature stabilization purposes. (See Part One, paragraph 5.4.)

(3) For Procedure III, based on the LCEP, identify the anticipated maximum non-operational temperature (exposure to high temperatures and solar loading) for the materiel, as well as the accompanying high ambient temperature. The LCEP should define whether or not the item will be operated at the maximum operational temperature immediately following the storage environment.

c. Tailoring. Necessary variations in the basic test procedures to accommodate environments identified in the LCEP.

3.2 During Test.

Collect the following information during conduct of the test:

a. General. Information listed in Part One, paragraph 5.10; and in Annex A, Tasks 405 and 406 of this Standard.

b. Specific to this Method.

(1) Record of chamber temperature-versus-time data (and humidity, if controlled) for the duration of the test.

(2) Record of the test item temperature-versus-time data for the duration of the test.

3.3 Post-Test.

The following post test data shall be included in the test report.

a. General. Information listed in Part One, paragraph 5.13; and in Annex A, Task 406 of this Standard.

b. Specific to this Method.

(1) Length of time required for each performance check.

(2) Temperature versus time data (test item and chamber).

(3) Any deviations from the original test plan.

Downloaded from http://www.everyspec.com

4. TEST PROCESS.

4.1 Test Facility.

a. The required apparatus consists of a chamber or cabinet together with auxiliary instrumentation capable of maintaining and monitoring the required conditions of high temperature (and humidity, where required) throughout an envelope of air surrounding the test item(s) (see Part One, paragraph 5.18).

b. Unless justified by the materiel platform environment and to prevent unrealistic heat transfer in the materiel, maintain the air velocity in the vicinity of the test item so as to not exceed 1.7 m/s (335 ft/min).

c. Continuously record chamber conditions and, if required, test item temperatures.

4.2 Controls.

a. Temperature. Unless otherwise specified in the test plan, if any action other than test item operation (such as opening the chamber door) results in a significant change of the test item temperature (more than 2 °C (3.6 °F)) or chamber air temperature, re-stabilize the test item at the required temperature before continuing the test. For Procedure II, if the operational check is not completed within 15 minutes, reestablish test item temperature/RH conditions before continuing.

b. Rate of temperature change. Unless otherwise specified or documented in the LCEP, use a rate of temperature change not exceeding 3 °C (5 °F) per minute to prevent thermal shock.

c. Temperature measurement. Install temperature sensor instrumentation on or in the test item to measure temperature stabilization data (see Part One, paragraph 5.4).

d. Data recording. Record chamber temperature (and humidity if controlled) in accordance with Part One, paragraphs 5.2 and 5.18, and at a sufficient rate to satisfy the post-test analysis (see Part One, paragraph 5.18)

4.3 Test Interruption.

Test interruptions can result from two or more situations, one being from failure or malfunction of test chambers or associated test laboratory equipment. The second type of test interruption results from failure or malfunction of the test item itself during required or optional performance checks.

4.3.1 Interruption Due to Chamber Malfunction.

a. General. See Part One, paragraph 5.11, of this Standard.

b. Specific to this Method.

(1) Undertest interruption.

(a) Cycling. If a cyclic high temperature test is being conducted and an unscheduled interruption occurs that causes the test conditions to fall out of allowable tolerances toward standard ambient temperatures, continue the test from the end of the last successfully-completed cycle.

(b) Steady state. If a steady state (non-cyclic) test is being conducted (only for items near constant-heat-producing sources), and an unscheduled interruption occurs that causes the test conditions to fall out of allowable tolerances toward standard ambient conditions, re-stabilize the test item at the required test temperature and continue the test from the point where test conditions were interrupted.

(2) Overtest interruption (e.g., loss of chamber control).

(a) Inspection and performance check. If an interruption in a cyclic or steady state test results in more extreme exposure of the test item than required by the materiel specifications, follow the interruption by a complete physical inspection and an operational check (where possible) before continuing the test.

(b) Safety, performance, materials problems. When these types of problems are discovered after an overtest, the preferable course of action is to terminate the test and re-initiate testing with a new test item. If this is not done and a test item failure occurs during the remainder of the test, the test

Downloaded from http://www.everyspec.com

results could be considered invalid because of the overtest conditions. If no problem has been encountered, reestablish pre-interruption conditions and continue from the point where the test tolerances were exceeded.

4.3.2 Interruption Due to Test Item Operation Failure.

Failure of the test item(s) to function as required during mandatory or optional performance checks during testing presents a situation with several possible options.

a. The preferable option is to replace the test item with a "new" one and restart from Step 1.

b. A second option is to replace / repair the failed or non-functioning component or assembly with one that functions as intended, and restart the entire test from Step 1.

> **NOTE**: When evaluating failure interruption, consider prior testing on the same test item and consequences of such.

4.4 Test Setup.

a. General. See Part One, paragraph 5.8.

b. Unique to this Method. Include in the test setup any additional heat sources or an appropriate simulation (see paragraph 2.3.2b).

4.5 Test Execution.

The following steps, alone or in combination, provide the basis for collecting necessary information concerning the materiel in a high temperature environment.

4.5.1 Preparation for Test.

4.5.1.1 Preliminary Steps.

Before starting the test, review pretest information in the test plan to determine test details (e.g., procedures, test item configuration, cycles, durations, parameter levels for storage/operation, etc.). (See paragraph 3.1, above.)

4.5.1.2 Pretest Standard Ambient Checkout.

All test items require a pretest standard ambient checkout to provide baseline data. Conduct the checkout as follows:

Step 1 Conduct a visual examination of the test item with special attention to stress areas, such as corners of molded cases, and document the results.

Step 2 In order to determine thermal response (paragraph 3.1c), install temperature sensors in, on, or around the test item as described in the test plan.

Step 3 Conduct an operational checkout (Part One, paragraph 5.8.2) at standard ambient conditions (Part One, paragraph 5.1) as described in the plan and record the results.

Step 4 If the test item operates satisfactorily, proceed to paragraph 4.5.2, 4.5.3, or 4.5.4 as appropriate. If not, resolve the problems and repeat Step 3 above. If resolution requires replacement of the item or removal of sensors in order to repair, then repeat Steps 1 through 3 above.

4.5.2 Procedure I - Storage.

> **NOTE**: If the LCEP has defined the need to operate the test item at the high operational temperature immediately following storage, consider using Procedure III.

Step 1 Place the test item in its storage configuration and install it in the chamber.

Step 2 Adjust the chamber environment to the required test conditions, either cyclic exposure (Tables 501.7-II or 501.7-III) or constant exposure (see paragraph 2.3.3.1), for the start of the test period at a rate not to exceed 3 °C/min (5 °F/min). Maintain for the specified time following temperature stabilization of the test item.

Downloaded from http://www.everyspec.com

Step 3 a. For cyclic storage, expose the test item to the temperature (and humidity, if applicable) conditions of the storage cycle for a minimum of seven continuous 24-hour cycles, or as specified in the LCEP and the test plan. Record the thermal response of the test item.

b. For constant temperature storage (to be used only for items situated in close proximity to equipment producing constant high temperatures; see paragraph 2.3.2b(2)), maintain the test temperature at least two hours following test item temperature stabilization (see Part One, paragraph 5.4). The additional two hours will help ensure unmeasured internal components actually reach stabilization. If not possible to instrument internal components, base any additional soak time on thermal analysis to ensure temperature stabilization throughout the test item.

Step 4 At the completion of the constant temperature soak or the last cycle, adjust the chamber air temperature to standard ambient conditions and maintain until the test item temperature is stabilized.

Step 5 Conduct a visual examination and operational checkout of the test item, and record the results for comparison with pretest data. See paragraph 5 for analysis of results.

4.5.3 Procedure II - Operation.

Step 1 With the test item in the chamber in its operational configuration, install any additional temperature sensors necessary to measure the maximum temperature response of the test item, ensuring the functioning components are included.

Step 2 If performing the constant temperature exposure, go to Step 3. For cycling temperature exposure, go to Step 8.

Step 3 Constant temperature exposure. Adjust the chamber air conditions to the required temperature (and humidity, if applicable) at which the materiel must operate at rate not to exceed 3 °C/min (5 °F/min).

Step 4 Maintain the chamber conditions at least two hours following test item temperature stabilization (see Part One, paragraph 5.4). If not possible to instrument internal components, base the additional soak time on thermal analysis or previously measured data to ensure temperature stabilization throughout the test item.

Step 5 Conduct as thorough a visual examination of the test item as possible considering chamber access limitations, and document the results for comparison with pretest data.

Step 6 Operate the test item and allow its temperature to re-stabilize. Conduct an operational checkout of the test item in accordance with the test plan and document the results for comparison with pretest data. If the test item fails to operate as intended, follow the guidance in paragraph 4.3.2 for test item failure.

Step 7 Skip Steps 8 through 10 and proceed directly to Step 11.

Step 8 Cycling temperature exposure. Adjust the chamber air temperature (and humidity, if applicable) to the initial conditions, of the operational cycle appropriate for materiel deployment, at a rate not to exceed 3 °C/min (5 °F/min). Maintain until the test item's temperature has stabilized.

Step 9 Expose the test item to at least three cycles or the number of cycles necessary to assure repeated test item response. Document the maximum test item response temperature. Conduct as complete a visual examination of the test item as possible considering chamber access limitations. Document the results.

Step 10 Operate the test item during the maximum test item temperature response period of the exposure cycle. If the test item fails to operate as intended, follow the guidance in paragraph 4.3.2 for test item failure. The maximum test item temperature response period may not coincide with the maximum temperature cycle conditions because of the thermal lag of the test item. Repeat until a successful operational checkout of the test item has been accomplished in accordance with the approved test plan, and the results have been documented.

Step 11 With the test item not operating, adjust the chamber air temperature to standard ambient conditions and maintain until the test item temperature has stabilized.

Downloaded from http://www.everyspec.com

Step 12 Conduct a complete visual examination and operational checkout in accordance with the approved test plan and document the results for comparison with pretest data. See paragraph 5 for analysis of results.

4.5.4 Procedure III - Tactical-Standby to Operational.

Step 1 With the test item in the chamber and in its tactical configuration, install any additional temperature sensors necessary to measure the temperature response of the test item, ensuring the functioning components are included.

Step 2 Adjust the chamber air temperature to the anticipated maximum non-operating temperature, and maintain this temperature until the test item temperature has stabilized, plus a minimum of two additional hours to ensure complete stabilization.

Step 3 Adjust the chamber air temperature to the high operational temperature identified in the LCEP as quickly as possible (at a rate no less than 2 ºC (3.6 ºF) per-minute). As soon as the chamber instrumentation indicates this temperature has been reached, operate the test item in accordance with the approved test plan and document the results for comparison with pretest data. If the test item fails to operate as intended, follow the guidance in paragraph 4.3.2 for test item failure. If identified in the LCEP that the item will be subjected to multiple exposures of this environment, repeat Steps 2 and 3 as required by the test plan.

Step 4 With the test item not operating, adjust the chamber air temperature to standard ambient conditions and maintain until the test item temperature has stabilized.

Step 5 Conduct a complete visual examination and operational checkout in accordance with the approved test plan, and document the results for comparison with pretest data. See paragraph 5 for analysis of results.

5. ANALYSIS OF RESULTS.

In addition to the guidance provided in Part One, paragraphs 5.14 and 5.17, the following information is provided to assist in the evaluation of the test results. Apply any data relative to failure of a test item to meet the requirements of the materiel specifications to the test analysis, and consider related information such as:

a. Results of nondestructive examinations (if any) of materiel at the temperature extreme.

b. Degradation or changes in operating characteristics allowed at the high extreme temperatures.

c. Necessity for special kits or special operating procedures for high temperature exposure.

d. Evidence of improper lubrication and assurance that the lubricants specified for the environmental condition were used.

e. For Procedure III, the amount of time required for the test item to become operational.

6. REFERENCE/RELATED DOCUMENTS.

6.1 Referenced Documents.

a. MIL-HDBK-310, Global Climatic Data for Developing Military Products.

b. NATO STANAG 4370, Allied Environmental Conditions and Test Publication (AECTP) 230; Climatic Conditions.

c. AR 70-38, Research, Development, Test and Evaluation of Materiel for Extreme Climatic Conditions.

d. MIL-STD-2105C, Test Method Standard – Hazard Assessment Tests for Non-Nuclear Munitions.

Downloaded from http://www.everyspec.com

6.2 Related Documents.

a. Synopsis of Background Material for MIL-STD-210B, Climatic Extremes for Military Equipment. Bedford, MA: Air Force Cambridge Research Laboratories, 24 January 1974. DTIC number AD-780-508.

b. NATO STANAG 4370, Environmental Testing.

c. Allied Environmental Conditions and Test Publication (AECTP) 300, Climatic Environmental Tests (under STANAG 4370), Method 302.

d. Egbert, Herbert W. "The History and Rationale of MIL-STD-810 (Edition 2)" January 2010," Institute of Environmental Sciences and Technology, Arlington Place One, 2340 S. Arlington Heights Road, Suite 100, Arlington Heights, IL 60005-4516.

(Copies of Department of Defense Specifications, Standards, and Handbooks, and International Standardization Agreements are available online at https://assist.dla.mil.

Requests for other defense-related technical publications may be directed to the Defense Technical Information Center (DTIC), ATTN: DTIC-BR, Suite 0944, 8725 John J. Kingman Road, Fort Belvoir VA 22060-6218, 1-800-225-3842 (Assistance--selection 3, option 2), http://www.dtic mil/dtic/ and the National Technical Information Service (NTIS), Springfield VA 22161, 1-800-553-NTIS (6847), http://www ntis.gov/.

Appendix B

Questionnaires

B.1 Questionnaire - Hospital conditions in LRSs

Hospitals conditions in low-resource settings

This survey aims to identify the conditions of Sub-Saharan hospitals. The survey consists of 9 sections, namely introduction, personal information, facility information, facility general characteristic, electrical access, human resources, facility environment, medical electrical equipment and database.

You may be an employee of the hospital (e.g., a nurse, a medical doctor, a biomedical technician) or any person who is familiar with the hospital.

The answers will be anonymized and used in a joint research study between the Applied Biomedical Signal Processing and Intelligent eHealth Lab (https://warwick.ac.uk/fac/sci/eng/research/grouplist/biomedicaleng/abspie) at the University of Warwick, led by Dr Leandro Pecchia, and the Research Center "E. Piaggio" (http://www.centropiaggio.unipi.it) at the University of Pisa, led by Prof Arti Ahluwalia.

Your answers will not be disclosed and your participation to this study will remain confidential.

In this survey, with the term health facility, we refer to any location where healthcare is provided. Health facilities range from small clinics and doctor's offices to urgent care centres and large hospitals with elaborate emergency rooms and trauma centres.

Thank you for taking time to respond to this questionnaire.

1. Pictures and videos of the interviewee, the medical locations and/or the medical devices may be taken before/during/after the interviews. They will be stored securely and may be used during seminars and as additional materials in journal publications. I hereby authorize the acquisition and treatment of such pictures and videos, as above mentioned.

   Mark only one oval.

   - ◯ Yes
   - ◯ No

2. I hereby authorize, according to the EU regulation 679/2016, the treatment of the transmitted personal data.

Mark only one oval.

- ◯ Accept
- ◯ Not accept

Personal Information

This section asks some general questions about your personal information.

3. Date:

_____

Example: 7 January 2019

4. DISTRICT and COUNTRY of the facility

_____

5. Age:

Mark only one oval.

- ◯ <20
- ◯ 21-30
- ◯ 31-40
- ◯ 41-50
- ◯ 51-60
- ◯ 61-70

6. Sex:

Mark only one oval.

- ◯ Female
- ◯ Male
- ◯ Prefer not to say

7. The highest GRADE or LEVEL OF SCHOOL/EDUCATION that you have completed:

Mark only one oval.

- ◯ Less than primary school
- ◯ Primary school
- ◯ Secondary school
- ◯ High school or equivalent
- ◯ College or university

8. ROLE within the facility:

Mark only one oval.

- ◯ Physician
- ◯ Nurse
- ◯ Medical Assistant
- ◯ Biomedical engineer/Biomedical Technician
- ◯ Other: _____

9. How long have you stayed in this role (years)?

Mark only one oval.

- ◯ 1-3
- ◯ 4-6
- ◯ 7-9
- ◯ 10 or more

10. Contact email (optional)

_____

Facility Information

This section of the questionnaire focuses on the facility information

11. Facility name:

_____

12. Classification of the facility:

Mark only one oval.

- ◯ Public
- ◯ Private
- ◯ Non-governamental organization (NGO)

13. Setting type:

Disease Control Priorities Project: terminology and definitions	Alternative terms commonly found in the literature
Primary-level hospital: few specialties—mainly internal medicine, obstetrics and gynaecology, paediatrics, and general surgery, or just general practice; limited laboratory services available for general but not specialized pathological analysis	District hospital Rural hospital Community hospital General hospital
Secondary-level hospital: highly differentiated by function with 5 to 10 clinical specialties; size ranges from 200 to 800 beds; often referred to as a *provincial hospital*	Regional hospital Provincial hospital (or equivalent administrative area such as county) General hospital
Tertiary-level hospital: highly specialized staff and technical equipment—for example, cardiology, intensive care unit, and specialized imaging units; clinical services highly differentiated by function; could have teaching activities; size ranges from 300 to 1,500 beds	National hospital Central hospital Academic or teaching or university hospital

Figure 1 - Description of different setting types

Mark only one oval.

- ◯ Primary level (rural)
- ◯ Secondary level (semi-urban)
- ◯ Third level (urban)

14. Department of belonging:

Facility general characteristics

This section of the questionnaire focuses on general characteristics of the facility including the availability of specific resources such as water, telephones and radios.

15. What is the MAIN SOURCE OF WATER in this facility? If more than one select all that apply

Tick all that apply.

- [ ] Piped water
- [ ] Water from open well
- [ ] Water from covered well or borehole
- [ ] Surface water
- [ ] Tanker water
- [ ] Rain water
- [ ] I don't know

16. Does the facility have a FUNCTIONING LAND LINE TELEPHONE?

Mark only one oval.

- ◯ Yes
- ◯ No
- ◯ I don't know

17. Does the facility have at least ONE FUNCTIONING MOBILE PHONE (either private or supported by the facility)?

Mark only one oval.

- ◯ Yes
- ◯ No
- ◯ I don't know

18. Does the facility have a FUNCTIONING SHORT WAVE RADIO for radio calls?

Mark only one oval.

- ◯ Yes
- ◯ No
- ◯ I don't know

19. Does the facility have at least ONE FUNCTIONING COMPUTER for staff use?

Mark only one oval.

- Yes
- No
- I don't know

20. Does the facility have a FUNCTIONING INTERNET SERVICE for staff use?

Mark only one oval.

- Yes
- No
- I don't know

21. Does the facility have AN AMBULANCE?

Mark only one oval.

- Yes
- No
- I don't know

Electrical Access

This section of the questionnaire asks about general resources available in the facility.

22. Does the facility have ACCESS to ELECTRICITY?

Mark only one oval.

- Yes
- No

23. Which is THE MAIN SOURCE OF ELECTRICITY in the facility?

Tick all that apply.

- [ ] Generator only
- [ ] Central supply
- [ ] Solar system
- [ ] Other: _____

24. How often have POWER OUTAGES happened in the last month?

Tick all that apply.

- [ ] 1-3
- [ ] 4-6
- [ ] 7-9
- [ ] 10 or more
- [ ] Other: _____

25. How good do you consider THE ACCESS TO THE MAIN SOURCE OF ELECTRICITY of the facility (power available during all regular service hours, with no outages exceeding 2 hours on a given day in the week prior to data collection)?

Mark only one oval.

- ◯ Very poor
- ◯ Poor
- ◯ Acceptable
- ◯ Good
- ◯ Very good
- ◯ I don't know

26. How good do you consider THE QUALITY AND RELIABILITY OF THE ELECTRICITY of the facility?

Mark only one oval.

- ◯ Very poor
- ◯ Poor
- ◯ Acceptable
- ◯ Good
- ◯ Very good
- ◯ I don't know

27. Which of the following SYSTEMS FOR ELECTRICAL SAFETY are available and functional of the facility?

Tick all that apply.

- ☐ Electrical grounding
- ☐ Equipotential nodes
- ☐ Isolation transformers
- ☐ I don't know

28. How good do you consider the availability and functionality of the ELECTRICAL SAFETY in the facility?

Mark only one oval.

- ◯ Very poor
- ◯ Poor
- ◯ Acceptable
- ◯ Good
- ◯ Very good
- ◯ I don't know

29. What is the NOMINAL VOLTAGE of the electricity available at the facility? (Nominal voltage means "expected" voltage)

_____

30. What is the FREQUENCY of the electricity available at the facility?

_____

31. How good do you consider the COMPATIBILITY of the WORKING VOLTAGE AND FREQUENCY required for the medical devices and the VOLTAGE AND FREQUENCY of the electricity of the facility?

Mark only one oval.

- ◯ Very poor
- ◯ Poor
- ◯ Acceptable
- ◯ Good
- ◯ Very good
- ◯ I don't know

Human resources

This section of the questionnaire asks about the human resources available in this facility. Questions ask about whether a human resource is available and the number present on the day of the interview.

32. How many medical DOCTORS/PHYSICIANS work in the facility?

_____

33. Which is the RATIO between PATIENTS and DOCTORS/PHYSICIANS in this facility?

Mark only one oval.

- ◯ 1 doctor for 1-2 patients
- ◯ 1 doctor for 2-5 patients
- ◯ 1 doctor for 5-10 patients
- ◯ 1 doctor for 10-15 patients
- ◯ 1 doctor for 15-20 patients
- ◯ 1 doctor for 20-30 patients
- ◯ 1 doctor for more than 30 patients

34. How good do you consider the RATIO between PATIENTS and DOCTORS/PHYSICIANS in this facility?

Mark only one oval.

- ◯ Very poor
- ◯ Poor
- ◯ Acceptable
- ◯ Good
- ◯ Very good
- ◯ I don't know

35. How many CLINICAL OFFICERS/ASSISTANT MEDICAL OFFICERS work in this facility? (A clinical officer (CO) is a licensed practitioner of medicine in East Africa and parts of Southern Africa who is trained and authorized to perform general or specialized medical duties such as diagnosis and treatment of disease and injury, ordering and interpreting medical tests, performing routine medical and surgical procedures, and referring patients to other practitioners.)

_____

36. Which is the RATIO between PATIENTS and CLINICAL OFFICERS/ASSISTANT MEDICAL OFFICERS in this facility?

Mark only one oval.

- ◯ 1 clinical officer for 1-2 patients
- ◯ 1 clinical officer for 2-5 patients
- ◯ 1 clinical officer for 5-10 patients
- ◯ 1 clinical officer for 10-15 patients
- ◯ 1 clinical officer for 15-20 patients
- ◯ 1 clinical officer for 20-30 patients
- ◯ 1 clinical officer for more than 30 patients

37. How good do you consider the RATIO between PATIENTS and CLINICAL OFFICERS/ASSISTANT MEDICAL OFFICERS in this facility?

Mark only one oval.

- ◯ Very poor
- ◯ Poor
- ◯ Acceptable
- ◯ Good
- ◯ Very good
- ◯ I don't know

38. How many NURSES work in this facility?

_____

39. Which is the RATIO between PATIENTS and NURSES in this facility?

Mark only one oval.

- ◯ 1 nurse for 1-2 patients
- ◯ 1 nurse for 2-5 patients
- ◯ 1 nurse for 5-10 patients
- ◯ 1 nurse for 10-15 patients
- ◯ 1 nurse for 15-20 patients
- ◯ 1 nurse for 20-30 patients
- ◯ 1 nurse for more than 30 patients

40. How good do you consider the RATIO between PATIENTS and NURSES in this facility?

Mark only one oval.

- Very poor
- Poor
- Acceptable
- Good
- Very good
- I don't know

41. How many LABORATORY TECHNICIANS/TECHNOLOGISTS work in this facility?

_____

42. How good do you consider the RATIO between LABORATORY TECHNICIANS/TECHNOLOGIST and MEDICAL DEVICES in this facility?

Mark only one oval.

- Very poor
- Poor
- Acceptable
- Good
- Very good
- I don't know

Facility environment

This section of the questionnaire focuses on the facility environment including the environment, occupancy, safety and patient movement. It also asks about the lighting, ventilation, public water supply

43. How good do you consider THE INSULATION OR DISTANCE from UNDUE NOISE?

Mark only one oval.

- Very poor
- Poor
- Acceptable
- Good
- Very good
- I don't know

44. How good do you consider THE INSULATION OR DISTANCE from SMOKE?

Mark only one oval.

- Very poor
- Poor
- Acceptable
- Good
- Very good
- I don't know

45. How good do you consider THE INSULATION OR DISTANCE from DUST?

Mark only one oval.

- Very poor
- Poor
- Acceptable
- Good
- Very good
- I don't know

46. How good do you consider THE INSULATION OR DISTANCE from FOUL ODORS?

Mark only one oval.

- Very poor
- Poor
- Acceptable
- Good
- Very good
- I don't know

47. How good do you consider THE LIGHTING (all areas shall be provided with sufficient illumination to promote comfort, healing and recovery of patients and to enable personnel in the performance of work)?

Mark only one oval.

- Very poor
- Poor
- Acceptable
- Good
- Very good
- I don't know

48. How good do you consider THE ADEQUATENESS OF VENTILATION?

Mark only one oval.

- Very poor
- Poor
- Acceptable
- Good
- Very good
- I don't know

49. How many TOILETS are there in this facility?

_____

50. How good do you consider THE DISPOSAL OF WASTE (liquid waste shall be discharged into an approved sewerage system if available and solid waste shall be collected, treated and disposed of in accordance with laws)? Please consider the table below as reference. It describes the categories of hospital waste according to the World Health Organization.

Waste category	Constituents
Risk waste	Infectious waste, pathological waste, sharps, pharmaceutical waste, genotoxic waste, chemical waste and radioactive waste.
Non-risk waste	Paper & cardboard, packaging, food waste, aerosols and so on.
Infectious waste	Waste contaminated by any type of pathogens and includes cultures from laboratory work, waste from surgeries and autopsies, waste from infected patients, discarded or disposable materials and equipment which have been in contact with such patients.
Pathological waste	Tissues, organs, body parts, fetuses, blood and body fluids.
Sharps	Include, whether infected or not, needles, syringes, scalpels, infusion sets, saws & knives, blades, broken glass and any other item that could cut or puncture.
Pharmaceutical waste	Expired or unused pharmaceutical products, surplus drugs, vaccines or sera and discarded items used in handling pharmaceutical waste such as bottles, boxes, gloves, masks, tubes or vials.
Genotoxic waste	Cytotoxic drugs and outdated materials, vomitus, feces or urine from patients treated with cytotoxic drugs or chemicals and materials such as syringes and vials contaminated from the preparation and administration of such drugs.
Chemical waste	Chemicals from diagnostic and experimental work, cleaning processes, housekeeping and disinfecting procedures, mercury waste such as from broken clinical equipment and spillage and cadmium waste from discarded batteries.
Radioactive waste	Liquid, solid and gaseous waste contaminated with radionuclides generated from in-vitro analysis of body tissue and fluid, in-vivo body organ imaging and tumor localization, and investigation and therapeutic procedures.

Figure 2 - Categories of hospital waste according to the World health Organization

Mark only one oval per row.

	Very poor	Poor	Acceptable	Good	Very good	I don't know
Risk waste	◯	◯	◯	◯	◯	◯
Non-risk waste	◯	◯	◯	◯	◯	◯
Infectious waste	◯	◯	◯	◯	◯	◯
Pathological waste	◯	◯	◯	◯	◯	◯
Sharps	◯	◯	◯	◯	◯	◯
Pharmaceutical waste	◯	◯	◯	◯	◯	◯
Genotoxic waste	◯	◯	◯	◯	◯	◯
Chemical waste	◯	◯	◯	◯	◯	◯
Radioactive waste	◯	◯	◯	◯	◯	◯

51. How often are the facility ENVIRONMENTS CLEANED?

Mark only one oval.

- Less than once a week
- 1-2 times per week
- 3-4 times per week
- 5 times per week or more

52. How good do you consider THE MATERIALS of the floors, walls and ceilings (they have to be sturdy, durable, of easy cleaning and resistant to fire)?

Mark only one oval.

- Very poor
- Poor
- Acceptable
- Good
- Very good
- I don't know

Medical Electrical Equipment

This section of the questionnaire explores the availability of specific health-related resources.

53. Do you have a well established CLINICAL/BIOMEDICAL ENGINEERING DEPARTMENT?

Mark only one oval.

- Yes
- No
- I don't know

54. Please indicate how many of the following medical devices are AVAILABLE and FUNCTIONAL in this facility:

Mark only one oval per row.

	0	1	2	3	4	5-10	more than 10	NA
X-ray machine								
Oxygen system/cylinders								
Autoclave for sterilization								
Operating theatre with basic equipment								
Anasthetic machine								
Hemocytometer (for total lymphocyte and full blood counts)								
Ultrasound machine								
Ambulance or other emergency transportation service								
Blood pressure machine/cuff								
Colonoscope								
Gastroscope								
ECG machine								
Scale for adult								
Scale for newborn								
Thermometer								

Defibrillator								
Syring pump								
Pulsoximeter								
Patient monitor								
Ventilator ICU								
Suction pump								
Fetal monitor								
Neonatal incubator								
CT-scanner								
Infant reanimation centre								
Mammograph								
Infant warmer								

55. Please indicate how do you consider THE RATIO between PATIENTS and THE NUMBER OF THESE MEDICAL DEVICES?

Mark only one oval per row.

	Very poor	Poor	Acceptable	Good	Very good	I don't know
X-ray machine						
Oxygen system/cylinders						
Autoclave for sterilization						
Operating theatre with basic equipment						
Anasthetic machine						
Hemocytometer (for total lymphocyte and full blood counts)						
Ultrasound machine						
Ambulance or other emergency transportation service						
Blood pressure machine/cuff						
Colonoscope						
Gastroscope						
ECG machine						
Scale for adult						
Scale for newborn						
Thermometer						
Defibrillator						
Syring pump						
Pulsoximeter						
Patient monitor						

Ventilator ICU						
Suction pump						
Fetal monitor						
Neonatal incubator						
CT-scanner						
Infant reanimation centre						
Mammograph						
Infant warmer						

56. Please indicate how many of the following medical devices are OUT OF SERVICE/AWAITING REPAIR in this facility:

Mark only one oval per row.

	0	1	2	3	4	5-10	more than 10	NA
X-ray machine	◯	◯	◯	◯	◯	◯	◯	◯
Oxygen system/cylinders	◯	◯	◯	◯	◯	◯	◯	◯
Autoclave for sterilization	◯	◯	◯	◯	◯	◯	◯	◯
Operating theatre with basic equipment	◯	◯	◯	◯	◯	◯	◯	◯
Anasthetic machine	◯	◯	◯	◯	◯	◯	◯	◯
Hemocytometer (for total lymphocyte and full blood counts)	◯	◯	◯	◯	◯	◯	◯	◯
Ultrasound machine	◯	◯	◯	◯	◯	◯	◯	◯
Ambulance or other emergency transportation service	◯	◯	◯	◯	◯	◯	◯	◯
Blood pressure machine/cuff	◯	◯	◯	◯	◯	◯	◯	◯
Colonoscope	◯	◯	◯	◯	◯	◯	◯	◯
Gastroscope	◯	◯	◯	◯	◯	◯	◯	◯
ECG machine	◯	◯	◯	◯	◯	◯	◯	◯
Scale for adult	◯	◯	◯	◯	◯	◯	◯	◯
Scale for newborn	◯	◯	◯	◯	◯	◯	◯	◯
Thermometer	◯	◯	◯	◯	◯	◯	◯	◯
	◯	◯	◯	◯	◯	◯	◯	◯

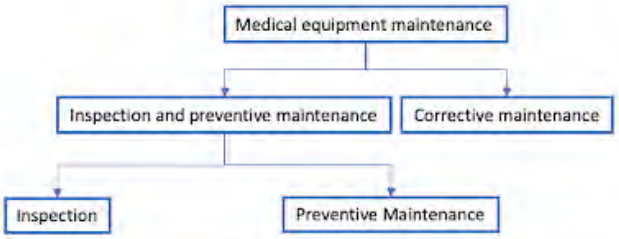
Defibrillator								
Syring pump								
Pulsoximeter								
Patient monitor								
Ventilator ICU								
Suction pump								
Fetal monitor								
Neonatal incubator								
CT-scanner								
Infant reanimation centre								
Mammograph								
Infant warmer								

57. How good do you consider THE RATIO between MEDICAL DOCTORS/NURSES able to use certain medical devices and THE NUMBER OF THESE MEDICAL DEVICES?

Mark only one oval.

- Very poor
- Poor
- Acceptable
- Good
- Very good
- I don't know

58. Does your facility provide a MAINTENANCE PROGRAMME for medical equipment? Please consider the image below as a reference for a correct maintenance programme.



Term	Definition
Inspection and preventive maintenance (IPM)	IPM refers to all the scheduled activity necessary to ensure a piece of medical equipment is functioning correctly and is well maintained. IPM therefore includes inspection and preventive maintenance (PM).
Inspection	Inspection refers to scheduled activities necessary to ensure a piece of medical equipment is functioning correctly. It includes both performance inspections and safety inspections. These occur in conjunction with preventive maintenance, corrective maintenance, or calibration but can also be completed as a stand-alone activity scheduled at specifi c intervals.
Preventive maintenance	PM involves maintenance performed to extend the life of the device and prevent failure. PM is usually scheduled at specifi c intervals and includes specifi c maintenance activities such as lubrication, cleaning (e.g. fi lters) or replacing parts that are expected to wear (e.g. bearings) or which have a fi nite life (e.g. tubing). The procedures and intervals are usually established by the manufacturer. In special cases the user may change the frequency to accommodate local environmental conditions. Preventive maintenance is sometimes referred to as 'planned maintenance' or 'scheduled maintenance'. This document uses these terms interchangeably.
Corrective maintenance (CM)	A process used to restore the physical integrity, safety and/or performance of a device after a failure. Corrective maintenance and unscheduled maintenance are regarded as equivalent to the term repair.

Figure 3 - Medical equipment maintenance program

Mark only one oval.

- ◯ Yes
- ◯ No
- ◯ I don't know

59. How is your MEDICAL EQUIPMENT MAINTENANCE PROGRAMME provided for the following medical devices?

Mark only one oval per row.

	IPM and CM at the facility	IPM at the facility and sent back to manufacturer for CM	IPM at the facility and sent back to "government store" for CM	Sent back to manufacturer for IPM and CM	Sent back to "government store" for IPM and CM	I don't know
X-ray machine						
Oxygen system/cylinders						
Autoclave for sterilization						
Operating theatre with basic equipment						
Anasthetic machine						
Hemocytometer (for total lymphocyte and full blood counts)						
Ultrasound machine						
Ambulance or other emergency transportation service						
Blood pressure machine/cuff						
Colonoscope						
Gastroscope						
ECG machine						
Scale for adult						
Scale for						

newborn						
Thermometer						
Defibrillato						
Syring pump						
Pulsoximeter						
Patient monitor						
Ventilator ICU						
Suction pump						
Fetal monitor						
Neonatal incubator						
CT-scanner						
Infant reanimation centre						
Mammograph						
Infant warmer						

60. According to the definition provided in Figure 3, which is the FREQUENCY of the INSPECTION PROCEDURES for the following medical devices?

Mark only one oval per row.

	Once a year or more	Less than once a year	Never	I don't know	NA
X-ray machine					
Autoclave for sterilization					
Operating theatre with basic equipment					
Anasthetic machine					
Hemocytometer (for total lymphocyte and full blood counts)					
Ultrasound machine					
Ambulance or other emergency transportation service					
Blood pressure machine/cuff					
Colonoscope					
Gastroscope					
ECG machine					
Scale for adult					
Scale for newborn					
Thermometer					
Defibrillator					
Syring pump					
Pulsoximeter					
Patient monitor					
Ventilator ICU					
Suction pump					

Fetal monitor					
Neonatal incubator					
CT-scanner					
Infant reanimation centre					
Mammograph					
Infant warmer					

61. According to the definition provided in Figure 3, which is the FREQUENCY of the PREVENTIVE MAINTENANCE PROCEDURES for the following medical devices?

Mark only one oval per row.

	Once a year or more	Less than once a year	Never	I don't know	NA
X-ray machine					
Autoclave for sterilization					
Operating theatre with basic equipment					
Anasthetic machine					
Hemocytometer (for total lymphocyte and full blood counts)					
Ultrasound machine					
Ambulance or other emergency transportation service					
Blood pressure machine/cuff					
Colonoscope					
Gastroscope					
ECG machine					
Scale for adult					
Scale for newborn					
Thermometer					
Defibrillator					
Syring pump					
Pulsoximeter					
Patient monitor					
Ventilator ICU					
Suction pump					

Fetal monitor					
Neonatal incubator					
CT-scanner					
Infant reanimation centre					
Mammograph					
Infant warmer					

62. According to the definition provided in Figure 3, which is the FREQUENCY of the CORRECTIVE MAINTENANCE PROCEDURES for the following medical devices?

Mark only one oval per row.

	Once a year or more	Less than once a year	Never	I don't know	NA
X-ray machine	◯	◯	◯	◯	◯
Autoclave for sterilization	◯	◯	◯	◯	◯
Operating theatre with basic equipment	◯	◯	◯	◯	◯
Anasthetic machine	◯	◯	◯	◯	◯
Hemocytometer (for total lymphocyte and full blood counts)	◯	◯	◯	◯	◯
Ultrasound machine	◯	◯	◯	◯	◯
Ambulance or other emergency transportation service	◯	◯	◯	◯	◯
Blood pressure machine/cuff	◯	◯	◯	◯	◯
Colonoscope	◯	◯	◯	◯	◯
Gastroscope	◯	◯	◯	◯	◯
ECG machine	◯	◯	◯	◯	◯
Scale for adult	◯	◯	◯	◯	◯
Scale for newborn	◯	◯	◯	◯	◯
Thermometer	◯	◯	◯	◯	◯
Defibrillator	◯	◯	◯	◯	◯
Syring pump	◯	◯	◯	◯	◯
Pulsoximeter	◯	◯	◯	◯	◯
Patient monitor	◯	◯	◯	◯	◯
Ventilator ICU	◯	◯	◯	◯	◯
Suction pump	◯	◯	◯	◯	◯

Fetal monitor	⬭	⬭	⬭	⬭	⬭
Neonatal incubator	⬭	⬭	⬭	⬭	⬭
CT-scanner	⬭	⬭	⬭	⬭	⬭
Infant reanimation centre	⬭	⬭	⬭	⬭	⬭
Mammograph	⬭	⬭	⬭	⬭	⬭
Infant warmer	⬭	⬭	⬭	⬭	⬭

63. What, if any, are the DIFFICULTIES in getting repairs to equipment done?

64. What percentage of CONSUMABLES is available in your facilities?

Mark only one oval per row.

	None	<25%	25-50%	50-75%	>75%	All
X-ray machine	◯	◯	◯	◯	◯	◯
Oxygen system/cylinders	◯	◯	◯	◯	◯	◯
Autoclave for sterilization	◯	◯	◯	◯	◯	◯
Operating theatre with basic equipment	◯	◯	◯	◯	◯	◯
Anasthetic machine	◯	◯	◯	◯	◯	◯
Hemocytometer (for total lymphocyte and full blood counts)	◯	◯	◯	◯	◯	◯
Ultrasound machine	◯	◯	◯	◯	◯	◯
Ambulance or other emergency transportation service	◯	◯	◯	◯	◯	◯
Blood pressure machine/cuff	◯	◯	◯	◯	◯	◯
Colonoscope	◯	◯	◯	◯	◯	◯
Gastroscope	◯	◯	◯	◯	◯	◯
ECG machine	◯	◯	◯	◯	◯	◯
Scale for adult	◯	◯	◯	◯	◯	◯
Scale for newborn	◯	◯	◯	◯	◯	◯
Thermometer	◯	◯	◯	◯	◯	◯
Defibrillator	◯	◯	◯	◯	◯	◯
Syring pump	◯	◯	◯	◯	◯	◯
Pulsoximeter	◯	◯	◯	◯	◯	◯
Patient monitor	◯	◯	◯	◯	◯	◯
Ventilator ICU	◯	◯	◯	◯	◯	◯
Suction pump	◯	◯	◯	◯	◯	◯

Fetal monitor						
Neonatal incubator						
CT-scanner						
Infant reanimation centre						
Mammograph						
Infant warmer						

65. What percentage of SPARE PARTS is available in your facilities?

Mark only one oval per row.

	None	<25%	25-50%	50-75%	>75%	All
X-ray machine	◯	◯	◯	◯	◯	◯
Oxygen system/cylinders	◯	◯	◯	◯	◯	◯
Autoclave for sterilization	◯	◯	◯	◯	◯	◯
Operating theatre with basic equipment	◯	◯	◯	◯	◯	◯
Anasthetic machine	◯	◯	◯	◯	◯	◯
Hemocytometer (for total lymphocyte and full blood counts)	◯	◯	◯	◯	◯	◯
Ultrasound machine	◯	◯	◯	◯	◯	◯
Ambulance or other emergency transportation service	◯	◯	◯	◯	◯	◯
Blood pressure machine/cuff	◯	◯	◯	◯	◯	◯
Colonoscope	◯	◯	◯	◯	◯	◯
Gastroscope	◯	◯	◯	◯	◯	◯
ECG machine	◯	◯	◯	◯	◯	◯
Scale for adult	◯	◯	◯	◯	◯	◯
Scale for newborn	◯	◯	◯	◯	◯	◯
Thermometer	◯	◯	◯	◯	◯	◯
Defibrillator	◯	◯	◯	◯	◯	◯
Syring pump	◯	◯	◯	◯	◯	◯
Pulsoximeter	◯	◯	◯	◯	◯	◯
Patient monitor	◯	◯	◯	◯	◯	◯
Ventilator ICU	◯	◯	◯	◯	◯	◯
Suction pump	◯	◯	◯	◯	◯	◯

Fetal monitor						
Neonatal incubator						
CT-scanner						
Infant reanimation centre						
Mammograph						
Infant warmer						

66. What percentage of COMPATIBILITY is there between PLUGS of donated medical devices and LOCAL SOCKETS?

Some medical devices could have a British plug in a hospital with French sockets

Mark only one oval.

- None
- <25%
- 25-50%
- 50-75%
- >75%
- All

Skip to question 67

DATABASE

67. Is there any INVENTORY OR DATABASE to keep track of all the available medical devices in the hospital?

Mark only one oval.

- Yes *Skip to question 68*
- No
- I don't know

Skip to question 67

DATABASE

This section of the questionnaire asks about general information about the database available in the facility.

68. Is the DATABASE computerised or paper-based?

Mark only one oval.

- Computerised
- Paper-based

69. How good you consider THE USE OF THE DATABASE at this facility?

Mark only one oval.

- Very poor
- Poor
- Acceptable
- Good
- Very good
- I don't know

70. Is the following information available?

Mark only one oval per row.

	Yes	No	I don't know
Funding	◯	◯	◯
Year of manufacture	◯	◯	◯
Type	◯	◯	◯
Serial Number	◯	◯	◯
Year of acquisition	◯	◯	◯
Under warranty	◯	◯	◯
Information on warranty duration/end date	◯	◯	◯
Class Function equipment	◯	◯	◯
Date of Service	◯	◯	◯
Routine servicing	◯	◯	◯
Reason of acquisition	◯	◯	◯
User manual	◯	◯	◯
Technical manual	◯	◯	◯
Technical characteristics	◯	◯	◯
CEE/EEC class	◯	◯	◯
Insulation/isolation type	◯	◯	◯

71. Please add any additional comment

B.2 Questionnaire - MD design criteria for LRSs

Medical device design criteria for low-resource settings

This short (10 min) survey aims to identify essential criteria that, in your opinion, should be considered while designing Medical Devices (MDs) that will be used in lower income settings. This survey aims to explore which elements should be considered during the design of MDs to make them more resilient to operational conditions that in lower-income settings are more challenging than in higher-income ones (e.g., lack of specialised staff, health technology management issues, poor supply chain etc.).

Your name has been suggested by your colleagues and IFMBE AC members, which consider you as one of the leading experts for medical device assessment, maintenance or regulation.

The answers will be anonymized and used by IFMBE (http://ifmbe.org) studies and in research studies within the Applied Biomedical Signal Processing and Intelligent eHealth Lab (https://warwick.ac.uk/fac/sci/eng/research/grouplist/biomedicaleng/abspie) at the University of Warwick, led by Dr Leandro Pecchia.

Your answers will not be disclosed and your participation to this study will remain confidential. Your email is collected only to share with you the final results of this survey. Since this is an electronic survey, taking part in the survey and transmitting your answers online, we assume that you give your consent and agree that we can use the information you provide us with for the purposes of our study.

This study was approved by the Biomedical & Scientific Research Ethics Committee (BSREC) at the University of Warwick (REGO-2018-2283).

*Required

1. **Email address** *

2. **In which nation do you work?** *

3. **What's your field of expertise?** *

4. **How many years of experience do you have in the field?** *

5. **USER TYPE: What is the importance of considering the END USERS' BACKGROUND (e.g., doctors, nurses, biomedical engineering technicians etc.) during the design of MD which will be used in low resource settings?** *

   Mark only one oval per row.

	Very low	Low	Medium	High	Very high	Do not know
Select an option						

6. **USER TYPE: What is the importance of considering the EASINESS OF USE (e.g., the MD requires a high specialized personnel, any operators can use it, or it is so intuitive that anyone can use it etc.) during the design of MD which will be used in low resource settings?** *

Mark only one oval per row.

	Very low	Low	Medium	High	Very high	Do not know
Select an option						

7. **USER TYPE: What is the importance of considering the TRAINING NEEDS (e.g., the training required to become skilled with this technology) during the design of MD which will be used in low resource settings?** *

Mark only one oval per row.

	Very low	Low	Medium	High	Very high	Do not know
Select an option						

8. **USER TYPE: What is the importance of considering the USER'S UNDERSTANDING OF THE TECHNICAL AND CLINICAL IMPACT of the technology during the design of MD which will be used in low resource settings?** *

Mark only one oval per row.

	Very low	Low	Medium	High	Very high	Do not know
Select an option						

9. **Do you suggest any other essential criterion/a for the USER TYPE domain? If yes, please include each below and rate its importance between brackets [e.g., "criteria 1 (Very low)" or "criteria 1 (High), criteria 2 (Medium), … "]** *

10. **HTM (Health Technology Management): What is the importance of considering the INSTALLATION REQUIREMENTS during the design of MD which will be used in low resource settings?** *

Mark only one oval per row.

	Very low	Low	Medium	High	Very high	Do not know
Select an option						

11. **HTM: What is the importance of considering the MAINTENANCE FREQUENCY during the design of MD which will be used in low resource settings?** *

Mark only one oval per row.

	Very low	Low	Medium	High	Very high	Do not know
Select an option						

12. **HTM: What is the importance of considering the MAINTENANCE COMPLEXITY during the design of MD which will be used in low resource settings?** *

Mark only one oval per row.

	Very low	Low	Medium	High	Very high	Do not know
Select an option						

13. **HTM: What is the importance of considering the need for CONSUMABLES during the design of MD which will be used in low resource settings?** *
Mark only one oval per row.

	Very low	Low	Medium	High	Very high	Do not know
Select an option						

14. **HTM: What is the importance of considering the need for SPARE PARTS during the design of MD which will be used in low resource settings?** *
Mark only one oval per row.

	Very low	Low	Medium	High	Very high	Do not know
Select an option						

15. **HTM: How important is the fact that consumables/spare parts are not necessarily from the same manufacturer (e.g., COMPATIBLE CONSUMABLES/SPARE PARTS CAN BE USED)?** *
Mark only one oval per row.

	Very low	Low	Medium	High	Very high	Do not know
Select an option						

16. **Do you suggest any other essential criterion/a for the HTM domain? If yes, please include each below and rate its importance between brackets [e.g., "criteria 1 (Very low)" or "criteria 1 (High), criteria 2 (Medium), … "]** *

17. **DESIGN: What is the importance of considering PORTABILITY, COMPACTNESS, ROBUSTNESS during the design of MD which will be used in low resource settings?** *
Mark only one oval per row.

	Very low	Low	Medium	High	Very high	Do not know
Select an option						

18. **DESIGN: What is the importance of LIMITING THE NUMBER OF COMPONENTS/SPARE PARTS during the design of MD which will be used in low resource settings?** *
Mark only one oval per row.

	Very low	Low	Medium	High	Very high	Do not know
Select an option						

19. **DESIGN: What is the importance of considering the REUSABILITY during the design of MD which will be used in low resource settings?** *
Mark only one oval per row.

	Very low	Low	Medium	High	Very high	Do not know
Select an option						

20. **Do you suggest any other essential criterion/a for the DESIGN domain? If yes, please include each below and rate its importance between brackets [e.g., "criteria 1 (Very low)" or "criteria 1 (High), criteria 2 (Medium), … "]** *

21. **RELIANCE ON EXTERNAL FACTORS: What is the importance of considering the RELIANCE ON POWER SOURCES during the design of MD which will be used in low resource settings?** *

Mark only one oval per row.

	Very low	Low	Medium	High	Very high	Do not know
Select an option						

22. **RELIANCE ON EXTERNAL FACTORS: What is the importance of considering the RELIANCE ON WATER DISTRIBUTION during the design of MD which will be used in low resource settings?** *

Mark only one oval per row.

	Very low	Low	Medium	High	Very high	Do not know
Select an option						

23. **RELIANCE ON EXTERNAL FACTORS: What is the importance of considering the RELIANCE ON MEDICAL LOCATION AIR (e.g. filtering, temperature, humidity, number of air-changes per hour) during the design of MD which will be used in low resource settings?** *

Mark only one oval per row.

	Very low	Low	Medium	High	Very high	Do not know
Select an option						

24. **RELIANCE ON EXTERNAL FACTORS: What is the importance of UNDERSTANDING/STATING THE DEPENDENCE OF THE MD FROM THE MEDICAL LOCATION CHARACTERISTICS (e.g. limited use in group 0, 2 or 3) during the design of MD which will be used in low resource settings?** *

Mark only one oval per row.

	Very low	Low	Medium	High	Very high	Do not know
Select an option						

25. **RELIANCE ON EXTERNAL FACTORS: What is the importance of considering the NEED FOR SAMPLE PREPARATION (when applicable) during the design of MD which will be used in low resource settings?** *

Mark only one oval per row.

	Very low	Low	Medium	High	Very high	Do not know
Select an option						

26. **Do you suggest any other essential criterion/a for the RELIANCE ON EXTERNAL FACTORS domain? If yes, please include each below and rate its importance between brackets [e.g., "criteria 1 (Very low)" or "criteria 1 (High), criteria 2 (Medium), … "]** *

27. **MATERIAL: What is the importance of considering the ROBUSTNESS OF THE MATERIAL used during the design of MD which will be used in low resource settings?** *
Mark only one oval per row.

	Very low	Low	Medium	High	Very high	Do not know
Select an option						

28. **MATERIAL: What is the importance of considering the DURABILITY OF THE CHOSEN MATERIAL during the design of MD which will be used in low resource settings?** *
Mark only one oval per row.

	Very low	Low	Medium	High	Very high	Do not know
Select an option						

29. **Do you suggest any other essential criterion/a for the MATERIAL domain? If yes, please include each below and rate its importance between brackets [e.g., "criteria 1 (Very low)" or "criteria 1 (High), criteria 2 (Medium), … "]** *

30. **COST: What is the importance of considering the INITIAL COST during the design of MD which will be used in low resource settings?** *
Mark only one oval per row.

	Very low	Low	Medium	High	Very high	Do not know
Select an option						

31. **COST: What is the importance of considering the MAINTENANCE COST during the design of MD which will be used in low resource settings?** *
Mark only one oval per row.

	Very low	Low	Medium	High	Very high	Do not know
Select an option						

32. **COST: What is the importance of considering the RUNNING COSTS during the design of MD which will be used in low resource settings?** *
Mark only one oval per row.

	Very low	Low	Medium	High	Very high	Do not know
Select an option						

33. **Do you suggest any other essential criterion/a for the COST domain? If yes, please include each below and rate its importance between brackets [e.g., "criteria 1 (Very low)" or "criteria 1 (High), criteria 2 (Medium), … "] ***

34. **LIFETIME: What is the importance of considering the MD LIFETIME during the design of MD which will be used in low resource settings? ***

Mark only one oval per row.

	Very low	Low	Medium	High	Very high	Do not know
Select an option						

35. **LIFETIME: What is the importance of considering the LIFETIME OF MD PARTS/COMPONENTS during the design of MD which will be used in low resource settings? ***

Mark only one oval per row.

	Very low	Low	Medium	High	Very high	Do not know
Select an option						

36. **Do you suggest any other essential criterion/a for the LIFETIME domain? If yes, please include each below and rate its importance between brackets [e.g., "criteria 1 (Very low)" or "criteria 1 (High), criteria 2 (Medium), … "] ***

37. **Please rate the importance of each domain for low resource settings ***

Mark only one oval per row.

	Very low	Low	Medium	High	Very high	Do not know
USER TYPE						
HTM						
DESIGN						
RELIANCE ON EXTERNAL FACTORS						
MATERIALS USED TO BUILD THE MD						
COST						
LIFETIME						

Send me a copy of my responses.

B.3 Screening questionnaire - Diabetic neuropathies

Pre-screening form

Name and Surname:

Age:

Sex:

Medical Conditions:

1) Were you diagnosed with diabetes?
   - If Yes, when?
   - If Yes, is it type 1 or 2?
2) Were you diagnosed with diabetic neuropathies?
3) Are you suffering from any of the following/ can you be included in any of the following groups? *Hypothyroidism, kidney disorders, recent injuries to the lower limbs, alcoholics, people exposed to heavy concentrations of toxic chemicals like glue, solvents or insecticides or heavy metals, Lyme disease, rheumatoid arthritis and lupus*

   - If yes, which?

If you answered **Yes** to 3), then you are not eligible for this study.

If you answered No to 3), then you are eligible for this study and you can set up an appointment.

Complete the following part on the day of the experiment:

- Have you or have you recently had any of these symptoms?
  - a high temperature – this means you feel hot to touch on your chest or back (you do not need to measure your temperature)
  - a new, continuous cough – this means coughing a lot for more than an hour, or 3 or more coughing episodes in 24 hours (if you usually have a cough, it may be worse than usual)
  - a loss or change to your sense of smell or taste – this means you've noticed you cannot smell or taste anything, or things smell or taste different to normal

- Is your current body temperature greater than 37.5°C?

If you have or have recently had any of the symptoms AND/OR if your current body temperature is greater than 37.5°C, then you will need to inform the researcher in advance and your appointment will be rescheduled.

Appendix C

Validation of MD design framework

The file attached below represents the protocol to test the framework. It is also an example of how it can be used. The first part presents a table with all the possible scores per domain and criterion.

	Criteria	Measurement scale		
User Type	End users' background	Medical doctors only	Any health care professional	Lay user
	Training needs	Low	Medium	High
HTM	Installation requirements	High	Medium	Low
	Maintenance frequency	Periodic	Seldom	No
	Maintenance complexity	Requires specialised personnel	Requires a trained local person	No
	Need for consumables	Frequent	Seldom	None
	Need for spare parts	Required specialised	Required easely avaliable	None
	Compatible consumables/spare parts	No		Yes
Design	Portability, compactness, robustness	Low	Medium	High
	Limiting the number of components/spare parts	High	Medium	Low
	Reusability	No		Yes
Reliance on external factors	Reliance on power sources	High	Medium	Low/None
	Reliance on water distribution	High	Medium	Low/None
	Reliance on medical location air	High	Medium	Low/None
	Need for sample preparation	Intensive	Medium	Minimal
	Resilience to dusty environments	Low	Medium	High
	Resilience to high-temperature environments	Low	Medium	High
	Resilience to high-humidity environments	Low	Medium	High
Materials	Robustness of the material	Low	Medium	High
	Durability of the material	Low	Medium	High

The second part includes an information table with the qualitative scoring of the MDs.

		User Type		
	Medical device	**End users' background**	**Training needs**	**User's understanding of the technical and clinical impact**
2014	**Low cost computed tomography scanner**	Physician, Technician or Radiologist	Initial training by manufacturer, and operator manuals	-
	Pulse oxymeter	Intended for use by physician, technician, midwife or nurse	No additional training required	-
	Anaesthesia delivery for low resource setting	A physician or technician	The manufacturer's representative in the region where the equipment is planned to be used will provide the training. The manufacturer will provide all the equipment required. Time required is 2 days.	-
	Mobile-enabled non-invasive measure-through motion and low perfusion pulse oximeter	Patient or any health care professional	Group training by a local health partner	-
2017	**Electrocardiogram, handheld, digital**	Trained caregiver (e.g family member), technician, nurse, general physician, specialised physician.	Device usage training needed	-
	Phototherapy, for jaundice	Nurse, general physician, specialised physician	No	-
	External Fixation for bone fracture	Physician, surgeon	Yes, orthopaedic surgeon training	-
	White blood cell counting system	Untrained individual, nurse, physician etc	No	-

	HTM					
Medical device	**Installation requirements**	**Maintenance frequency**	**Maintenance complexity**	**Need for consumables**	**Need for spare parts**	**Compatible consumables/spare parts**
Low cost computed tomography scanner	Medium	Requires regular maintenance 3 times annually by trained engineer, technician or manufacturer	Require specialised personnel	None	Requires specialised	-
Pulse oxymeter	Low	No scheduled maintenance required	No	None	Easily available	Yes
Anaesthesia delivery for low resource setting	Medium	Calibration required at time of use, along with scheduled annual maintenance.	Medium	Inalation agent,delivery gases	-	-
Mobile-enabled non-invasive measure-through motion and low perfusion pulse oximeter	Low	Clean the sensor, cable and connector by wiping with a 70% isopropyl alcohol pad.	No	Batteries and cable with sensor	-	-
Electrocardiogram, handheld, digital	Low	No	No	Ag/AgCl ECG gel	-	-
Phototherapy, for jaundice	Low	No	No	None	-	-
External Fixation for bone fracture	NA	No	No	Yes, bone pins	-	-
White blood cell counting system	Low	**No**	**No**	Microcuvettes, reagent and cleaner	-	-

	Design		
Medical device	**Portability, compactness, robustness**	**Limiting the number of components/spare parts**	**Reusability**
Low cost computed tomography scanner	Low	-	Yes
Pulse oxymeter	High	Low	Yes
Anaesthesia delivery for low resource setting	High	-	Yes
Mobile-enabled non-invasive measure-through motion and low perfusion pulse oximeter	High	Low	Yes
Electrocardiogram, handheld, digital	High	Low	Yes
Phototherapy, for jaundice	Medium	Low	Yes
External Fixation for bone fracture	High	Low	Yes
White blood cell counting system	High	Low	Yes

	Reliance on external factors						
Medical device	**Reliance on power sources**	**Reliance on water distribution**	**Reliance on medical location air**	**Resilience to dusty environments**	**Resilience to high-temperature environments**	**Resilience to high-humidity environments**	**Need for sample preparation**
Low cost computed tomography scanner	High	No	No	-	No	No	NA
Pulse oxymeter	Medium	No	No	-	-	-	NA
Anaesthesia delivery for low resource setting	Runs off either batteries or continuous power supply of 100-120V.	No	No	-	-	-	NA
Mobile-enabled non-invasive measure-through motion and low perfusion pulse oximeter	Draws power from attached mobile device	No	No	If rugged smartphone	If rugged smartphone	If rugged smartphone	NA
Electrocardiogram, handheld, digital	Medium	No	No	-	-	-	NA
Phototherapy, for jaundice	Low (power supply, solar panel, battery)	No	No	-	No	No	NA
External Fixation for bone fracture	Low	No	No	Yes	Yes	-	NA
White blood cell counting system	Power supply and batteries	No	No	-	-	-	NA

	Materials	
Medical device	**Robustness of the material**	**Durability of the material**
Low cost computed tomography scanner	-	-
Pulse oxymeter	High	-
Anaesthesia delivery for low resource setting	-	-
Mobile-enabled non-invasive measure-through motion and low perfusion pulse oximeter	If rugged smartphone	If rugged smartphone
Electrocardiogram, handheld, digital	-	-
Phototherapy, for jaundice	-	-
External Fixation for bone fracture	-	-
White blood cell counting system	-	-

	Cost			Lifetime	
Medical device	**Initial cost**	**Maintenance costs**	**Running costs**	**MD lifetime**	**Lifetime of MD parts/components**
Low cost computed tomography scanner	300 000	-	-	-	-
Pulse oxymeter	250	-	25 for probes, 10 for batteries	2 to 5	-
Anaesthesia delivery for low resource setting	24650	-	-	10	-
Mobile-enabled non-invasive measure-through motion and low perfusion pulse oximeter	490			5	
Electrocardiogram, handheld, digital	500	-	-	5 to 10	-
Phototherapy, for jaundice	950	-	-	5 to 10	-
External Fixation for bone fracture	200	-	-	2 to 5	-
White blood cell counting system	-	-	-	-	-

	RED (including -) (%)	Yellow (%)	Green (%)	NA (%)	
Low cost computed tomography scanner	66.67	9.52	19.05	4.76	
Pulse oxymeter	23.81	14.29	57.14	4.76	
Anesthesia	52.38	23.81	19.05	4.76	
Mobile-enabled non-invasive measure-through motion and low perfusion pulse oximeter	14.29	33.33	47.62	4.76	
Electrocardiogram, handheld, digital	42.86	9.52	42.86	4.76	
Phototherapy, for jaundice	38.10	9.52	47.62	4.76	
External Fixation for bone fracture	35.09	10.03	50.13	4.76	
White blood cell counting system	42.86	4.76	47.62	4.76	

Appendix D

Pupillometer

D.1 Pupil and iris recognition

D.1.1 Determining crop properties

In order to obtain a more reliable and efficient recognition of the pupil with the blob detection algorithm, avoiding potentially bigger blobs to be in the frame. For instance, from the videos I acquired with the smartphone a potentially bigger blob was generated by the eyebrow. Hence, it was decided to ask the subject to keep the area around the eye spread open with the thumb and index fingers. Moreover, in the processing phase, it was decided that cropping around the region of interest (i.e, the actual eye) would facilitate the algorithm. Similar considerations were made for the iris detection. The cropping function works as follows. The user is asked to draw a rectangle around the region of interest (i.e., the eye) (see Figure D.1) and the first three frames of the video are loaded and cropped accordingly (see Figure D.2).

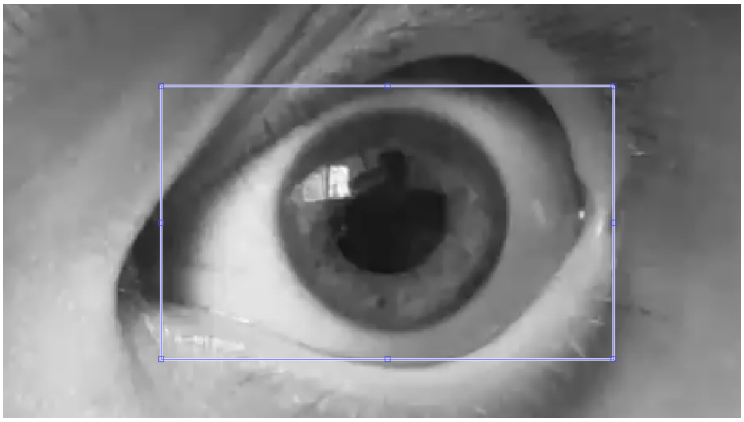


Figure D.1: The first frame of the video on which the user is asked to draw a rectangle to highlight the region of interest. The blue rectangle can be modified by dragging the handles.

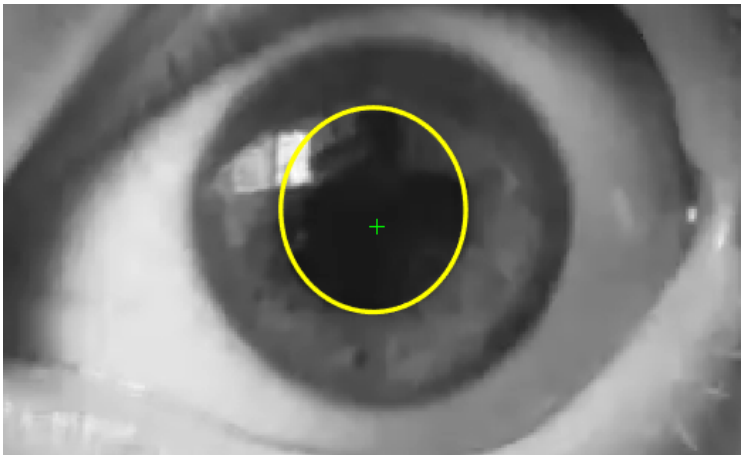


Figure D.2: One of the frames cropped according to the manually selected region.

The algorithm then preprocesses the frames and runs the pupil recognition algorithm (i.e., blob detection algorithm). The center of the pupil is noted as well as the mean pupil diameter that is the baseline (i.e., the average of the three diameters related to the three frames). Afterward, a new square cropping region is determined (see Figure D.3). Its width and height are calculated as four times the mean pupil diameter baseline. This automatic cropping will increase the precision of the cropping, compared to a manual one.

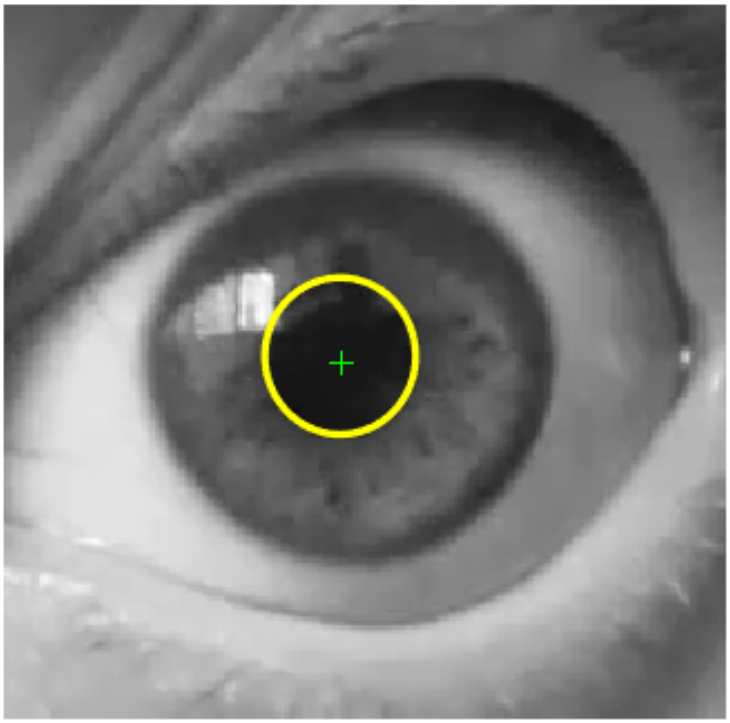


Figure D.3: One of the frames cropped according to the automatically selected square region.

D.1.2 Identification of the flash-related frames

As mentioned in the main text, the frames related to the flash were removed and substituted with a linear interpolation, because the double-threshold binarization method proved to be not completely robust and could fail to switch to the correct threshold in the first and final frames of the flash, when it is not at full brightness. As aforementioned, this would not affect the overall performance as the first part of the constriction phase of the photopupillary reaction is steep and approximately linear. In order to identify the start and end frames of the flash, the average pixel intensity of the frames was analysed and stored in an array. Moreover, the differences between the adjacent elements of this array were calculated and stored in a different array (see Figure D.4). Whenever one of the differences resulted over or below a certain empirically determined threshold (i.e., 5 or -5), the frames, respectively related to the start and the end of the flash, were saved. In order to ensure the capture of the whole flash sequence, a padding of 8 frames in total was added to the flash frames: 4 preceding the flash start frame and 4 following the flash end frame.

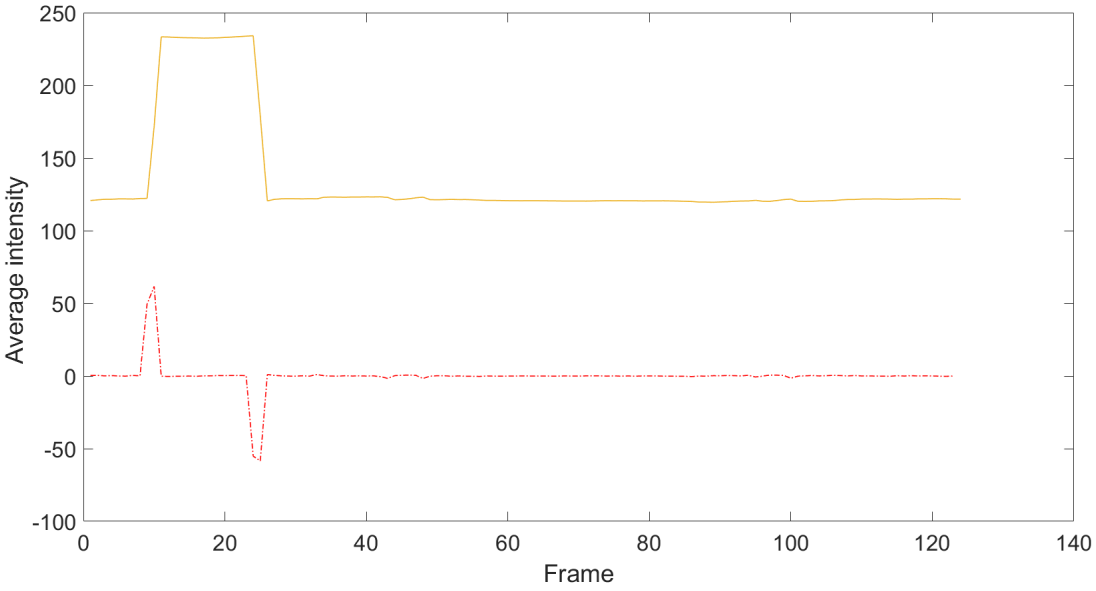


Figure D.4: The average pixel intensity over the frames (yellow) and the signal of the differences between the adjacent elements of the intensity array (red). The spike represents the flash.

D.1.3 Identification of the blink-related frames

As blinking can occur when the eye is flashed, there can be artefacts affecting the resulting signal. For this reason, identifying the frames related to possible blinks is essential. In order to do so, the pupil diameter signal was detrended and, similarly to flash identification process, the absolute values of the differences between the adjacent elements of this array were calculated and stored in a different array (see Figure D.5). Whenever one of the differences resulted over a certain empirically determined threshold (i.e., 2), the frames, related to the blink, were deleted from the signal, and the gaps were linearly interpolated. The pupil diameter signal without flash and blink artefacts can be seen in Figure D.6.

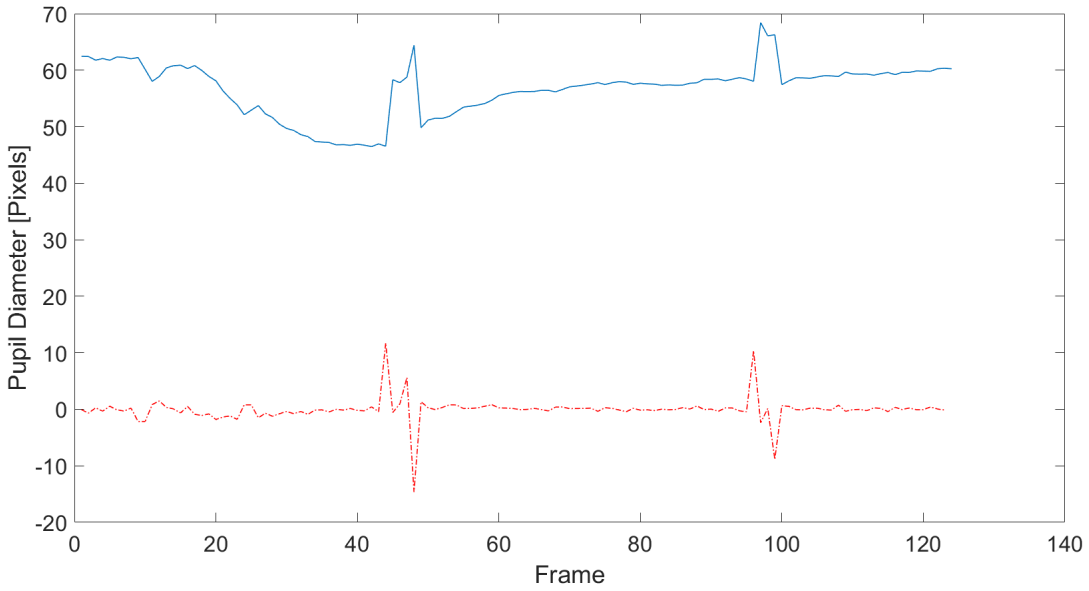


Figure D.5: The pupil diameter signal over the frames (blue) and the signal of the differences between the adjacent elements of the pupil diameter array array (red). The two spikes represent the flash blinks.

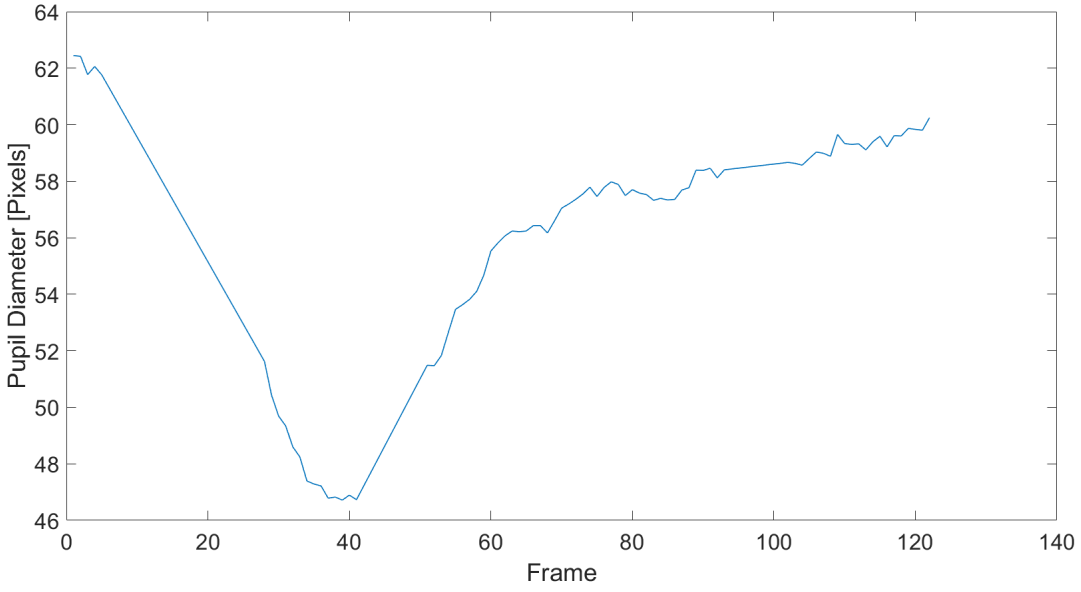


Figure D.6: The pupil diameter signal without artefacts.

D.1.4 Iris signal processing

The signal related to the iris diameter, resulting from the first feasibility study, was relatively shaky, although there was no sensible relative movement between the smartphone and the eye during the experiment. For this reason, a low pass filtering was envisioned. As no filtering frequency for this type of specific signal was found on the internet, a fast Fourier transform was applied in order to obtain the power spectra and find the significant frequencies empirically. In particular, the frequencies containing 70%, 80% and 90% (F70, F80 and F90) of the power spectra were individuated (see Figure D.7). F70 resulted to be 0.484 Hz, F80 3.871 Hz, and F90 10.16 Hz. Upon comparison, filtering at F80 with a low-pass fourth order Butterworth filter, characterised by a frequency response as flat as possible in the passband [330], resulted in a smoother and yet not compromised signal, compared to F90 filtering. Moreover, the filtering at F80 was preferred to that at F70, as the latter was not introducing much improvement, while compromising the signal (see Figure D.8).

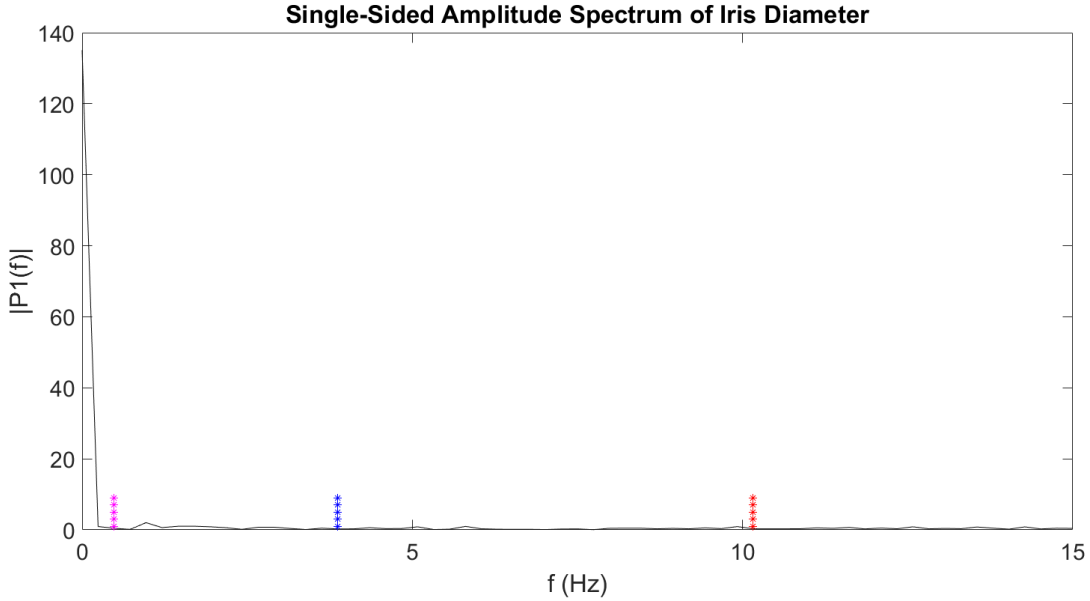


Figure D.7: The power spectra and the relevant frequencies, namely F70 (magenta), F80 (blue), and F90 (red).

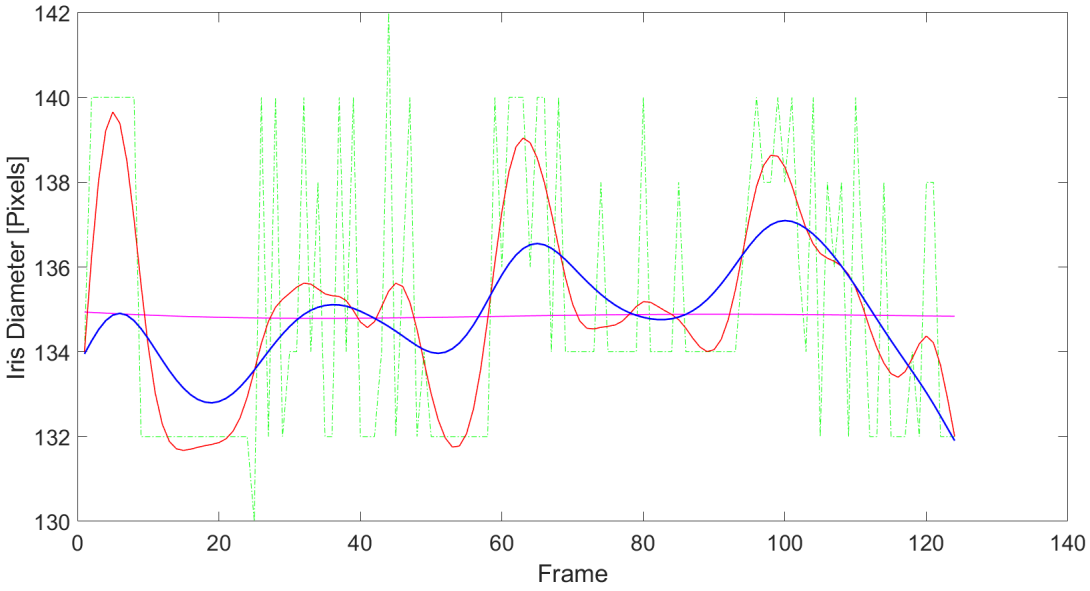


Figure D.8: The raw signal of the iris diameter (dashed green) with the filtered signals superimposed, the one filtered at F70 in magenta, the one at F80 in blue, and the one at F90 in red.

D.2 Bland-Altman Plots

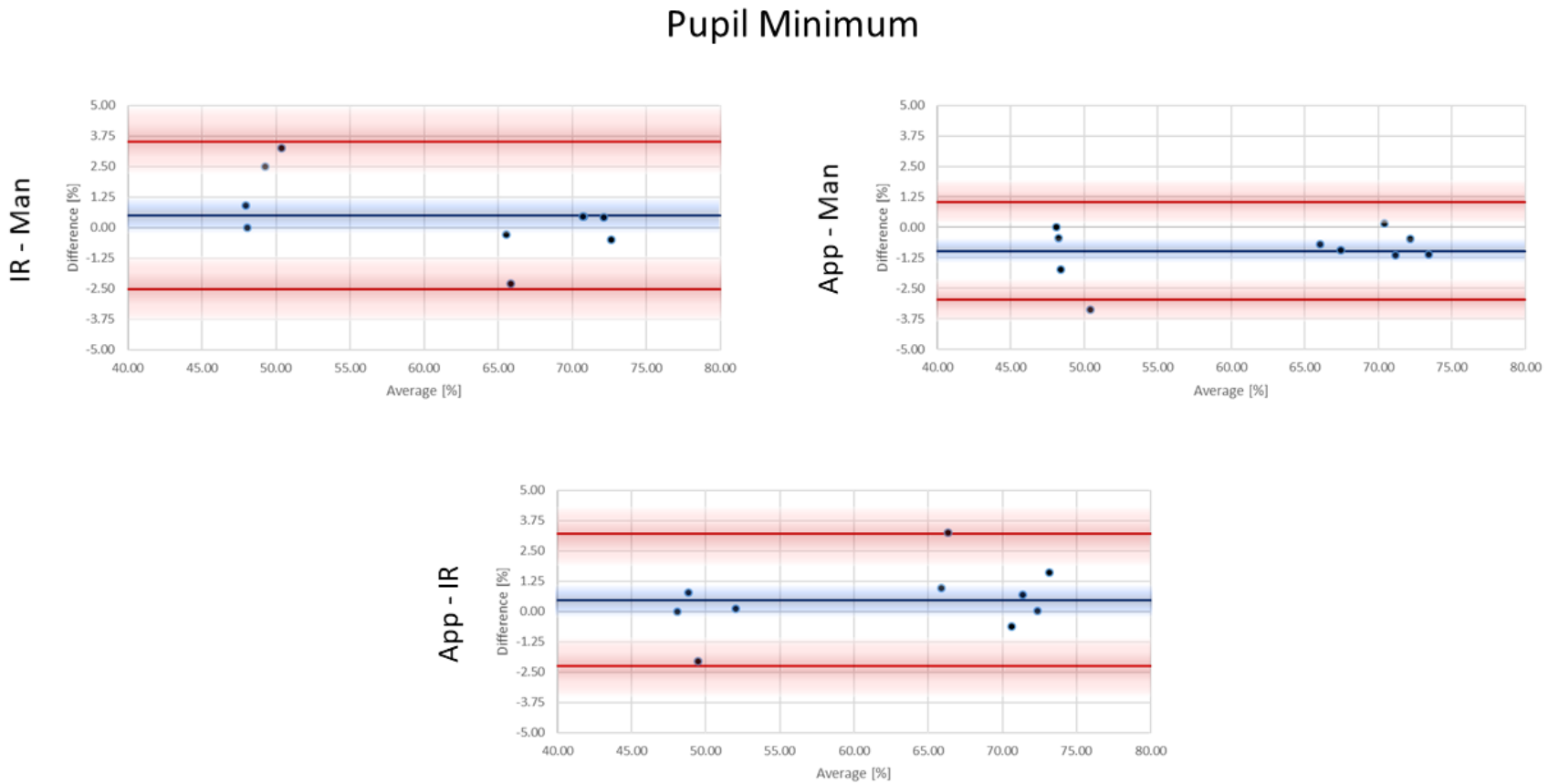


Figure D.9: Bland-Altman plots for the pupil minimum and three methods. The continuous blue line represents the bias, the continuous red lines the 95% limits of agreement. The red and blue halos are the 90% confidence level of the limits of agreement and of the bias, respectively.

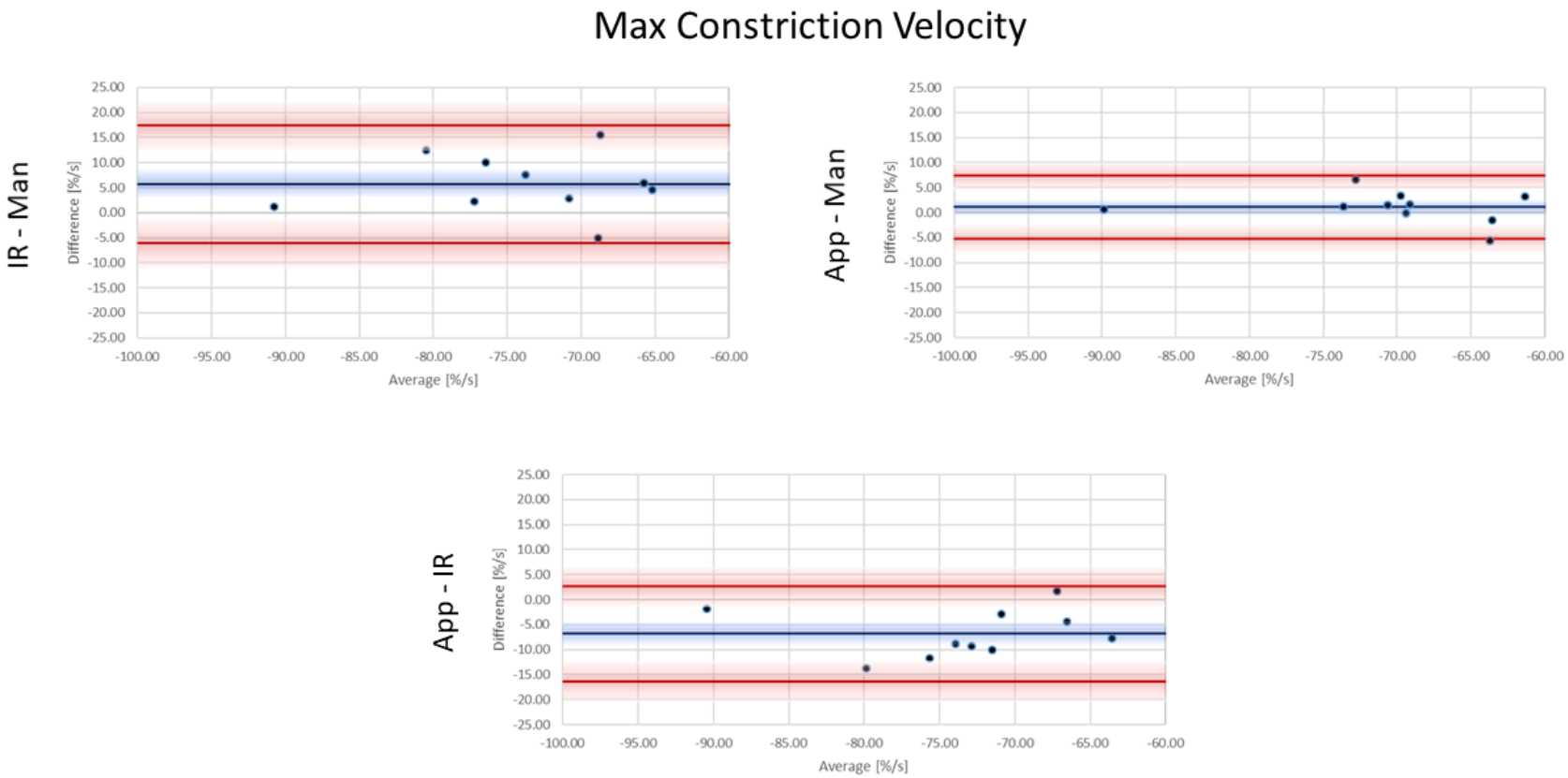


Figure D.10: Bland-Altman plots for the maximum constriction velocity and three methods. The continuous blue line represents the bias, the continuous red lines the 95% limits of agreement. The red and blue halos are the 90% confidence level of the limits of agreement and of the bias, respectively.

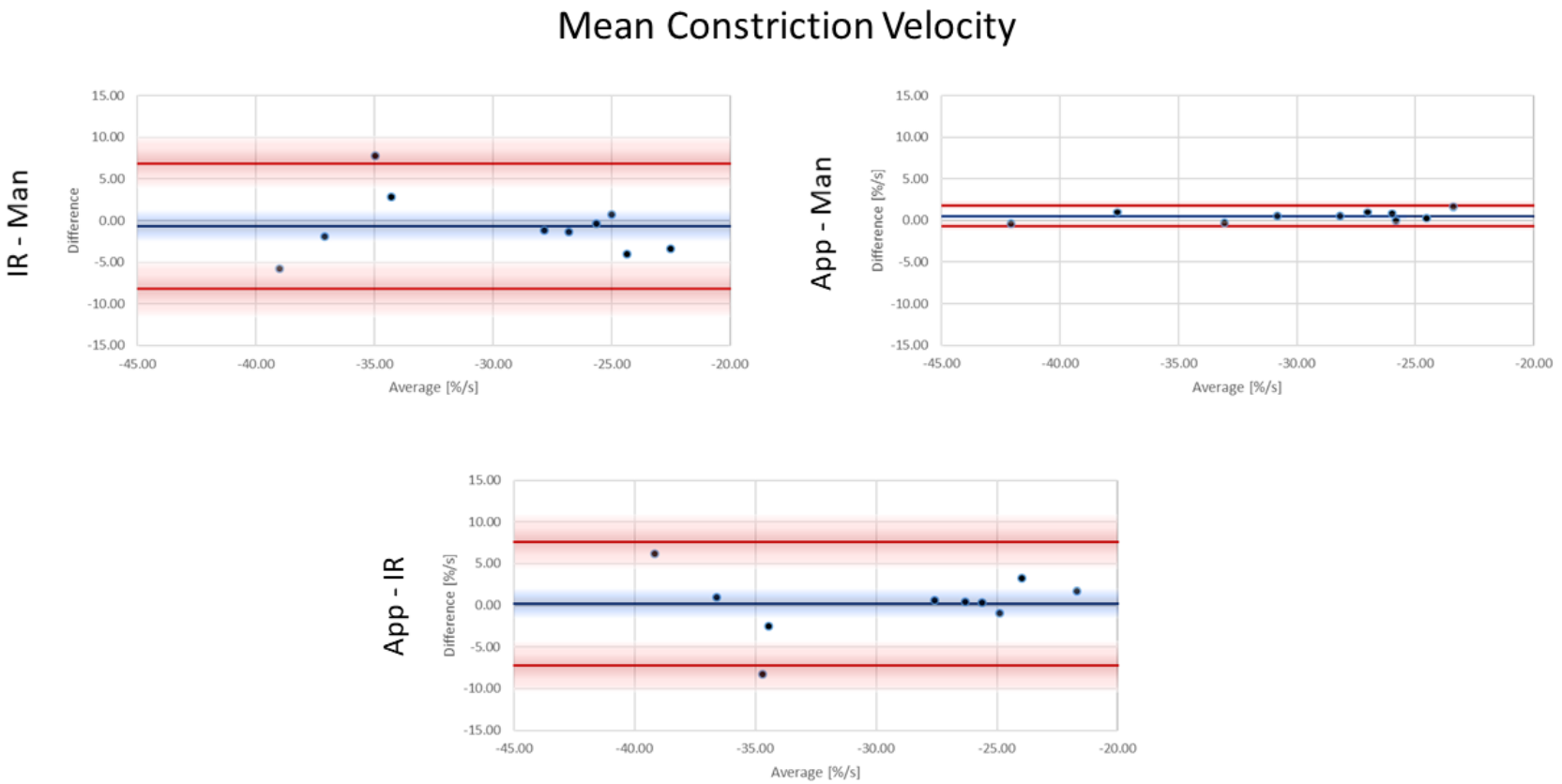


Figure D.11: Bland-Altman plots for the mean constriction velocity and three methods. The continuous blue line represents the bias, the continuous red lines the 95% limits of agreement. The red and blue halos are the 90% confidence level of the limits of agreement and of the bias, respectively.

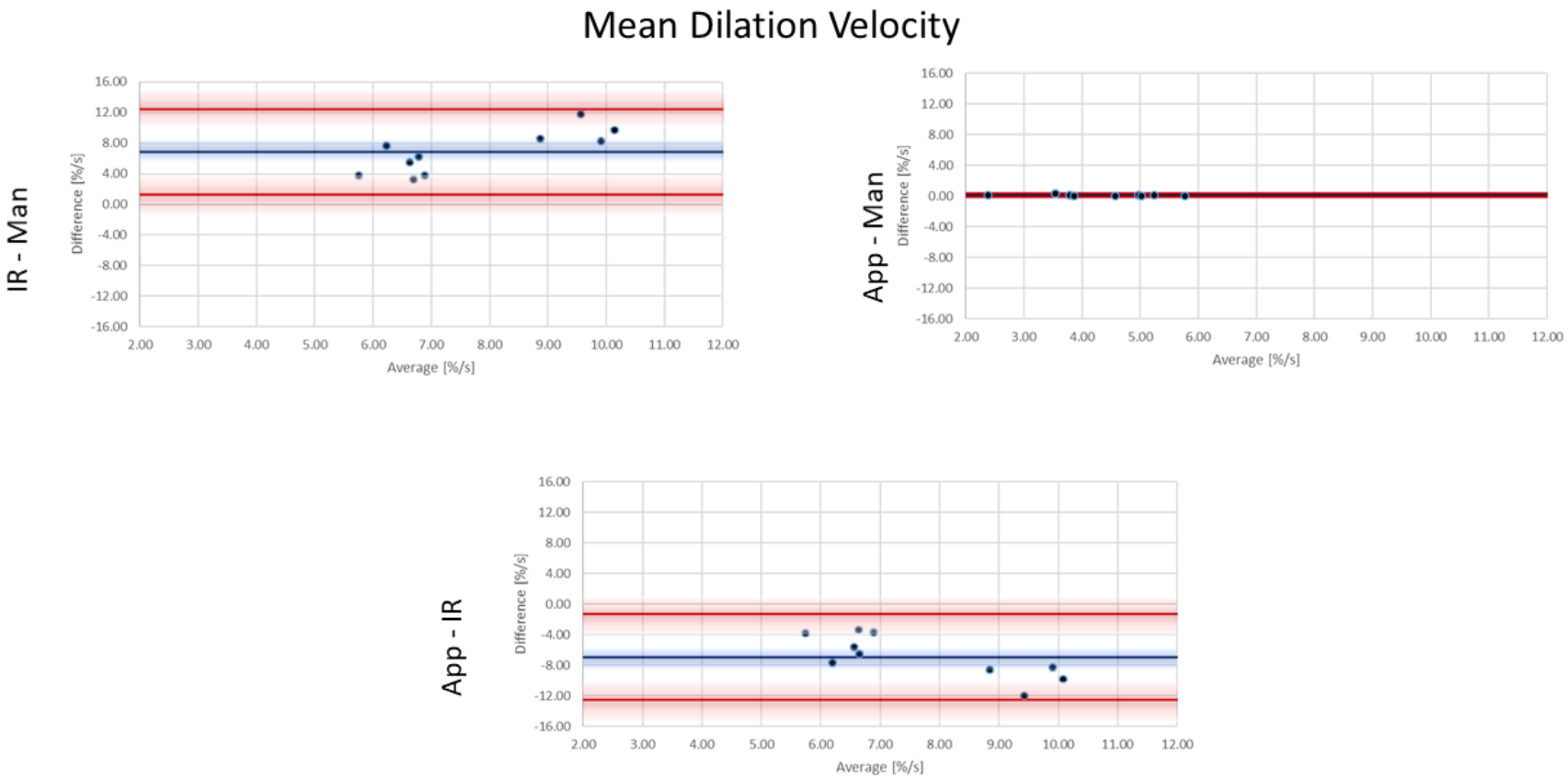


Figure D.12: Bland-Altman plots for the mean dilation velocity and three methods. The continuous blue line represents the bias, the continuous red lines the 95% limits of agreement. The red and blue halos are respectively the 90% confidence level of the limits of agreement and of the bias.

D.3 Future add-ons

In order to by pass the problem of a non-fixed distance between the eye and the smartphone, a 3D printed cone that can be attached to the smartphone was designed on Autodesk Fusio360. There are two versions, one characterised by different lateral holes (windowed) that will allow a minimum amount of light to enter the cone, and one that has no holes but could be 3D printed using transparent polyactic acid filaments (see Figure D.13). The former was also printed, however it resulted to increase the reflections on the eye (this could be improved by applying a sheet of paper around it, to diffuse the ambient light and reduce the reflections).

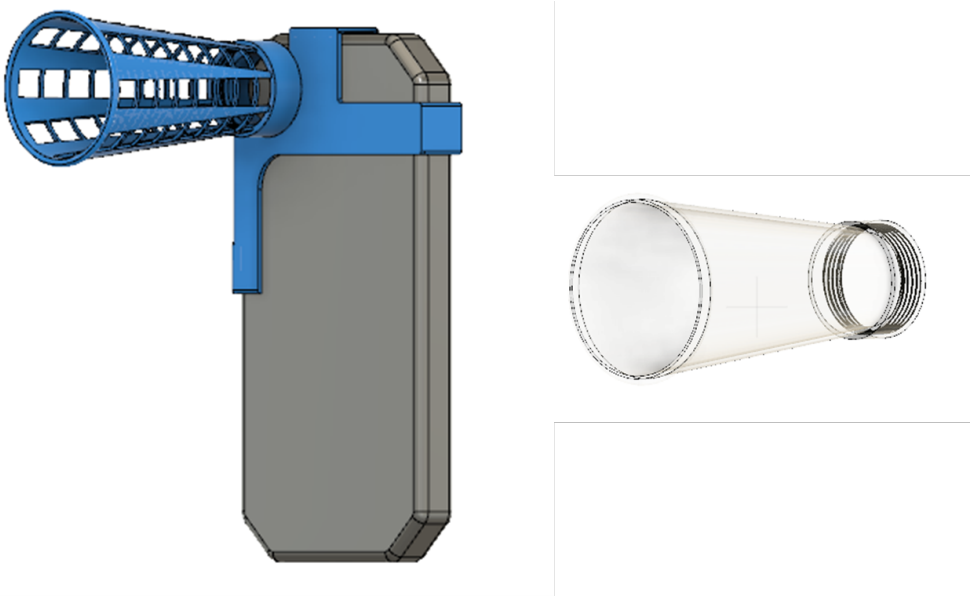


Figure D.13: The 3D printed cone: first windowed version installed on a smartphone model (left) and semi-transparent version (right)

Appendix E

Tool for screening diabetic neuropathies

E.1 Pre-screening form

Pre-screening form

Name and Surname:

Age:

Sex:

Medical Conditions:

1) Were you diagnosed with diabetes?
   - If Yes, when?
   - If Yes, is it type 1 or 2?
2) Were you diagnosed with diabetic neuropathies?
3) Are you suffering from any of the following/ can you be included in any of the following groups? *Hypothyroidism, kidney disorders, recent injuries to the lower limbs, alcoholics, people exposed to heavy concentrations of toxic chemicals like glue, solvents or insecticides or heavy metals, Lyme disease, rheumatoid arthritis and lupus*

   - If yes, which?

If you answered **Yes** to 3), then you are not eligible for this study.

If you answered No to 3), then you are eligible for this study and you can set up an appointment.

Complete the following part on the day of the experiment:

- Have you or have you recently had any of these symptoms?
  - a high temperature – this means you feel hot to touch on your chest or back (you do not need to measure your temperature)
  - a new, continuous cough – this means coughing a lot for more than an hour, or 3 or more coughing episodes in 24 hours (if you usually have a cough, it may be worse than usual)
  - a loss or change to your sense of smell or taste – this means you've noticed you cannot smell or taste anything, or things smell or taste different to normal

- Is your current body temperature greater than 37.5°C?

If you have or have recently had any of the symptoms AND/OR if your current body temperature is greater than 37.5°C, then you will need to inform the researcher in advance and your appointment will be rescheduled.

Appendix F

A vest for treating jaundice in LRSs

The following protocol aims to evaluate the requirements R.L.1-3 and R.S.2, besides comparing and finding the best effective LED light source for photo-ionisation at skin surface level. In particular, the following cases were investigated:

- **Case F.1.** Modelled absorption at an interpolated or extrapolated skin thickness (to assess the level of light penetration).
- **Case F.2.** safe phototherapy emission bandwidth verification.
- **Case F.3.** LED performance and efficacy comparison.
- **Case F.4.** fibre-optic loss prediction aand hence required number of LEDs to achieve effective phototherapy.

These tests were performed in accordance with the American Society for Testing and Materials (ASTM) standards, namely G138-12 (Standard Test Method for Calibration of a Spectroradiometer Using a Standard Source of Irradiance) and E824 - 10 (Standard Test Method for Transfer of Calibration From Reference to Field Radiometers), and in accordance with the British Standards Institute standards, namely BS EN 62471-5:2015 (Photobiological safety of lamps and lamp systems - Part 5: Image projectors). Also a document by Schneider and Young [331] informed the tests. In order to perform such tests, the following equipment/devices were used:

- Optical Barrier (100mmx100mmx2mm synthetic skin sample).
- Vertical frame for the barrier suited to the specific dimensions of the skin sample.

- Clamps for the alignment of the light source to the detector (RM Laptop P10).
- Calibrated absolute Spectroradiometer (EKO Spectroradiometer LS-100).
- Monochromatic light source. In this case, a range of single light surface mount LEDs, namely LXML-PE01-0070 (LED1), LXML-PB01-0040 (LED2), LXML-PB02 (LED3), LXML-PR01-0500 (LED4), SunPlus L1SP-RYL0003500000 (LED5), and Luxeon C Colour L1C1-RYL1000000000 (LED6) (see Table F.1 for a summary of the characteristics of such LEDs).
- Power source with a voltage and current readout (VOLTCRAFT Power supply LSP-1403).
- Multimeter to verify current readout on power supply and take LED voltage (VOLTCRAFT Multimeter VC265).
- Laptop/Computer/Processing unit for data measurement and storage (RM Laptop P10).
- Ruler for apparatus distance setting.
- Thermometer and relative humidity sensor (Anymeter Thermometer and Hygrometer TH101E).

Table F.1: The summary characteristics of the selected LEDs. In particular, the spectral halfwidth is the wavelength band which becomes half level of energy to peak wavelength; the viewing angle is the space covered by the "cone of light" prior to losing half of its peak illumination level; the maximum LED junction temperature is the safe upper limit of temperature over which the LED can be damaged.

LED	**Dominant or peak wavelength (Min; Max)(nm)**	**Typical spectral halfwidth**	**Typical viewing angle (°)**	**Maximum LED junction temperature (°C)**
LED1	490; 515	30	125	150
LED2	460; 485	20	125	150
LED3	460; 485	20	125	150
LED4	440; 460	20	125	150
LED5	440; 455	25	115	125
LED6	440; 460	20	165	135

While performing these experiments environmental control factors were taken into account. Firstly, the experiment should take place in an environment without reflective surfaces and, ideally, without any light source within the relevant wavelength range (in this case, general ambient visible light was minimised but was not managed to be extricated). Secondly, temperature and humidity should be maintained or adjusted to reflect practical working conditions (in this case, they were kept constant to room conditions as this

is a difficult control factor to adjust otherwise). The detector is especially considered to be the most sensitive component to temperature changes. Lastly, the receiver should be fixed, and should not be subject to vibration or shock during the measurement. Moreover, the following safety precautions were applied, in order to minimise the risks of harm to the experimenter:

- Avoiding staring at the LED directly, and placing the control apparatus behind or aside from the LED, as the maximum emission intensities of the LEDs are expected to surpass the limit for causing retinal damage by direct observation at operating current (as per BS EN 62471-5:2015).
- The operating temperatures of the LEDs are low enough to allow for sustained contact whilst operational. However, to avoid temperature discomfort, a precautionary waiting time of up to 2 minutes for the LED to cool down after use may be appropriate (as per BS EN 60601-1-11:2015).

F.1 Modelled light absorption at skin level

The absorption at varying thicknesses of the synthetic skin can be calculated using Beer-Lambert's equations (F.1 and F.2).

$$A = \varepsilon \cdot c \cdot l \tag{F.1}$$

where A is the arbitrary absorption (per wavelength), ϵ is the molar absorptivity coefficient (per wavelength), c is the concentration of the absorbing species, and l is the path length (i.e., the skin barrier thickness).

$$A = \log_{10} \frac{I_0}{I} \tag{F.2}$$

where I_0 is the intensity of light without barrier, I is the intensity of light with the barrier, A is the absorption.

Equation F.2 can be used to calculate the absorption across a wavelength spectra for a particular skin thickness. The absorbance can then be used with F.1 to predict the product $\varepsilon \cdot c$. This can be averaged with the repeated absorbance readings between different skin thickness and LEDs. After deriving the product $\varepsilon \cdot c$, a plot of equation F.1 for different values of l can allow the derivation of interpolated or extrapolated absorbance at different skin thicknesses.

The following assumptions needs to be taken into consideration:

- the product $\varepsilon \cdot c$ is roughly constant, as the material does not change
- the incident light is parallel and focuses onto the emitter
- the emission wavelength bandwidth is narrow

- there is no optical boundary between additional layers of synthetic skin (i.e., they are solidly joined)
- the absorption and scattering due to room temperature air is negligible

However, this approach might be limited, because the Beer-Lambert law basis itself on the conditions that the absorbing media does not scatter radiation [332]. For real skin, this does not hold, as the non-uniform distribution of its dermal composite molecules causes the scattering of light [333].

The six above mentioned LEDs were tested. As 4mm-thick synthetic skin impeded most of the LEDs' irradiance on the spectroradiometer, with most repeated measurements, showing no receptivity, the reported results are only related to the absorbance of 2mm-thick skin. Figure F.1 shows the relative absorption of each of them. Higher relative absorptions indicate LEDs that may not be suitable for phototherapy. As regards the relative absorption, LED 3 and 4 resulted to be the best performing ones.

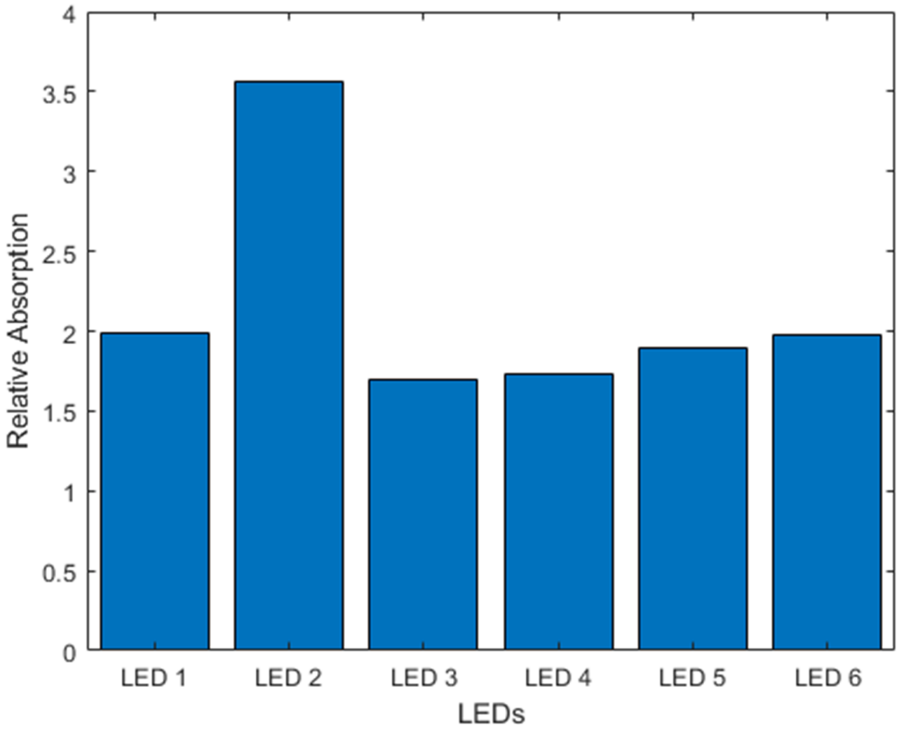


Figure F.1: Relative absorption comparison between LEDs.

F.2 Safe phototherapy emission bandwidth verification

For the LED emission bandwidth to be safe, it should be within the visible spectrum, and should not spread beyond it, either into ultraviolet (UV) nor

IR regions. To this purpose, the spectral distributions of each of the LEDs, placed directly on the receiver, were measured and plotted. However, the spectroradiometer may not detect light emissions outside of its own sensitivity range. This is unlikely to be relevant if the main lobe emission peak is captured, and can be verified using the light source's data sheet as council. Figure F.2 shows an example of spectral distribution for all the LEDs at operation current; Figure F.3 shows the spectral distribution as well as the change in irradiance with increasing input power for LED4. Relatively small residual peaks in the IR and UV wavelengths after pre-processing may be assumed negligible as noise.

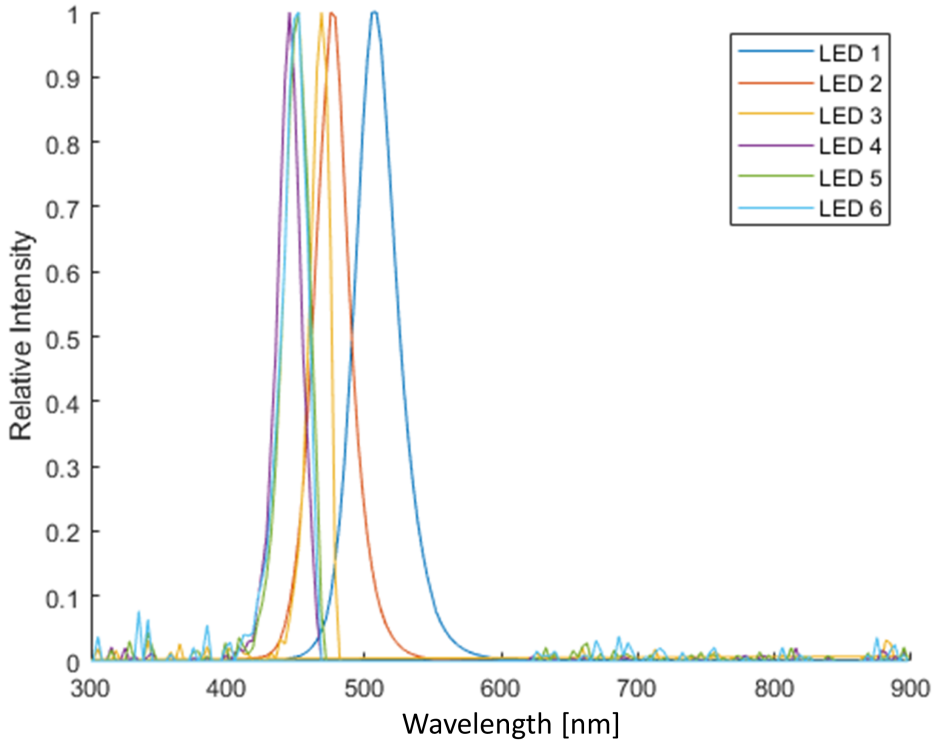


Figure F.2: Emission bandwidth spectrum of all the LEDs at operation current.

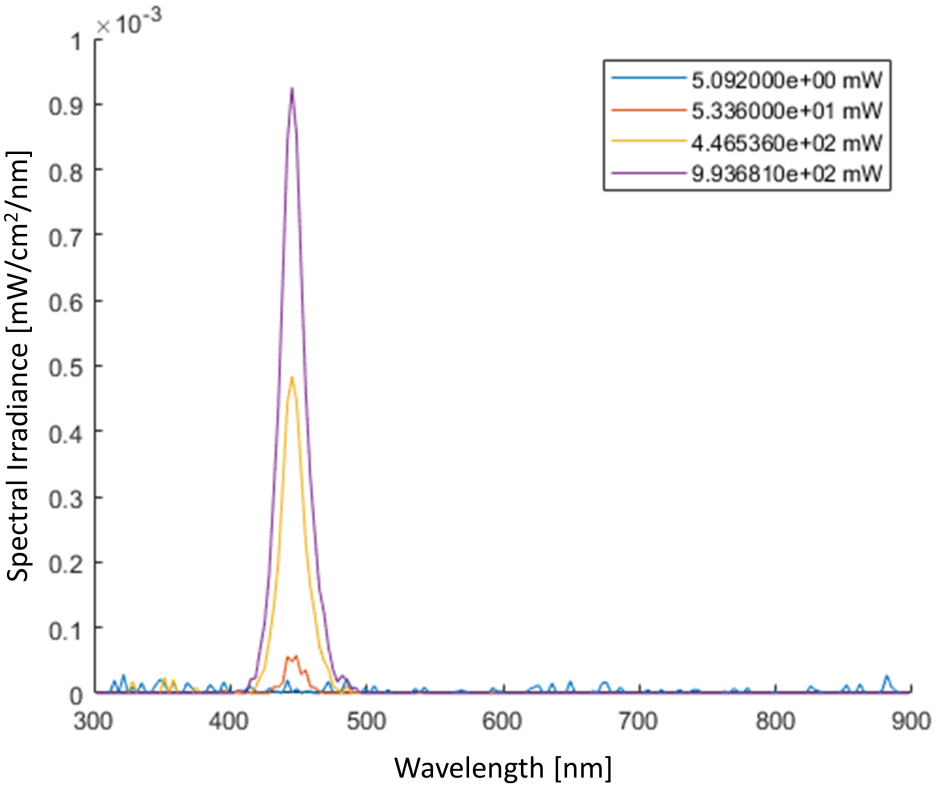


Figure F.3: Change in irradiance with increasing input power for LED4.

F.3 LED performance and efficacy comparison

LED performance comparison encompasses the efficiency of the LEDs to emit similar irradiance, whilst the efficacy comparison assesses the appropriateness of the LEDs to provide effective phototherapy - being defined as 30 $\mu W/cm^2/nm$ across 430-490 nm wavelength R.L.2.. The power required by the LED can be measured using equation F.3:

$$P = I \cdot V \tag{F.3}$$

where P is the input power in Watts, V is the voltage across the LED in Volts, I is the current through the LED in Ampere. As regards the irradiance of the LED, it can be calculated by integrating the spectral irradiance between the minimum and maximum wavelengths of the main lobe (see equation F.4, which can be deduced from the LED data sheets.

$$W = \int_{\lambda_1}^{\lambda_2} I(\lambda) d\lambda \tag{F.4}$$

where I(λ) is the spectral irradiance as a function of wavelength, $\lambda_{1,2}$ main lobe minimum and maximum wavelength, respectively, W is the irradiance. Afterwards, the irradiance was plotted against the input power for the six LEDs (see Figure F.4), as well as the spectral irradiance against wavelength at increasing input powers (see Figure F.3).

These calculations are based on the assumption that the ambient temperature and humidity and external light noise were constant between all of the LEDs tests. In regard to this, the temperature of the LEDs themselves would have fluctuated during measurement, but these can be considered negligible, considering the short on-time periods required for the measurements.

F.4 Fibre-optic loss prediction and required number of LEDs to achieve effective phototherapy

Fibre-optic loss can be assessed by comparing the loss between the measurements of the LED through no media, and through the fibre-optic and the vest. The specific wavelength loss may also be compared by calculating the ratio of the two. Using equation F.4, the difference of the irradiance between the two test modes will represent the loss of the fibre-optic cables. This loss per LED per fibre-optic cable is a measure of the efficiency of the phototherapy delivery system. The ratio between the spectral irradiance without and with the fibre-optic cables is calculated by dividing the former by the latter, element-wise.

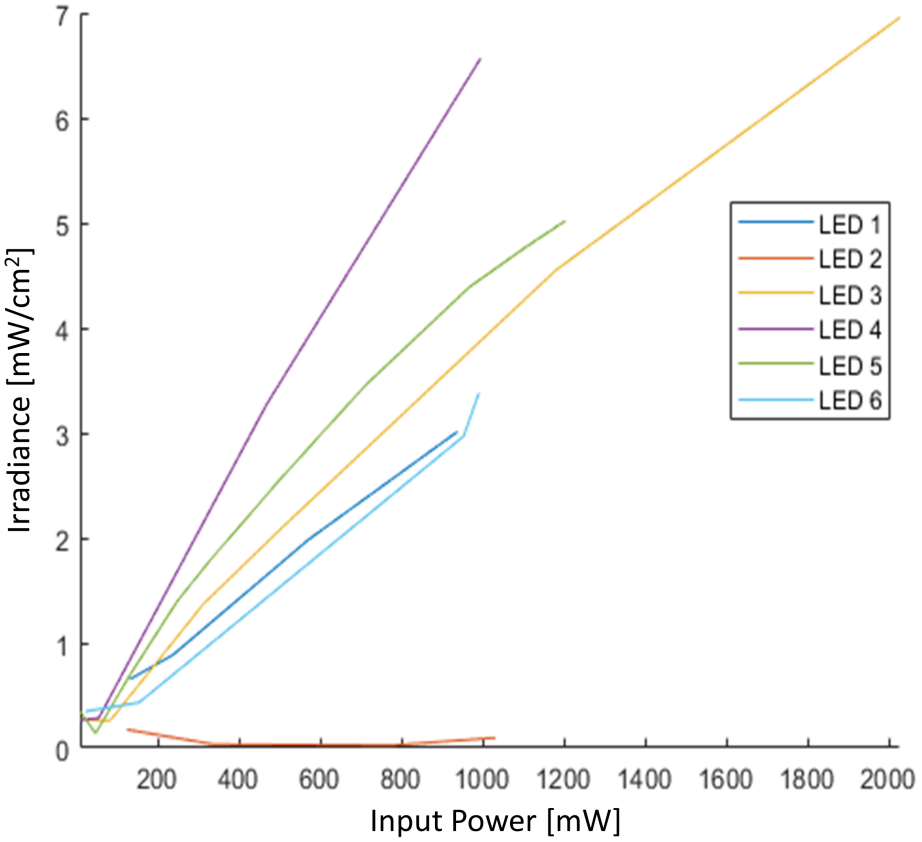


Figure F.4: Comparison of efficiency with irradiance compared to input power.

The vector of ratios may then be plotted against wavelength to show if there are any particular extreme wavelength attenuations because of the coupling and delivery. The required number of LEDs to achieve effective phototherapy may be, then, calculated by dividing the target phototherapy requirement, i.e., 30 $\mu/cm^2/nm$, by the peak spectral irradiation, and then rounding up the result. As a result, the required number of LEDs per set number of fibre-optic cables (four in this case), will be retrieved. The following assumptions are made:

1. The loss is constant between different LED couplings to a set number of fibre-optic cables.

2. The LED coupling is consistent.

3. The loss due to the bending of the fibre-optic cables is consistent between measurements.

4. The final assumption will mean that the predicted number of LEDs required to satisfy effective phototherapy will be an overestimate at worst as there can be additional superposition of light from adjacent fibre-optic cables within the vest, increasing the skin surface illuminance. During the measurements taken with the spectroradiometer beneath the vest, results for the conclusion Case F.4 were largely variant and, therefore, inconclusive. This is likely due to the spectroradiometer having a relatively large aperture diameter (i.e., 7mm). In fact, the fibre-optic cables themselves are scarcely spread and only 0.5mm in diameter across the vest in the prototype, reasons as to why the readings are inconsistent and weak, as the irradiance area incident on the spectroradiometer from the fibre-optics is relatively negligible. Therefore, conclusion case F.4 has been suspended from this project, and left for future investigations. In fact, this may be solved by using a spectroradiometer of smaller aperture diameter (<3mm) may suffice. Alternatively, a higher density of embedded POFs may rectify this and would require further production from Footfalls&Heartbeats.Regardless, once this has been resolved, predicting the solution for meeting the irradiance criteria may then be fully realised and further testing may continue.

F.5 Conclusion on cases

The tests explained above proved how LED4, i.e., LXML-PR01-0500, is the overall optimal choice for the vest prototype. Table 6.2 summarises the performance indicators for the LEDs. In particular, LED4 is the best option in regards to the 'safe phototherapy emission spectrum' criterion, the 'efficiency' criterion,

and the 'appropriate emission spectrum with varying power' criterion. When comparing the emission bandwidth spectrum for LED4 with the relative fraction of light absorbed by bilirubin in a blood sample (see Figure 6.5), it can be noted how the wavelengths are almost superimposable.

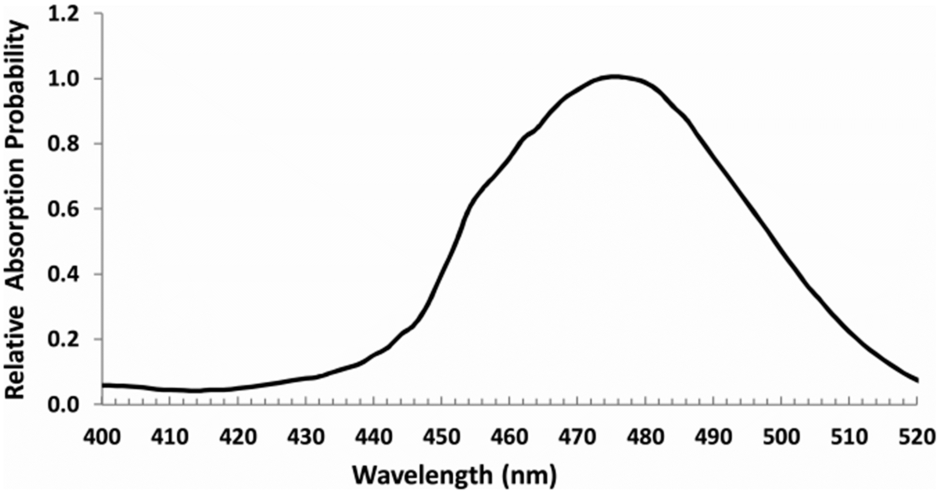


Figure 6.5: The relative fraction of light absorbed by bilirubin in a blood sample [334].

Table 6.2: Comparison of all the tested LEDs performance indicators, resulting both from the testing and from the related LEDs datasheets. Each criterion is ranked from 1 to 6, where 1 is best and 6 is worst.

	Alternatives						
Criteria	**LED1**	**LED2**	**LED3**	**LED4**	**LED5**	**LED6**	**Weighting**
Minimum absorption	5	6	1	2	3	4	1.5
Safe phototherapy emission spectrum	1	1	1	1	1	1	2
Efficiency	4	6	3	1	2	5	2
Appropriate emission spectrum with varying power	1	0	1	1	1	1	0.5
Maximum operating junction temperature	3	3	3	3	1	2	0.2
Typical viewing angle	2	2	2	2	1	3	1
Lifetime at operating current	2	2	3	2	1	2	1.5
Total	**24**	**29**	**17**	**13**	**14**	**25**	

6.6 Flowchart of an envisioned method of treatment outside of a health centre with the final prototype the vest

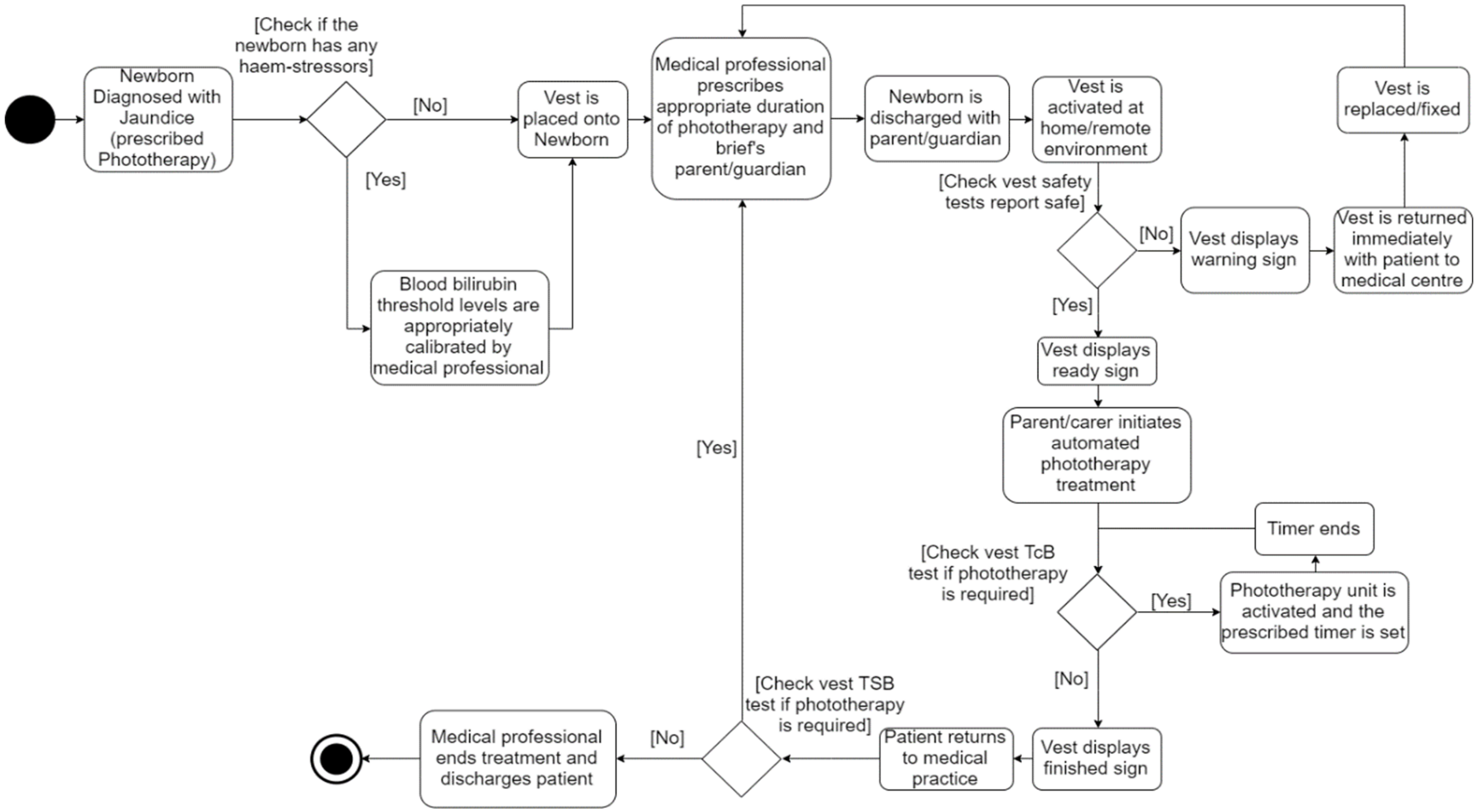


Figure 6.6: Flow chart of conceptual method of treatment outside of a health centre, beginning from diagnosis (at a health facility or otherwise) through to clinical clearance of Jaundice.

Bibliography

[1] D. Piaggio, D. Medenou, R. C. Houessouvo, and L. Pecchia, "Donation of medical devices in low-income countries: preliminary results from field studies," in *International Conference on Medical and Biological Engineering*, pp. 423–427, Springer, 2019.

[2] L. Di Pietro, D. Piaggio, I. Oronti, A. Maccaro, R. C. Houessouvo, D. Medenou, C. De Maria, L. Pecchia, and A. Ahluwalia, "A framework for assessing healthcare facilities in low-resource settings: Field studies in benin and uganda," *Journal of Medical and Biological Engineering*, vol. 40, no. 4, pp. 526–534, 2020.

[3] L. Pecchia, D. Piaggio, A. Maccaro, C. Formisano, and E. Iadanza, "The inadequacy of regulatory frameworks in time of crisis and in low-resource settings: Personal protective equipment and covid-19," *Health and Technology*, p. 1, 2020.

[4] D. Piaggio, R. Castaldo, M. Cinelli, S. Cinelli, A. Maccaro, and L. Pecchia, "A framework for designing medical devices resilient to low-resource settings," *Globalization and Health*, vol. 17, no. 1, pp. 1–13, 2021.

[5] D. Piaggio, G. Namm, P. Melillo, F. Simonelli, E. Iadanza, and L. Pecchia, "Pupillometry via smartphone for low-resource settings," *Biocybernetics and Biomedical Engineering*, 2021.

[6] D. Piaggio, M. Andellini, M. Taher, and L. Pecchia, "A vest for treating jaundice in lrss," *Proceedings of IEEE MetroInd4.0&IOT*, 2021.

[7] E. Williams, D. Piaggio, M. Andellini, and L. Pecchia, "3d-printed activated charcoal inlet filters for oxygen concentrators: A circular economy approach," *Development Engineering*, p. 100094, 2022.

[8] D. Piaggio, S. Hyland, A. Orfeo, A. Maccaro, and L. Pecchia, "A 3d-printed condom intrauterine balloon tamponade," *BioMedical Engineering OnLine*, Under review.

[9] D. Piaggio, C. Rossana, G. Garibizzo, and L. Pecchia, "A smartphone-based screening tool for diabetic neuropathies: a mhealth and 3d printing approach.," *Biocybernetics and biomedical engineering*, Under review.

[10] General Assembly of the United Nations, "Transforming our world: the 2030 agenda for sustainable development," *Division for Sustainable Development Goals: New York, NY, USA*, 2015.

[11] D. A. Jaffray, *World congress on medical physics and biomedical engineering, june 7-12, 2015, Toronto, Canada*, vol. 51. Springer, 2015.

[12] P. Ghisellini, C. Cialani, and S. Ulgiati, "A review on circular economy: the expected transition to a balanced interplay of environmental and economic systems," *Journal of Cleaner production*, vol. 114, pp. 11–32, 2016.

[13] T. P. Gross, C. M. Witten, and C. Uldriks, "Medical device regulation in the usa," *Medical device epidemiology and surveillance*, pp. 5–19, 2007.

[14] World Health Organization and others, "Regulatory system strengthening for medical products," *Proceedings of the 67th World Health Assembly*, vol. 28, 2014.

[15] C. Altenstetter, "Medical device regulation in the european union, japan and the united states. commonalities, differences and challenges," *Innovation: The European Journal of Social Science Research*, vol. 25, no. 4, pp. 362–388, 2012.

[16] L. Pecchia, D. Piaggio, R. Castaldo, L. Radice, and N. Pallikarakis, "Medical device regulation and assessment: new challenges for biomedical engineers," in *XXXVIIIa Scuola di Bressanone*, pp. 177–192, Patron editore, 2019.

[17] Food and Drug Administration, *A History of Medical Device Regulation and Oversight in the United States*. Available at `https://www.fda.gov/medical-devices/overview-device-regulation/history-medical-device-regulation-oversight-united-states` accessed: 26/10/2020.

[18] European Commission, "90/385/eec of 20 june 1990 concerning active implantable medical devices," *Official Journal of the European Community L*, vol. 189, July 1990.

[19] European Commission, "93/42/eec of 14 june 1993 concerning medical devices," *Official Journal of the European Community L*, vol. 169, July 1993.

[20] MedTech Europe, "The european medical technology industry 2019." Available at https://www.medtecheurope.org/resource-library/the-european-medical-technology-industry-in-figures-2019/ accessed: 05/03/2021.

[21] P. Herman, J. Horowitz, and M. Torsekar, "Competitive conditions affecting us exports of medical technology to key emerging markets," *US International Trade Commission, Washington, DC*, 2018.

[22] Statista, *Medical device market size in Africa*. Available at https://www.statista.com/statistics/890876/medical-device-market-size-africa/.

[23] World Health Organization and others, *Global atlas of medical devices*. World Health Organization, 2017.

[24] World Health Organisation, *Regulations*. Available at https://www.who.int/medical_devices/safety/en/,accessed:26/10/2020.

[25] M. Kedwani, J. Schröttner, and C. Baumgartner, "Analysis of regulatory requirements of medical devices and in-vitro diagnostics worldwide for the development of an efficient procedure of registration for manufacturers of medical products," *Current Directions in Biomedical Engineering*, vol. 5, no. 1, pp. 609–612, 2019.

[26] S. K. Markwell, "Mandatory medical device reporting, medsun, and medwatch: What are the differences?," *Journal of Clinical Engineering*, vol. 38, no. 3, pp. 123–124, 2013.

[27] R. A. Bright, M. N. Flack, and S. N. Gardner, "The medical product surveillance network (medsun)," *Medical device epidemiology and surveillance. Chichester, UK: John Wiley & Sons*, pp. 63–77, 2007.

[28] R. A. Bright, "Surveillance of adverse medical device events," in *Medical device epidemiology and surveillance*, pp. 43–61, Wiley Online Library, 2007.

[29] P. Malataras and N. Pallikarakis, "Comparing the eu and usa medical devices vigilance systems transparency," in *XIV Mediterranean Conference on Medical and Biological Engineering and Computing 2016*, pp. 1061–1065, Springer, 2016.

[30] T. Saidi and T. Douglas, "Medical device regulation in africa," *Biomedical Engineering for Africa*, p. 175, 2019.

[31] Cambridge University Press, "Regulation," in *Cambridge Dictionary*, Cambridge University Press, 2020.

[32] Cambridge University Press, "Standard," in *Cambridge Dictionary*, Cambridge University Press, 2020.

[33] Cambridge University Press, "Requirement," in *Cambridge Dictionary*, Cambridge University Press, 2020.

[34] International Organization for Standardization/International Electrotechnical Commission and others, "Iso/iec directives part 2: 2004 (rules for the structure and drafting of international standards)," 2004.

[35] L. Pecchia, "Health technology assessment of medical devices in low and middle income countries: study design and preliminary results.," in *EMBEC & NBC 2017*, pp. 225–228, Springer, 2017.

[36] Department of Health, *Health Building Note 04-02*. Available at `https://www.gov.uk/government/collections/health-building-notes-core-elements` accessed: 05/03/2021.

[37] J. Locke, *Second treatise of government*. Strelbytskyy Multimedia Publishing, 2020.

[38] M. C. Nussbaum, *Frontiers of justice: Disability, nationality, species membership*. Harvard University Press, 2009.

[39] P. Legrand, "The impossibility of 'legal transplants'," *Maastricht Journal of European and Comparative Law*, vol. 4, no. 2, pp. 111–124, 1997.

[40] A. Watson, *Legal transplants: an approach to comparative law*. University of Georgia Press, 1993.

[41] M. Nussbaum and A. Sen, *The quality of life*. Clarendon Press, 1993.

[42] J. N. Mandl, C. Schneider, D. S. Schneider, and M. L. Baker, "Going to bat (s) for studies of disease tolerance," *Frontiers in immunology*, vol. 9, p. 2112, 2018.

[43] A. J. Rodriguez-Morales, D. K. Bonilla-Aldana, G. J. Balbin-Ramon, A. A. Rabaan, R. Sah, A. Paniz-Mondolfi, P. Pagliano, and S. Esposito, "History is repeating itself: Probable zoonotic spillover as the cause of the 2019 novel coronavirus epidemic," *Infez Med*, vol. 28, no. 1, pp. 3–5, 2020.

[44] A. Maccaro, D. Piaggio, C. A. Dodaro, and L. Pecchia, "Biomedical engineering and ethics: reflections on medical devices and ppe during the first wave of covid-19," *BMC Medical Ethics*, vol. 22, no. 1, pp. 1–7, 2021.

[45] H. Legido-Quigley, J. T. Mateos-García, V. R. Campos, M. Gea-Sánchez, C. Muntaner, and M. McKee, "The resilience of the spanish health system against the covid-19 pandemic," *The lancet public health*, vol. 5, no. 5, pp. e251–e252, 2020.

[46] A. Remuzzi and G. Remuzzi, "Covid-19 and italy: what next?," *The lancet*, vol. 395, no. 10231, pp. 1225–1228, 2020.

[47] R. Horton, "Offline: Covid-19 and the nhs—"a national scandal"," *Lancet (London, England)*, vol. 395, no. 10229, p. 1022, 2020.

[48] A. Borges, "French health system under pressure with covid-19 cases still soaring," Mar 2020.

[49] E. Mahase, "Covid-19: hoarding and misuse of protective gear is jeopardising the response, who warns," 2020.

[50] L. O. Gostin, E. A. Friedman, and S. A. Wetter, "Responding to covid-19: how to navigate a public health emergency legally and ethically," *Hastings Center Report*, vol. 50, no. 2, pp. 8–12, 2020.

[51] J. Steiner, L. Woods, and P. Watson, *Steiner & Woods EU Law*. Oxford University Press, 2012.

[52] K. Alexander and P. Clarkson, "Good design practice for medical devices and equipment, part i: a review of current literature," *Journal of medical engineering & technology*, vol. 24, no. 1, pp. 5–13, 2000.

[53] P. Sripaiboonkij, N. Sripaiboonkij, W. Phanprasit, and M. S. Jaakkola, "Respiratory and skin health among glass microfiber production workers: a cross-sectional study," *Environmental health*, vol. 8, no. 1, pp. 1–10, 2009.

[54] D. B. Williams, J. C. Kohler, A. Howard, Z. Austin, and Y.-L. Cheng, "A framework for the management of donated medical devices based on perspectives of frontline public health care staff in ghana," *Medicine Access@ Point of Care*, vol. 4, p. 2399202620941367, 2020.

[55] D. Medenou, L. A. Fagbemi, R. C. Houessouvo, T. R. Jossou, M. H. Ahouandjinou, D. Piaggio, C.-D. A. Kinnouezan, G. A. Monteiro, M. A. Idrissou, E. Iadanza, *et al.*, "Medical devices in sub-saharan africa: optimal assistance via a computerized maintenance management system (cmms) in benin," *Health and Technology*, vol. 9, no. 3, pp. 219–232, 2019.

[56] P. L, "Assessment of medical devices in low income settings," *Third WHO global forum on medical devices: international conference centre Geneva: Geneva, Switzerland 10–12 May 2017*, 2018.

[57] L. Lhotska, L. Sukupova, I. Lacković, and G. S. Ibbott, *World Congress on Medical Physics and Biomedical Engineering 2018: June 3-8, 2018, Prague, Czech Republic (Vol. 1)*. Springer, 2018.

[58] WHO, "Fourth who global forum on medical devices: report: Amtzkalam convention centre, visakhapatnam, india 13 to 15 december 2018," tech. rep., World Health Organization, 2019.

[59] US Department of Defence, "Test method standard for environmental engineering considerations and laboratory tests," *US Department of Defense, Defense Technical Information Center, Fort Belvoir, VA, Military Specification MIL-STD-810H*, 2019.

[60] S. Chawla, S. Kurani, S. M. Wren, B. Stewart, G. Burnham, A. Kushner, and T. McIntyre, "Electricity and generator availability in lmic hospitals: improving access to safe surgery," *Journal of Surgical Research*, vol. 223, pp. 136–141, 2018.

[61] S. Bergamasco, D. Williams, L. Pecchia, and A. Hussein, "Extending the lifespan of donated medical devices.," *Fourth Global WHO Forum on Medical Devices*, Dec 2018.

[62] D. Piaggio and L. Pecchia, "A device for tracking the photopupillary reflex via smartphone in lmics.," *Global Clinical Engineering Journal*, 2019.

[63] M. T. Shah, M. Joshipura, J. Singleton, P. LaBarre, H. Desai, E. Sharma, and C. Mock, "Assessment of the availability of technology for trauma care in india," *World journal of surgery*, vol. 39, no. 2, pp. 363–372, 2015.

[64] J. C. Rusatira, B. Tomaszewski, V. Dusabejambo, V. Ndayiragije, S. Gonsalves, A. Sawant, A. Mumararungu, G. Gasana, E. Amendezo, A. Haake, *et al.*, "Enabling access to medical and health education in rwanda using mobile technology: Needs assessment for the development of mobile medical educator apps," *JMIR medical education*, vol. 2, no. 1, p. e7, 2016.

[65] A. W. LaVigne, S. A. Triedman, T. C. Randall, E. L. Trimble, and A. N. Viswanathan, "Cervical cancer in low and middle income countries: addressing barriers to radiotherapy delivery," *Gynecologic oncology reports*, vol. 22, pp. 16–20, 2017.

[66] A. Taylor, P. Muelenaer, K. Kochersberger, A. Muelenaer, L. Bickford, and K. Redican, "Innovating for global health: Study of healthcare technology failure in southern malawi," *Annals of Global Health*, vol. 82, no. 3, 2016.

[67] S. McDonald, A. Fabbri, L. Parker, J. Williams, and L. Bero, "Medical donations are not always free: an assessment of compliance of medicine and medical device donations with world health organization guidelines (2009–2017)," *International health*, vol. 11, no. 5, pp. 379–402, 2019.

[68] K. Mitzner, B. DOE, A. Akulin, A. Suponin, and D. Müller, "Chapter 4 - introduction to industry standards," in *Complete PCB Design Using OrCAD® Capture and PCB Editor (Second Edition)* (K. Mitzner, B. DOE, A. Akulin, A. Suponin, and D. Müller, eds.), pp. 67 – 81, Academic Press, second edition ed., 2019.

[69] Department of Defense, "Manual 4120.24, defense standardization program procedures," 2018.

[70] "Mil-std-810," Sep 2020. Available at `https://en.wikipedia.org/wiki/MIL-STD-810` accessed: 11/03/2021.

[71] "Ip code," Nov 2020. `https://en.wikipedia.org/wiki/IP_Code` accessed: 11/03/2021.

[72] D. Adler, O. Heller, and M. Vosk, "Medical devices for military use," *Military medicine*, vol. 158, no. 10, pp. 677–680, 1993.

[73] E. Bompan and I. N. Brambilla, *Che cosa è l'economia circolare*. Edizioni Ambiente, 2016.

[74] C. Weetman, *A circular economy handbook for business and supply chains: Repair, remake, redesign, rethink*. Kogan Page Publishers, 2016.

[75] E. D. Santibanez Gonzalez, L. Koh, and J. Leung, "Towards a circular economy production system: trends and challenges for operations management," 2019.

[76] G. Reday and W. R. Stahel, *Potential for Substituting Manpower for Energy*. Battelle Memorial Institute, 1976.

[77] A. Heshmati, "A review of the circular economy and its implementation," *International Journal of Green Economics*, vol. 11, no. 3-4, pp. 251–288, 2017.

[78] M. Kay, J. Santos, and M. Takane, "mhealth: New horizons for health through mobile technologies," *World Health Organization*, vol. 64, no. 7, pp. 66–71, 2011.

[79] World Health Organization, *Global diffusion of eHealth: making universal health coverage achievable: report of the third global survey on eHealth*. World Health Organization, 2017.

[80] H. Edgcombe, C. Paton, and M. English, "Enhancing emergency care in low-income countries using mobile technology-based training tools," *Archives of disease in childhood*, vol. 101, no. 12, pp. 1149–1152, 2016.

[81] "Mobile cellular subscriptions (per 100 people)."

[82] World Health Organization and others, *Compendium of innovative health technologies for low-resource settings: assistive devices, eHealth solutions, medical devices*. World Health Organization, 2014.

[83] M. Cremer, J. Garai, L. Taxa, M. Salinas, J. Felix, K. Alfaro, M. Haas, and A. Zevallos, "Cryopen®, a gasless cryotherapy system adapted for low-resource settings," in *2016 IEEE Healthcare Innovation Point-Of-Care Technologies Conference (HI-POCT)*, pp. 130–133, IEEE, 2016.

[84] A. Bastawrous, "Increasing access to eye care... there's an app for that. peek: smartphone technology for eye health," *International journal of epidemiology*, vol. 45, no. 4, pp. 1040–1043, 2016.

[85] J. A. Blaya, H. S. Fraser, and B. Holt, "E-health technologies show promise in developing countries," *Health Affairs*, vol. 29, no. 2, pp. 244–251, 2010.

[86] C. B. Aranda-Jan, N. Mohutsiwa-Dibe, and S. Loukanova, "Systematic review on what works, what does not work and why of implementation of mobile health (mhealth) projects in africa," *BMC public health*, vol. 14, no. 1, p. 188, 2014.

[87] K. Sertoglu, P. Hanaphy, H. Everett, and M. Petch, "The free beginner's guide," Aug 2018.

[88] J. C. Najmon, S. Raeisi, and A. Tovar, "Review of additive manufacturing technologies and applications in the aerospace industry," *Additive manufacturing for the aerospace industry*, pp. 7–31, 2019.

[89] D. Grygier, M. Kujawa, and P. Kowalewski, "Deposition of biocompatible polymers by 3d printing (fdm) on titanium alloy," *Polymers*, vol. 14, no. 2, p. 235, 2022.

[90] A. Aimar, A. Palermo, and B. Innocenti, "The role of 3d printing in medical applications: a state of the art," *Journal of healthcare engineering*, vol. 2019, 2019.

[91] J. Maric, F. Rodhain, and Y. Barlette, "Frugal innovations and 3d printing: insights from the field," *Journal of Innovation Economics Management*, no. 3, pp. 57–76, 2016.

[92] R. Tino, R. Moore, S. Antoline, P. Ravi, N. Wake, C. N. Ionita, J. M. Morris, S. J. Decker, A. Sheikh, F. J. Rybicki, *et al.*, "Covid-19 and the role of 3d printing in medicine," 2020.

[93] "Frugal innovation," Jan 2022.

[94] T. Weyrauch and C. Herstatt, "What is frugal innovation? three defining criteria," *Journal of frugal innovation*, vol. 2, no. 1, pp. 1–17, 2017.

[95] R. A. Malkin, "Barriers for medical devices for the developing world," *Expert review of medical devices*, vol. 4, no. 6, pp. 759–763, 2007.

[96] R. Y. Hsia, N. A. Mbembati, S. Macfarlane, and M. E. Kruk, "Access to emergency and surgical care in sub-saharan africa: the infrastructure gap," *Health policy and planning*, vol. 27, no. 3, pp. 234–244, 2012.

[97] K. Albutt, R. R. Yorlets, M. Punchak, P. Kayima, D. B. Namanya, G. A. Anderson, and M. G. Shrime, "You pray to your god: A qualitative analysis of challenges in the provision of safe, timely, and affordable surgical care in uganda," *Plos one*, vol. 13, no. 4, p. e0195986, 2018.

[98] D. Dovlo and H. Karamagi, "Life-saving hospitals-a role in uhc for africa. building health dreams," *World Hosp Health Serv*, vol. 52, pp. 12–6, 2016.

[99] S. Murthy, A. Leligdowicz, and N. K. Adhikari, "Intensive care unit capacity in low-income countries: a systematic review," *PloS one*, vol. 10, no. 1, p. e0116949, 2015.

[100] J. Tumukunde, C. Sendagire, and S. S. Ttendo, "Development of intensive care in low-resource regions," *Current Anesthesiology Reports*, vol. 9, no. 1, pp. 15–17, 2019.

[101] P. Firth and S. Ttendo, "Intensive care in low-income countries—a critical need," *N Engl J Med*, vol. 367, no. 21, pp. 1974–6, 2012.

[102] W. Mutale, S. Bosomprah, P. Shankalala, O. Mweemba, R. Chilengi, S. Kapambwe, C. Chishimba, M. Mukanu, D. Chibutu, and D. Heimburger, "Assessing capacity and readiness to manage ncds in primary

care setting: Gaps and opportunities based on adapted who pen tool in zambia," *PloS one*, vol. 13, no. 8, p. e0200994, 2018.

[103] G. Musinguzi, H. Bastiaens, R. K. Wanyenze, A. Mukose, F. Nuwaha, *et al.*, "Capacity of health facilities to manage hypertension in mukono and buikwe districts in uganda: Challenges and recommendations," *PloS one*, vol. 10, no. 11, p. e0142312, 2015.

[104] H. D. Report, *Beyond income, beyond averages, beyond today: Inequalities in human development in the 21st century*. United Nations Development Programme New York, 2019.

[105] J. Harrington, *From the Solomon Islands to Liberia*. PhD thesis, these are the 25 poorest countries in the world. USA Today, 2018.

[106] "Healthcare in uganda," Oct 2019. `https://en.wikipedia.org/w/index.php?title=Healthcare_in_Uganda&oldid=922014431` accessed: 11/03/2021.

[107] S. Singh, "Location & layout of hospital," 2008.

[108] Academy for Architecture for Health & Facilities Guidelines Institute, "Guidelines for design and construction of hospital and health care facilities."

[109] "Priority medical devices," May 2020. `https://www.who.int/medical_devices/priority/en/.`, journal=World Health Organization accessed: 11/03/2021.

[110] "Medical equipment maintenance programme overview," Jul 2019. `https://www.who.int/medical_devices/publications/medical-equipment-maintenance/en/` accessed: 11/03/2021.

[111] C. De Maria, L. Di Pietro, A. D. Lantada, J. Madete, P. N. Makobore, M. Mridha, A. Ravizza, J. Torop, and A. Ahluwalia, "Safe innovation: On medical device legislation in europe and africa," *Health Policy and Technology*, vol. 7, no. 2, pp. 156–165, 2018.

[112] G. J. Buckley, J. E. Riviere, *et al.*, *Ensuring safe foods and medical products through stronger regulatory systems abroad*. National Academies Press, 2012.

[113] D. R. Lustick and M. H. Zaman, "Biomedical engineering education and practice challenges and opportunities in improving health in developing countries," in *2011 Atlanta conference on science and innovation policy*, pp. 1–5, IEEE, 2011.

[114] C. De Maria, D. Mazzei, and A. D. Ahluwalia, "Improving african healthcare through open source biomedical engineering," *International Journal On Advances in Life Sciences*, 2015.

[115] C. De Maria, L. Di Pietro, A. D. Lantada, A. Ravizza, M. Mridha, J. Torop, J. Madete, P. Makobore, and A. Ahluwalia, "The ubora e-infrastructure for open source innovation in medical technology," in *Mediterranean conference on medical and biological engineering and computing*, pp. 878–882, Springer, 2019.

[116] L. Di Pietro, C. De Maria, A. Ravizza, and A. Ahluwalia, "Co-design open-source medical devices: how to minimize the human error using ubora e-infrastructure," in *2019 41st annual international conference of the IEEE engineering in medicine and biology society (EMBC)*, pp. 3730–3733, IEEE, 2019.

[117] C. Aranda Jan, S. Jagtap, and J. Moultrie, "Towards a framework for holistic contextual design for low-resource settings," *International Journal of Design*, 2016.

[118] R. Richards-Kortum and M. Oden, "Devices for low-resource health care," *Science*, vol. 342, no. 6162, pp. 1055–1057, 2013.

[119] A. Arasaratnam and G. Humphreys, "Emerging economies drive frugal innovation," *World Health Organization. Bulletin of the World Health Organization*, vol. 91, no. 1, p. 6, 2013.

[120] A. J. Nimunkar, J. Baran, D. Van Sickle, N. K. Pagidimarry, and J. G. Webster, "Medical devices for developing countries: Design constraints and approaches," in *2009 Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, pp. 7048–7051, IEEE, 2009.

[121] A. K. Gauthier, G. Cruz, L. Medina, and S. Duke, "Design factors for medical device functionality in developing countries," in *IIE Annual Conference. Proceedings*, p. 2227, Institute of Industrial and Systems Engineers (IISE), 2013.

[122] M. Zeschky, B. Widenmayer, and O. Gassmann, "Frugal innovation in emerging markets," *Research-Technology Management*, vol. 54, no. 4, pp. 38–45, 2011.

[123] World Health Organization, *WHO compendium of innovative health technologies for low resource settings, 2011-2014: assistive devices, eHealth solutions, medical devices, other technologies, technologies for outbreaks*. World Health Organization, 2015.

[124] C. Pope and N. Mays, "Qualitative research: reaching the parts other methods cannot reach: an introduction to qualitative methods in health and health services research," *bmj*, vol. 311, no. 6996, pp. 42–45, 1995.

[125] W. Goddard and S. Melville, *Research methodology: An introduction*. Juta and Company Ltd, 2004.

[126] D. S. Triangulation, "The use of triangulation in qualitative research," in *Oncology nursing forum*, vol. 41, p. 545, 2014.

[127] J. Ritchie, J. Lewis, C. M. Nicholls, R. Ormston, *et al.*, *Qualitative research practice: A guide for social science students and researchers*. sage, 2013.

[128] J. Polisena, R. Castaldo, O. Ciani, C. Federici, S. Borsci, M. Ritrovato, D. Clark, and L. Pecchia, "Health technology assessment methods guidelines for medical devices: how can we address the gaps? the international federation of medical and biological engineering perspective," *International journal of technology assessment in health care*, vol. 34, no. 3, pp. 276–289, 2018.

[129] "Kick-off of the first african scientific society of medical and biological engineering.."

[130] J. Waggoner, J. D. Carline, and S. J. Durning, "Is there a consensus on consensus methodology? descriptions and recommendations for future consensus research," *Academic Medicine*, vol. 91, no. 5, pp. 663–668, 2016.

[131] I. Staff, "Bandwagon effect definition," Dec 2020. `https://www.investopedia.com/terms/b/bandwagon-effect.asp` accessed: 11/03/2021.

[132] "Bandwagon effect," Jan 2021. `https://en.wikipedia.org/wiki/Bandwagon_effect` accessed: 11/03/2021.

[133] C. Okoli and S. D. Pawlowski, "The delphi method as a research tool: an example, design considerations and applications," *Information & management*, vol. 42, no. 1, pp. 15–29, 2004.

[134] W. Revelle and D. M. Condon, "Reliability from α to ω: A tutorial.," *Psychological assessment*, vol. 31, no. 12, p. 1395, 2019.

[135] M. Cinelli, S. R. Coles, O. Sadik, B. Karn, and K. Kirwan, "A framework of criteria for the sustainability assessment of nanoproducts," *Journal of Cleaner Production*, vol. 126, pp. 277–287, 2016.

[136] M. Furr, *Scale construction and psychometrics for social and personality psychology*. SAGE Publications Ltd, 2011.

[137] A. Bonanomi, M. N. Ruscone, and S. A. Osmetti, "The polychoric ordinal alpha, measuring the reliability of a set of polytomous ordinal items," in *SIS 2013 Conference: Advances in latent variables: Methods, models and applications, Brescia, Italy*, pp. 19–21, Citeseer, 2013.

[138] B. D. Zumbo, A. M. Gadermann, and C. Zeisser, "Ordinal versions of coefficients alpha and theta for likert rating scales," *Journal of modern applied statistical methods*, vol. 6, no. 1, p. 4, 2007.

[139] "Cronbach's alpha: Simple definition, use and interpretation."

[140] W. H. Organization, "Who compendium of innovative health technologies for low-resource settings: 2016-2017: medical devices, ehealth/mhealth, medical simulation devices, personal protective equipment, assistive products, other technologies," in *WHO compendium of innovative health technologies for low-resource settings: 2016-2017: medical devices, eHealth/mHealth, medical simulation devices, personal protective equipment, assistive products, other technologies*, WHO, 2018.

[141] S. Pugh, "Concept selection–a method that works, chapter 14 from "creating innovative products using total design"," 1996.

[142] E. G. Carayannis, J. J. Ferreira, M. S. Jalali, and F. A. Ferreira, "Mcda in knowledge-based economies: Methodological developments and real world applications," *Technological Forecasting and Social Change*, vol. 131, pp. 1–3, 2018.

[143] E. G. Carayannis, Y. Goletsis, and E. Grigoroudis, "Composite innovation metrics: Mcda and the quadruple innovation helix framework," *Technological Forecasting and Social Change*, vol. 131, pp. 4–17, 2018.

[144] A. González, E. Ortigoza, C. Llamosas, G. Blanco, and R. Amarilla, "Multi-criteria analysis of economic complexity transition in emerging economies: The case of paraguay," *Socio-Economic Planning Sciences*, vol. 68, p. 100617, 2019.

[145] N. Lerche, I. Wilkens, M. Schmehl, S. Eigner-Thiel, and J. Geldermann, "Using methods of multi-criteria decision making to provide decision support concerning local bioenergy projects," *Socio-Economic Planning Sciences*, vol. 68, p. 100594, 2019.

[146] S.-H. Chen and W.-T. Lin, "Analyzing determinants for promoting emerging technology through intermediaries by using a danp-based mcda

framework," *Technological Forecasting and Social Change*, vol. 131, pp. 94–110, 2018.

[147] Z. Bauman, "On glocalization: Or globalization for some, localization for some others," *Thesis Eleven*, vol. 54, no. 1, pp. 37–49, 1998.

[148] M. Augé, *Non-lieux. Introduction à une anthropologie de la: Introduction à une anthropologie de la surmodernité*. Média Diffusion, 2015.

[149] J. E. Hall and M. E. Hall, *Guyton and Hall textbook of medical physiology e-Book*. Elsevier Health Sciences, 2020.

[150] A. Adoni and M. McNett, "The pupillary response in traumatic brain injury: a guide for trauma nurses," *Journal of Trauma Nursing— JTN*, vol. 14, no. 4, pp. 191–196, 2007.

[151] J. W. Chen, Z. J. Gombart, S. Rogers, S. K. Gardiner, S. Cecil, and R. M. Bullock, "Pupillary reactivity as an early indicator of increased intracranial pressure: The introduction of the neurological pupil index," *Surgical neurology international*, vol. 2, 2011.

[152] D. Wildemeersch, N. Peeters, V. Saldien, M. Vercauteren, and G. Hans, "Pain assessment by pupil dilation reflex in response to noxious stimulation in anaesthetized adults," *Acta Anaesthesiologica Scandinavica*, vol. 62, no. 8, pp. 1050–1056, 2018.

[153] D. Wildemeersch, M. Baeten, N. Peeters, V. Saldien, M. Vercauteren, and G. Hans, "Pupillary dilation reflex and pupillary pain index evaluation during general anaesthesia: a pilot study," *Romanian journal of anaesthesia and intensive care*, vol. 25, no. 1, pp. 19–23, 2018.

[154] C. D. Bryant, *Handbook of death and dying*, vol. 1. Sage, 2003.

[155] C. A. Hall and R. P. Chilcott, "Eyeing up the future of the pupillary light reflex in neurodiagnostics," *Diagnostics*, vol. 8, no. 1, p. 19, 2018.

[156] L. Sharpe, W. Pickworth, and W. Martin, "Actions of amphetamine and antagonists on pupil diameter in the chronic sympathectomized dog," *Psychopharmacology*, vol. 53, no. 2, pp. 115–120, 1977.

[157] M. D. Rollins, J. R. Feiner, J. M. Lee, S. Shah, and M. Larson, "Pupillary effects of high-dose opioid quantified with infrared pupillometry," *Anesthesiology*, vol. 121, no. 5, pp. 1037–1044, 2014.

[158] J. C. Park, Y.-F. Chen, N. P. Blair, F. Y. Chau, J. I. Lim, Y. I. Leiderman, M. Shahidi, and J. J. McAnany, "Pupillary responses in non-proliferative diabetic retinopathy," *Scientific reports*, vol. 7, no. 1, pp. 1–10, 2017.

[159] B. Liew, K. Zainab, A. Cecilia, Y. Zarina, and T. Clement, "Early management of head injury in adults in primary care," *Malaysian family physician: the official journal of the Academy of Family Physicians of Malaysia*, vol. 12, no. 1, p. 22, 2017.

[160] I. Moppett, "Traumatic brain injury: assessment, resuscitation and early management," *British Journal of Anaesthesia*, vol. 99, no. 1, pp. 18–31, 2007.

[161] N. I. for Health and C. E. G. Britain), *Head injury: assessment and early management*. National Institute for Health and Care Excellence (NICE), 2017.

[162] P. Melillo, A. de Benedictis, E. Villani, M. C. Ferraro, E. Iadanza, M. Gherardelli, F. Testa, S. Banfi, P. Nucci, and F. Simonelli, "Toward a novel medical device based on chromatic pupillometry for screening and monitoring of inherited ocular disease: A pilot study," in *World Congress on Medical Physics and Biomedical Engineering 2018*, pp. 387–390, Springer, 2019.

[163] E. Iadanza, R. Fabbri, A. Luschi, F. Gavazzi, P. Melillo, F. Simonelli, and M. Gherardelli, "Oráo: Restful cloud-based ophthalmologic medical record for chromatic pupillometry," in *International Conference on Medical and Biological Engineering*, pp. 713–720, Springer, 2019.

[164] E. Iadanza, R. Fabbri, A. Luschi, P. Melillo, and F. Simonelli, "A collaborative restful cloud-based tool for management of chromatic pupillometry in a clinical trial," *Health and Technology*, vol. 10, no. 1, pp. 25–38, 2020.

[165] E. Iadanza, F. Goretti, M. Sorelli, P. Melillo, L. Pecchia, F. Simonelli, and M. Gherardelli, "Automatic detection of genetic diseases in pediatric age using pupillometry," *IEEE Access*, vol. 8, pp. 34949–34961, 2020.

[166] T.-H. Kim and J.-I. Youn, "Development of a smartphone-based pupillometer," *Journal of the Optical Society of Korea*, vol. 17, no. 3, pp. 249–254, 2013.

[167] A. Mariakakis, J. Baudin, E. Whitmire, V. Mehta, M. A. Banks, A. Law, L. Mcgrath, and S. N. Patel, "Pupilscreen: using smartphones to assess traumatic brain injury," *Proceedings of the ACM on Interactive, Mobile, Wearable and Ubiquitous Technologies*, vol. 1, no. 3, pp. 1–27, 2017.

[168] J. J. McAnany, B. M. Smith, A. Garland, and S. L. Kagen, "iphone-based pupillometry: a novel approach for assessing the pupillary light reflex," *Optometry and Vision Science*, vol. 95, no. 10, p. 953, 2018.

[169] R. Vigário, M. Santos, R. Vences, and C. Quintão, "Towards a mobile phone pupillometer," in *International Conference on Applied Human Factors and Ergonomics*, pp. 194–206, Springer, 2019.

[170] K. Sluss, R. Rao, and J. Schuler, "Evaluation of reflex and its applications in medicine," *Brightlamp, Inc, IN, USA*, 2019.

[171] P. Melillo, L. Pecchia, F. Testa, S. Rossi, J. Bennett, and F. Simonelli, "Pupillometric analysis for assessment of gene therapy in leber congenital amaurosis patients," *Biomedical engineering online*, vol. 11, no. 1, pp. 1–13, 2012.

[172] D. Li, D. Winfield, and D. J. Parkhurst, "Starburst: A hybrid algorithm for video-based eye tracking combining feature-based and model-based approaches," in *2005 IEEE Computer Society Conference on Computer Vision and Pattern Recognition (CVPR'05)-Workshops*, pp. 79–79, IEEE, 2005.

[173] A. Ferone, M. Frucci, A. Petrosino, and G. S. di Baja, "Iris detection through watershed segmentation," in *International Workshop on Biometric Authentication*, pp. 57–65, Springer, 2014.

[174] A. A. Jarjes, K. Wang, and G. J. Mohammed, "Gvf snake-based method for accurate pupil contour detection," *Information Technology Journal*, vol. 9, no. 8, pp. 1653–1658, 2010.

[175] S. Minaee and A. Abdolrashidi, "Deepiris: Iris recognition using a deep learning approach," *arXiv preprint arXiv:1907.09380*, 2019.

[176] H. Saidi, B. K. Mutiso, and J. Ogengo, "Mortality after road traffic crashes in a system with limited trauma data capability," *Journal of trauma management & outcomes*, vol. 8, no. 1, pp. 1–6, 2014.

[177] WHO, "The top 10 causes of death." Available at `https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death` accessed: 12/03/2021.

[178] D. Couret, D. Boumaza, C. Grisotto, T. Triglia, L. Pellegrini, P. Ocquidant, N. J. Bruder, and L. J. Velly, "Reliability of standard pupillometry practice in neurocritical care: an observational, double-blinded study," *Critical Care*, vol. 20, no. 1, pp. 1–9, 2016.

[179] D. M. Fetterman, "Ethnography (vol. 17)," *Thousand Oaks, Ca*, 1998.

[180] H. Eskola, O. Väisänen, J. Viik, and J. Hyttinen, *EMBEC & NBC 2017: Joint Conference of the European Medical and Biological Engineering*

Conference (EMBEC) and the Nordic-Baltic Conference on Biomedical Engineering and Medical Physics (NBC), Tampere, Finland, June 2017, vol. 65. Springer, 2017.

[181] K. J. Ciuffreda, N. R. Joshi, and J. Q. Truong, "Understanding the effects of mild traumatic brain injury on the pupillary light reflex," *Concussion*, vol. 2, no. 3, p. CNC36, 2017.

[182] D. M. Calandra, S. Di Martino, D. Riccio, and A. Visconti, "Smartphone based pupillometry: an empirical evaluation of accuracy and safety," in *International Conference on Image Analysis and Processing*, pp. 433–443, Springer, 2017.

[183] Y. D. Shin, J. H. Bae, E. J. Kwon, H. T. Kim, T.-S. Lee, and Y. J. Choi, "Assessment of pupillary light reflex using a smartphone application," *Experimental and therapeutic medicine*, vol. 12, no. 2, pp. 720–724, 2016.

[184] N. Voudoukis and S. Oikonomidis, "Inverse square law for light and radiation: A unifying educational approach," *European Journal of Engineering and Technology Research*, vol. 2, no. 11, pp. 23–27, 2017.

[185] T. Knapen, J. W. de Gee, J. Brascamp, S. Nuiten, S. Hoppenbrouwers, and J. Theeuwes, "Cognitive and ocular factors jointly determine pupil responses under equiluminance," *PloS one*, vol. 11, no. 5, p. e0155574, 2016.

[186] Statscounter, "Mobile & tablet android version market share worldwide." Available at `https://gs.statcounter.com/android-version-market-share/mobile-tablet/worldwide`, Accessed: 15/03/2021.

[187] S. S. Shapiro and M. B. Wilk, "An analysis of variance test for normality (complete samples)," *Biometrika*, vol. 52, no. 3/4, pp. 591–611, 1965.

[188] C. De Maria, L. Di Pietro, A. Ravizza, A. D. Lantada, and A. D. Ahluwalia, "Open-source medical devices: Healthcare solutions for low-, middle-, and high-resource settings," in *Clinical Engineering Handbook*, pp. 7–14, Elsevier, 2020.

[189] S. O'Dea, "Mobile os share in africa 2018-2021," Feb 2021. Available at: `https://www.statista.com/statistics/1045247/share-of-mobile-operating-systems-in-africa-by-month/`, Accessed: 15/03/2021.

[190] S. Borsci, J. Kuljis, J. Barnett, and L. Pecchia, "Beyond the user preferences: Aligning the prototype design to the users' expectations," *Human*

Factors and Ergonomics in Manufacturing & Service Industries, vol. 26, no. 1, pp. 16–39, 2016.

[191] S. Firsing, "How severe is africa's brain drain?," *Africa at LSE*, 2016.

[192] J. M. Bland and D. Altman, "Statistical methods for assessing agreement between two methods of clinical measurement," *The lancet*, vol. 327, no. 8476, pp. 307–310, 1986.

[193] D. Giavarina, "Understanding bland altman analysis," *Biochemia medica*, vol. 25, no. 2, pp. 141–151, 2015.

[194] D. Piaggio, M. Taher, F. Marinozzi, F. Bini, L. Pecchia, *et al.*, "A matlab app to assess, compare and validate new methods against their benchmarks," in *European Medical and Biological Engineering Conference*, pp. 10–21, Springer, 2020.

[195] R. E. McKay, M. A. Kohn, E. S. Schwartz, and M. D. Larson, "Evaluation of two portable pupillometers to assess clinical utility," *Concussion*, vol. 5, no. 4, p. CNC82, 2020.

[196] A. E. Neice, C. Fowler, R. A. Jaffe, and J. G. Brock-Utne, "Feasibility study of a smartphone pupillometer and evaluation of its accuracy," *Journal of Clinical Monitoring and Computing*, pp. 1–9, 2020.

[197] A. Verrotti, G. Prezioso, R. Scattoni, and F. Chiarelli, "Autonomic neuropathy in diabetes mellitus," *Frontiers in endocrinology*, vol. 5, p. 205, 2014.

[198] S. Yagihashi, H. Mizukami, and K. Sugimoto, "Mechanism of diabetic neuropathy: where are we now and where to go?," *Journal of diabetes investigation*, vol. 2, no. 1, pp. 18–32, 2011.

[199] N. E. Cameron and M. A. Cotter, "Metabolic and vascular factors in the pathogenesis of diabetic neuropathy," *Diabetes*, vol. 46, no. Supplement 2, pp. S31–S37, 1997.

[200] C. F. Packer, B. Sonani, and B. Manna, "Diabetic ulcer," *StatPearls [Internet]*, 2020.

[201] N. Papanas, "Diabetic neuropathy collection: progress in diagnosis and screening," 2020.

[202] E. L. Feldman, B. C. Callaghan, R. Pop-Busui, D. W. Zochodne, D. E. Wright, D. L. Bennett, V. Bril, J. W. Russell, and V. Viswanathan, "Diabetic neuropathy," *Nature Reviews Disease Primers*, vol. 5, no. 1, pp. 1–18, 2019.

[203] "Sensorimotor polyneuropathy: Medlineplus medical encyclopedia." Available at: =https://medlineplus.gov/ency/article/000750.htm, Accessed: 24/03/2021.

[204] K. A. Williams, R. W. Hurley, E. E. Lin, and C. L. Wu, "Neuropathic pain syndromes," in *Raj's Practical Management of Pain*, pp. 427–443, Elsevier Inc., 2008.

[205] D. J. Margolis, L. Allen-Taylor, O. Hoffstad, and J. A. Berlin, "Diabetic neuropathic foot ulcers and amputation," *Wound Repair and Regeneration*, vol. 13, no. 3, pp. 230–236, 2005.

[206] I. Mantey, R. Hill, A. Foster, S. Wilson, J. Wade, M. Edmonds, *et al.*, "Infection of foot ulcers with staphylococcus aureus associated with increased mortality in diabetic patients," *Communicable disease and public health*, vol. 3, pp. 288–290, 2000.

[207] H. N. Gouda, F. Charlson, K. Sorsdahl, S. Ahmadzada, A. J. Ferrari, H. Erskine, J. Leung, D. Santamauro, C. Lund, L. N. Aminde, *et al.*, "Burden of non-communicable diseases in sub-saharan africa, 1990–2017: results from the global burden of disease study 2017," *The Lancet Global Health*, vol. 7, no. 10, pp. e1375–e1387, 2019.

[208] S. D. Pastakia, C. R. Pekny, S. M. Manyara, and L. Fischer, "Diabetes in sub-saharan africa–from policy to practice to progress: targeting the existing gaps for future care for diabetes," *Diabetes, metabolic syndrome and obesity: targets and therapy*, vol. 10, p. 247, 2017.

[209] M. J. Snyder, L. M. Gibbs, and T. J. Lindsay, "Treating painful diabetic peripheral neuropathy: an update," *American family physician*, vol. 94, no. 3, pp. 227–234, 2016.

[210] Z. Abbas and L. Archibals, "The diabetic foot in sub-saharan africa: A new management paradigm," *Diabetic Foot*, vol. 10, no. 3, p. 128, 2007.

[211] K. Feingold, B. Anawalt, A. Boyce, G. Chrousos, K. Dungan, A. Grossman, J. Hershman, G. Kaltsas, C. Koch, P. Kopp, *et al.*, "Diabetic neuropathies–endotext," *Endotext*, 2000.

[212] A. Gordois, P. Scuffham, A. Shearer, A. Oglesby, and J. A. Tobian, "The health care costs of diabetic peripheral neuropathy in the us," *Diabetes care*, vol. 26, no. 6, pp. 1790–1795, 2003.

[213] J. Røikjer, C. D. Mørch, and N. Ejskjaer, "Diabetic peripheral neuropathy: Diagnosis and treatment.," *Current drug safety*, 2020.

[214] E. Chicharro-Luna, F. J. Pomares-Gómez, A. B. Ortega-Ávila, M. Coheña-Jiménez, and G. Gijon-Nogueron, "Variability in the clinical diagnosis of diabetic peripheral neuropathy," *Primary care diabetes*, vol. 14, no. 1, pp. 53–60, 2020.

[215] E. J. Bastyr III, K. L. Price, V. Bril, M. S. Group, *et al.*, "Development and validity testing of the neuropathy total symptom score-6: questionnaire for the study of sensory symptoms of diabetic peripheral neuropathy," *Clinical therapeutics*, vol. 27, no. 8, pp. 1278–1294, 2005.

[216] W. H. Organization *et al.*, *WHO List of Priority medical devices for cardiovascular diseases & diabetes*. World Health Organization, 2021.

[217] R. Fernández-Torres, M. Ruiz-Muñoz, A. J. Pérez-Panero, J. García-Romero, and M. Gónzalez-Sánchez, "Instruments of choice for assessment and monitoring diabetic foot: a systematic review," *Journal of clinical medicine*, vol. 9, no. 2, p. 602, 2020.

[218] N. Arteaga-Marrero, A. Hernández, E. Villa, S. González-Pérez, C. Luque, and J. Ruiz-Alzola, "Segmentation approaches for diabetic foot disorders," *Sensors*, vol. 21, no. 3, p. 934, 2021.

[219] H. Yang, G. Sloan, Y. Ye, S. Wang, B. Duan, S. Tesfaye, and L. Gao, "New perspective in diabetic neuropathy: from the periphery to the brain, a call for early detection, and precision medicine," *Frontiers in endocrinology*, vol. 10, p. 929, 2020.

[220] C. C. Robinson, R. P. G. Barreto, and R. D. M. Plentz, "Effects of whole body vibration in individuals with diabetic peripheral neuropathy: a systematic review," *Journal of musculoskeletal & neuronal interactions*, vol. 18, no. 3, p. 382, 2018.

[221] N. J. Akbari, M. Hosseinifar, S. S. Naimi, S. Mikaili, and S. Rahbar, "The efficacy of physiotherapy interventions in mitigating the symptoms and complications of diabetic peripheral neuropathy: A systematic review," *Journal of Diabetes & Metabolic Disorders*, pp. 1–10, 2020.

[222] E. Lindholm, M. Löndahl, K. Fagher, J. Apelqvist, and L. B. Dahlin, "Strong association between vibration perception thresholds at low frequencies (4 and 8 hz), neuropathic symptoms and diabetic foot ulcers," *Plos one*, vol. 14, no. 2, p. e0212921, 2019.

[223] W. D. Rinkel, D. Rizopoulos, M. H. Aziz, J. W. Van Neck, M. C. Cabezas, and J. H. Coert, "Grading the loss of sensation in diabetic patients: a psychometric evaluation of the rotterdam diabetic foot study test battery," *Muscle & nerve*, vol. 58, no. 4, pp. 559–565, 2018.

[224] J. B. Zwaferink, J. M. Hijmans, C. M. Schrijver, L. K. Schrijver, K. Postema, and J. J. van Netten, "Mechanical noise improves the vibration perception threshold of the foot in people with diabetic neuropathy," *Journal of diabetes science and technology*, vol. 14, no. 1, pp. 16–21, 2020.

[225] A. I. Vinik, "Diabetic neuropathies," *Controversies in Treating Diabetes*, pp. 135–156, 2008.

[226] A. J. Boulton, A. I. Vinik, J. C. Arezzo, V. Bril, E. L. Feldman, R. Freeman, R. A. Malik, R. E. Maser, J. M. Sosenko, and D. Ziegler, "Diabetic neuropathies: a statement by the american diabetes association," *Diabetes care*, vol. 28, no. 4, pp. 956–962, 2005.

[227] J. Doupis, G. Festas, C. Tsilivigos, V. Efthymiou, and A. Kokkinos, "Smartphone-based technology in diabetes management," *Diabetes Therapy*, vol. 11, no. 3, pp. 607–619, 2020.

[228] Ö. Kap, V. Kilic, J. G. Hardy, and N. Horzum, "Smartphone-based colorimetric detection systems for glucose monitoring in the diagnosis and management of diabetes," *Analyst*, 2021.

[229] B. Najafi, N. D. Reeves, and D. G. Armstrong, "Leveraging smart technologies to improve the management of diabetic foot ulcers and extend ulcer-free days in remission," *Diabetes/metabolism research and reviews*, vol. 36, p. e3239, 2020.

[230] J. D. May and M. W. J. Morris, "Mobile phone generated vibrations used to detect diabetic peripheral neuropathy," *Foot and Ankle Surgery*, vol. 23, no. 4, pp. 281–284, 2017.

[231] G. J. Bönhof, C. Herder, A. Strom, N. Papanas, M. Roden, and D. Ziegler, "Emerging biomarkers, tools, and treatments for diabetic polyneuropathy," *Endocrine reviews*, vol. 40, no. 1, pp. 153–192, 2019.

[232] P. G. Jacobs, P. Hanaway, J. Leitschuh, J. Condon, U. Rajhbeharrysingh, C. Mosquera-Lopez, C. Guidarelli, and K. Winters-Stone, "Design and evaluation of a portable smart-phone based peripheral neuropathy test platform," in *2018 40th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)*, pp. 1–4, IEEE, 2018.

[233] C. Chute and T. French, "Introducing care 4.0: an integrated care paradigm built on industry 4.0 capabilities," *International journal of environmental research and public health*, vol. 16, no. 12, p. 2247, 2019.

[234] P. Rea, "Chapter 8—spinal tracts—ascending/sensory pathways," *Essential clinical anatomy of the nervous system*, pp. 133–160, 2015.

[235] L. Bickley and P. G. Szilagyi, *Bates' guide to physical examination and history-taking*. Lippincott Williams & Wilkins, 2012.

[236] C. Dumontier and R. Tubiana, "Physical examination of the hand," in *Plastic Surgery Secrets Plus*, pp. 749–754, Mosby, 2010.

[237] R. Periyasamy, M. Manivannan, and V. B. R. Narayanamurthy, "Changes in two point discrimination and the law of mobility in diabetes mellitus patients," *Journal of brachial plexus and peripheral nerve injury*, vol. 3, no. 1, pp. 1–6, 2008.

[238] F. J. Domínguez-Muñoz, J. C. Adsuar, S. Villafaina, M. A. García-Gordillo, M. Á. Hernández-Mocholí, D. Collado-Mateo, and N. Gusi, "Test-retest reliability of vibration perception threshold test in people with type 2 diabetes mellitus," *International journal of environmental research and public health*, vol. 17, no. 5, p. 1773, 2020.

[239] S. M. Lanting, M. J. Spink, P. E. Tehan, S. Vickers, S. L. Casey, and V. H. Chuter, "Non-invasive assessment of vibration perception and protective sensation in people with diabetes mellitus: inter-and intra-rater reliability," *Journal of foot and ankle research*, vol. 13, no. 1, pp. 1–7, 2020.

[240] T. O'Brien and J. Karem, "An initial evaluation of a proof-of-concept 128-hz electronic tuning fork in the detection of peripheral neuropathy," *Journal of the American Podiatric Medical Association*, vol. 104, no. 2, pp. 134–140, 2014.

[241] A. Kaneko, N. Asai, and T. Kanda, "The influence of age on pressure perception of static and moving two-point discrimination in normal subjects," *Journal of hand therapy*, vol. 18, no. 4, pp. 421–425, 2005.

[242] P. Wiles, S. Pearce, P. Rice, and J. Mitchell, "Vibration perception threshold: influence of age, height, sex, and smoking, and calculation of accurate centile values," *Diabetic medicine*, vol. 8, no. 2, pp. 157–161, 1991.

[243] I. Willits, H. Cole, R. Jones, P. Dimmock, M. Arber, J. Craig, and A. Sims, "Vibratip™ for testing vibration perception to detect diabetic peripheral neuropathy: a nice medical technology guidance," *Applied health economics and health policy*, vol. 13, no. 4, pp. 315–324, 2015.

[244] R. Drake, A. W. Vogl, and A. W. Mitchell, *Gray's anatomy for students E-book*. Elsevier Health Sciences, 2009.

[245] A. J. Wheeler and A. R. Ganji, *Introduction to engineering experimentation*, ch. 6, pp. 163–164. Prentice Hall New Jersey, 2010.

[246] F. J. Massey Jr, "The kolmogorov-smirnov test for goodness of fit," *Journal of the American statistical Association*, vol. 46, no. 253, pp. 68–78, 1951.

[247] S. J. Lederman and R. L. Klatzky, "Haptic perception: A tutorial," *Attention, Perception, & Psychophysics*, vol. 71, no. 7, pp. 1439–1459, 2009.

[248] K. J. Tietze, *Clinical skills for pharmacists-E-book: A patient-focused approach*, ch. 4, p. 49. Elsevier Health Sciences, 2011.

[249] Y. Bakri, B. Christopher, and S. Alouini, "Second generation of intrauterine balloon tamponade: new perspective," *BMJ innovations*, vol. 6, no. 1, 2020.

[250] 2019.

[251] W. H. Organization, "Trends in maternal mortality 2000 to 2017: estimates by who, unicef, unfpa, world bank group and the united nations population division," 2019.

[252] E. Kondoh, Y. Chigusa, A. Ueda, H. Mogami, and M. Mandai, "Novel intrauterine balloon tamponade systems for postpartum hemorrhage," *Acta Obstetricia et Gynecologica Scandinavica*, vol. 98, no. 12, pp. 1612–1617, 2019.

[253] E. T. Maya, K. A. Buntugu, L. Ako, and E. K. Srofenyoh, "Condom tamponade in the management of primary postpartum haemorrhage: a report of three cases in ghana," *African Journal of Reproductive Health*, vol. 19, no. 3, pp. 151–157, 2015.

[254] A. Aderoba, B. Olagbuji, A. Akintan, O. Oyeneyin, O. Owa, and J. Osaikhuwuomwan, "Condom-catheter tamponade for the treatment of postpartum haemorrhage and factors associated with success: a prospective observational study," *BJOG: An International Journal of Obstetrics & Gynaecology*, vol. 124, no. 11, pp. 1764–1771, 2017.

[255] A. Evensen, J. M. Anderson, and P. Fontaine, "Postpartum hemorrhage: prevention and treatment," *American family physician*, vol. 95, no. 7, pp. 442–449, 2017.

[256] W. H. Organization, *WHO recommendations for the prevention and treatment of postpartum haemorrhage*. World Health Organization, 2012.

[257] UN, "Transforming our world: the 2030 agenda for sustainable development." Available at `https://sustainabledevelopment.un.org/post2015/transformingourworld` accessed: 16/04/2021.

[258] A. L. L. Alves, J. C. Senra, C. R. Gonçalves, B. R. Ribeiro, C. N. de São José, E. B. Candido, L. B. Silva, and A. L. Silva-Filho, "Uterine tamponade in postpartum hemorrhage: A new handmade intrauterine balloon," *International Journal of Gynecology & Obstetrics*, vol. 149, no. 2, pp. 248–250, 2020.

[259] G. B. Theron, "Management of postpartum hemorrhage with free-flow pressure controlled uterine balloon," *International Journal of Gynecology & Obstetrics*, vol. 142, no. 3, pp. 371–373, 2018.

[260] M. Mvundura, D. Kokonya, E. Abu-Haydar, E. Okoth, T. Herrick, J. Mukabi, L. Carlson, M. Oguttu, and T. Burke, "Cost-effectiveness of condom uterine balloon tamponade to control severe postpartum hemorrhage in kenya," *International Journal of Gynecology & Obstetrics*, vol. 137, no. 2, pp. 185–191, 2017.

[261] A. Natarajan, J. Kamara, R. Ahn, B. D. Nelson, M. J. Eckardt, A. M. Williams, S. A. Kargbo, and T. F. Burke, "Provider experience of uterine balloon tamponade for the management of postpartum hemorrhage in sierra leone," *International Journal of Gynecology & Obstetrics*, vol. 134, no. 1, pp. 83–86, 2016.

[262] S. Suarez, A. Conde-Agudelo, A. Borovac-Pinheiro, D. Suarez-Rebling, M. Eckardt, G. Theron, and T. F. Burke, "Uterine balloon tamponade for the treatment of postpartum hemorrhage: a systematic review and meta-analysis," *American Journal of Obstetrics and Gynecology*, 2020.

[263] A. Ramanathan, M. J. Eckardt, B. D. Nelson, M. Guha, M. Oguttu, Z. Altawil, and T. Burke, "Safety of a condom uterine balloon tamponade (esm-ubt) device for uncontrolled primary postpartum hemorrhage among facilities in kenya and sierra leone," *BMC pregnancy and childbirth*, vol. 18, no. 1, p. 168, 2018.

[264] H. A. Anger, R. Dabash, J. Durocher, N. Hassanein, S. Ononge, L. Frye, A. Diop, S. Beye, G. Burkhardt, and E. Darwish, "The effectiveness and safety of introducing condom-catheter uterine balloon tamponade for postpartum haemorrhage at secondary level hospitals in uganda, egypt and senegal: a stepped wedge, cluster-randomised trial," *BJOG:*

An International Journal of Obstetrics & Gynaecology, vol. 126, no. 13, pp. 1612–1621, 2019.

[265] S. Matsubara, H. Takahashi, and A. K. Lefor, "Re: The effectiveness and safety of introducing condom-catheter uterine balloon tamponade for postpartum haemorrhage at secondary level hospitals in uganda, egypt and senegal: a stepped wedge, cluster-randomised trial: Difficulty evaluating the efficacy of introducing the condom-catheter," *Bjog: an International Journal of Obstetrics and Gynaecology*, vol. 127, no. 3, pp. 425–425, 2019.

[266] A. Weeks, "Does balloon tamponade really make postpartum haemorrhage worse?," *BJOG: An International Journal of Obstetrics & Gynaecology*, vol. 126, no. 13, pp. 1622–1622, 2019.

[267] D. Piaggio, D. Medenou, R. C. Houessouvo, and L. Pecchia, "Donation of medical devices in low-income countries: Preliminary results from field studies," in *International Conference on Medical and Biological Engineering*, pp. 423–427, Springer, 2019.

[268] L. Di Pietro, D. Piaggio, I. Oronti, A. Maccaro, R. C. Houessouvo, D. Medenou, C. De Maria, L. Pecchia, and A. Ahluwalia, "A framework for assessing healthcare facilities in low-resource settings: Field studies in benin and uganda," *Journal of Medical and Biological Engineering*, pp. 1–9, 2020.

[269] Oberk, "How different seals work and best applications of each." Available at `https://www.oberk.com/packaging-crash-course/dispensing-closures-sealing-systems` accessed: 16/04/2021.

[270] K. Mollazadeh-Moghaddam, M. Dundek, A. Bellare, A. Borovac-Pinheiro, A. Won, and T. F. Burke, "Mechanical properties of the every second matters for mothers-uterine balloon tamponade (esm-ubt) device: In vitro tests," *American Journal of Perinatology Reports*, vol. 9, no. 04, pp. e376–e383, 2019.

[271] C. Georgiou, "Balloon tamponade in the management of postpartum haemorrhage: a review," *BJOG: An International Journal of Obstetrics & Gynaecology*, vol. 116, no. 6, pp. 748–757, 2009.

[272] A. S., P. D., T. M., and et al., ""a matlab app to assess, compare, and validate new methods against their benchmarks"," *8th European Medical and Biological Engineering Conference. In press.*, 2020.

[273] S. Verma, "Frugal innovation in medical devices: Key to growth in emerging economies," *Journal of Medical Marketing*, vol. 16, no. 2, pp. 66–73, 2017.

[274] D. Yadav, R. K. Garg, A. Ahlawat, and D. Chhabra, "3d printable biomaterials for orthopedic implants: Solution for sustainable and circular economy," *Resources Policy*, vol. 68, p. 101767, 2020.

[275] P. Schroeder, K. Anggraeni, and U. Weber, "The relevance of circular economy practices to the sustainable development goals," *Journal of Industrial Ecology*, vol. 23, no. 1, pp. 77–95, 2019.

[276] K. M. Antony, D. A. Racusin, M. A. Belfort, and G. A. Dildy III, "Under pressure: intraluminal filling pressures of postpartum hemorrhage tamponade balloons," *AJP reports*, vol. 7, no. 2, p. e86, 2017.

[277] C. Georgiou, "Intraluminal pressure readings during the establishment of a positive 'tamponade test'in the management of postpartum haemorrhage," *BJOG: An International Journal of Obstetrics & Gynaecology*, vol. 117, no. 3, pp. 295–303, 2010.

[278] C. Georgiou, "A review of current practice in using balloon tamponade technology in the management of postpartum haemorrhage," *Hypertension Research in Pregnancy*, vol. 2, no. 1, pp. 1–10, 2014.

[279] S. Matsubara, "An effective addition of uterine balloon tamponade (condom-balloon) in rural settings," *Rural and Remote Health*, 2016.

[280] T. Kim and H. Lee, "Uterine compression sutures with intrauterine balloon tamponade," *Acta Obstetricia et Gynecologica Scandinavica*, vol. 93, no. 3, pp. 313–314, 2013.

[281] H. Y. Kwon, Y.-H. Kim, Y.-W. Park, and J.-Y. Kwon, "Efficacy of bakri balloon tamponade in massive postpartum hemorrhage: a series of 57 cases," *Perinatology*, vol. 27, no. 4, pp. 236–243, 2016.

[282] T. M. Rankin, N. A. Giovinco, D. J. Cucher, G. Watts, B. Hurwitz, and D. G. Armstrong, "Three-dimensional printing surgical instruments: are we there yet?," *Journal of Surgical Research*, vol. 189, no. 2, pp. 193–197, 2014.

[283] S. Kondor, C. Grant, P. Liacouras, M. Schmid, L. Michael Parsons, V. K. Rastogi, L. S. Smith, B. Macy, B. Sabart, and C. Macedonia, "On demand additive manufacturing of a basic surgical kit," *Journal of Medical Devices*, vol. 7, no. 3, 2013.

[284] S. Mitra and J. Rennie, "Neonatal jaundice: aetiology, diagnosis and treatment," *British Journal of Hospital Medicine*, vol. 78, no. 12, pp. 699–704, 2017.

[285] V. K. Bhutani, "Building evidence to manage newborn jaundice worldwide," *The Indian Journal of Pediatrics*, vol. 79, pp. 253–255, 2012.

[286] NHS, "Newborn jaundice," 2017. Available at: `https://www.nhs.uk/conditions/jaundice-newborn/`, Accessed: 26/04/2021.

[287] M.-T. Tsai and D.-C. Tarng, "Beyond a measure of liver function—bilirubin acts as a potential cardiovascular protector in chronic kidney disease patients," *International journal of molecular sciences*, vol. 20, no. 1, p. 117, 2019.

[288] T. L. Gomella, M. Cunningham, and F. Eyal, "Management, procedures, on-call problems, diseases, and drugs," 2004.

[289] B. Ansong-Assoku, "Neonatal jaundice," Jun 2020. Available at: `http://knowledge.statpearls.com/chapter/0/23803/`, Accessed: 26/04/2021.

[290] B. O. Olusanya, S. Teeple, and N. J. Kassebaum, "The contribution of neonatal jaundice to global child mortality: findings from the gbd 2016 study," *Pediatrics*, vol. 141, no. 2, 2018.

[291] T. M. Slusher, T. G. Zamora, D. Appiah, J. U. Stanke, M. A. Strand, B. W. Lee, S. B. Richardson, E. M. Keating, A. M. Siddappa, and B. O. Olusanya, "Burden of severe neonatal jaundice: a systematic review and meta-analysis," *BMJ paediatrics open*, vol. 1, no. 1, 2017.

[292] V. K. Bhutani, A. Zipursky, H. Blencowe, R. Khanna, M. Sgro, F. Ebbesen, J. Bell, R. Mori, T. M. Slusher, N. Fahmy, *et al.*, "Neonatal hyperbilirubinemia and rhesus disease of the newborn: incidence and impairment estimates for 2010 at regional and global levels," *Pediatric research*, vol. 74, pp. 86–100, 2013.

[293] S. E. Mir, B. A. Van Der Geest, and J. V. Been, "Management of neonatal jaundice in low-and lower-middle-income countries," *BMJ paediatrics open*, vol. 3, no. 1, 2019.

[294] R. K. Pejaver and J. Vishwanath, "An audit of phototherapy units," *The Indian Journal of Pediatrics*, vol. 67, no. 12, pp. 883–884, 2000.

[295] C. Greco, G. Arnolda, N.-Y. Boo, I. F. Iskander, A. A. Okolo, R. Rohsiswatmo, S. M. Shapiro, J. Watchko, R. P. Wennberg, C. Tiribelli, *et al.*,

"Neonatal jaundice in low-and middle-income countries: lessons and future directions from the 2015 don ostrow trieste yellow retreat," *Neonatology*, vol. 110, no. 3, pp. 172–180, 2016.

[296] B. K. Cline, H. J. Vreman, K. Faber, H. Lou, K. M. Donaldson, E. Amuabunosi, G. Ofovwe, V. K. Bhutani, B. O. Olusanya, and T. M. Slusher, "Phototherapy device effectiveness in nigeria: irradiance assessment and potential for improvement," *Journal of tropical pediatrics*, vol. 59, no. 4, pp. 321–325, 2013.

[297] V. K. Bhutani, B. K. Cline, K. M. Donaldson, and H. J. Vreman, "The need to implement effective phototherapy in resource-constrained settings," in *Seminars in perinatology*, vol. 35, pp. 192–197, Elsevier, 2011.

[298] "What are jaundice and kernicterus?," Dec 2020. Available at: `https://www.cdc.gov/ncbddd/jaundice/facts.html`, Accessed: 26/04/2021.

[299] NHS, "The nhs long term plan," 2019. Available at: `https://www.longtermplan.nhs.uk/publication/nhs-long-term-plan/`, Accessed: 26/04/2021.

[300] P. W. Chang and W. M. Waite, "Evaluation of home phototherapy for neonatal hyperbilirubinemia," *The Journal of pediatrics*, vol. 220, pp. 80–85, 2020.

[301] NHS, "Delivering home based phototherapy to babies with physiological jaundice," 2018. Available at: `https://www.england.nhs.uk/atlas_case_study/delivering-home-based-phototherapy-to-babies-with-physiological-jaundice/`, Accessed: 26/04/2021.

[302] B. O. Olusanya, T. A. Ogunlesi, P. Kumar, N.-Y. Boo, I. F. Iskander, M. F. B. de Almeida, Y. E. Vaucher, and T. M. Slusher, "Management of late-preterm and term infants with hyperbilirubinaemia in resource-constrained settings," *BMC pediatrics*, vol. 15, no. 1, pp. 1–12, 2015.

[303] American Academy of Pediatrics Subcommittee on Hyperbilirubinemia and others, "Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation," *Pediatrics*, vol. 114, no. 1, pp. 297–316, 2004.

[304] E. A. Sully, A. Biddlecom, and J. E. Darroch, "Not all inequalities are equal: differences in coverage across the continuum of reproductive health services," *BMJ global health*, vol. 4, no. 5, p. e001695, 2019.

[305] B. Compton, D. M. Barash, J. Farrington, C. Hall, D. Herzog, V. Meka, E. Rafferty, K. Taylor, and A. Varghese, "Access to medical devices in low-income countries: addressing sustainability challenges in medical device donations," *NAM Perspectives*, 2018.

[306] S. Eze, W. Ijomah, and T. C. Wong, "Accessing medical equipment in developing countries through remanufacturing," *Journal of Remanufacturing*, vol. 9, no. 3, pp. 207–233, 2019.

[307] A. Montealegre, N. Charpak, A. Parra, C. Devia, I. Coca, and A. M. Bertolotto, "Effectiveness and safety of two phototherapy devices for the humanised management of neonatal jaundice," *Anales de Pediatría (English Edition)*, vol. 92, no. 2, pp. 79–87, 2020.

[308] K. Hodal, "Portable kit to treat babies with jaundice goes on trial in peru," Apr 2019. Available at: `https://www.theguardian.com/global-development/2019/apr/16/portable-kit-to-treat-babies-with-jaundice-goes-on-trial-in-peru`, Accessed: 26/04/2021.

[309] Brezinski, "Little sparrows technologies bili-hut," 2016. Available at: `https://www.engineeringforchange.org/solutions/product/little-sparrows-technologies-bili-hut/`, Accessed: 26/04/2021.

[310] N. Shahroni and M. M. Addi, "An automatic and portable phototherapy garment (appg) with integrated non-invasive bilirubin detector," in *TENCON 2018-2018 IEEE Region 10 Conference*, pp. 1999–2004, IEEE, 2018.

[311] B. M. Quandt, M. S. Pfister, J. F. Lübben, F. Spano, R. M. Rossi, G.-L. Bona, and L. F. Boesel, "Pof-yarn weaves: controlling the light outcoupling of wearable phototherapy devices," *Biomedical optics express*, vol. 8, no. 10, pp. 4316–4330, 2017.

[312] Z. Gong, Z. Xiang, X. OuYang, J. Zhang, N. Lau, J. Zhou, and C. C. Chan, "Wearable fiber optic technology based on smart textile: A review," *Materials*, vol. 12, no. 20, p. 3311, 2019.

[313] C. V. Hulzebos, D. E. Vader-van Imhoff, A. F. Bos, and P. H. Dijk, "Should transcutaneous bilirubin be measured in preterm infants receiving phototherapy? the relationship between transcutaneous and total serum bilirubin in preterm infants with and without phototherapy," *PloS one*, vol. 14, no. 6, p. e0218131, 2019.

[314] "Transcutaneous bilirubin measurements in newborns: Clinical and costeffectiveness, and guidelines." Available at: `https:`

//www.cadth.ca/sites/default/files/pdf/htis/2017/RB1164%20Transcutaneous%20Bilirubin%20Measurement%20Final.pdf, Accessed: 21/05/2021.

[315] S. R. Howie, B. E. Ebruke, M. Gil, B. Bradley, E. Nyassi, T. Edmonds, S. Boladuadua, S. Rasili, E. Rafai, G. Mackenzie, *et al.*, "The development and implementation of an oxygen treatment solution for health facilities in low and middle-income countries," *Journal of global health*, vol. 10, no. 2, 2020.

[316] M. Andellini, S. De Santis, F. Nocchi, E. Bassanelli, L. Pecchia, and M. Ritrovato, "Clinical needs and technical requirements for ventilators for covid-19 treatment critical patients: an evidence-based comparison for adult and pediatric age," *Health and Technology*, vol. 10, no. 6, pp. 1403–1411, 2020.

[317] "The life-saving power of medical oxygen.." Available at: https://www.who.int/news-room/feature-stories/detail/the-life-saving-power-of-medical-oxygen, Accessed: 21/05/2021.

[318] "Portable oxygen concentrators market: Covid-19 impact on global market demand, opportunities, and analysis & forecast to 2026.." Available at: https://www.biospace.com/article/portable-oxygen-concentrators-market-covid-19-impact-on-global-market-demand-o
Accessed: 21/05/2021.

[319] B. D. Bradley, S. Chow, Y.-L. Cheng, E. Nyassi, S. R. Howie, and D. Peel, "The use of oxygen concentrators in the gambia: A study of over 5 years of experience in," *Second WHO Global Forum on Medical Devices*, 2013.

[320] B. D. Bradley, S. Chow, E. Nyassi, Y.-L. Cheng, D. Peel, and S. R. Howie, "A retrospective analysis of oxygen concentrator maintenance needs and costs in a low-resource setting: experience from the gambia," *Health and Technology*, vol. 4, no. 4, pp. 319–328, 2015.

[321] W. H. Organization *et al.*, *Technical Specifications for Oxygen Concentrators: WHO Medical Device Technical Series*. World Health Organization, 2016.

[322] R. Friesen, M. Raber, and D. Reimer, "Oxygen concentrators: a primary oxygen supply source," *Canadian Journal of Anesthesia*, vol. 46, no. 12, p. 1185, 1999.

[323] B. Bradley, J. Light, A. Ebonyi, P. N'Jai, R. Ideh, B. Ebruke, E. Nyassi, D. Peel, and S. Howie, "Implementation and 8-year follow-up of an

uninterrupted oxygen supply system in a hospital in the gambia," *The International Journal of Tuberculosis and Lung Disease*, vol. 20, no. 8, pp. 1130–1134, 2016.

[324] B. Bradley, J. Light, B. Singhateh, D. Koli, D. Peel, Y.-L. Cheng, and S. Howie, "Temperature and humidity trends in a health centre in the gambia: Implications for back up battery-life in tropical settings," in *7th International Conference on Appropriate Healthcare Technologies for Developing Countries*, pp. 1–5, IET, 2012.

[325] S. Rismani, V. der Loos, H. Machiel, *et al.*, "The competitive advantage of using 3d-printing in low-resource healthcare settings," in *International Conference on Engineering Design, ICED15*, 2015.

[326] A. Beroza, "3d printing in low resource healthcare settings: Analysis of potential implementations," Master's thesis, Michigan technological university, 2019.

[327] E. C. Dillon Jr, J. H. Wilton, J. C. Barlow, and W. A. Watson, "Large surface area activated charcoal and the inhibition of aspirin absorption," *Annals of emergency medicine*, vol. 18, no. 5, pp. 547–552, 1989.

[328] "How to make activated charcoal (with pictures).." Available at: `https://homesteadsurvivalsite.com/make-activated-charcoal/`, Accessed: 21/05/2021.

[329] W. H. Organization *et al.*, "Technical specifications for invasive and non-invasive ventilators for covid-19: Interim guidance," *COVID-19: Clinical care*, 2020.

[330] S. Butterworth *et al.*, "On the theory of filter amplifiers," *Wireless Engineer*, vol. 7, no. 6, pp. 536–541, 1930.

[331] W. E. Schneider and R. Young, "Spectroradiometry methods," *Handbook of Applied Photometry, ed. Casimer De Cusatis*, p. 252, 1997.

[332] W. Emery and A. Camps, *Introduction to satellite remote sensing: atmosphere, ocean, land and cryosphere applications*. Elsevier, 2017.

[333] T. Lister, P. A. Wright, and P. H. Chappell, "Optical properties of human skin," *Journal of biomedical optics*, vol. 17, no. 9, p. 090901, 2012.

[334] A. A. Lamola and M. Russo, "Fluorescence excitation spectrum of bilirubin in blood: a model for the action spectrum for phototherapy of neonatal jaundice," *Photochemistry and photobiology*, vol. 90, no. 2, pp. 294–296, 2014.