# Understanding Ancillary Care in the Global South: Examining Practice, current Ethical Guidance, and Stakeholder Perspectives in Malawi

**Blessings Msango Kapumba**

**A thesis submitted in accordance with the requirements for the degree of Doctor of Philosophy of the**

**University of London**

**July 2023**

**Department of Global Health and Development**

**Faculty of Public Health and Policy**

**LONDON SCHOOL OF HYGIENE & TROPICAL MEDICINE**

The work contained in this thesis was supported by the Global Health Bioethics Network (Wellcome Trust Strategic Award - 096527)

**Declaration by student**

I, Blessings Msango Kapumba, declare that I have read and understood the school's definition of plagiarism and cheating given in the Research Degrees Handbook. I confirm that the work presented in this thesis has been written by me and that it is the record of work carried out by me, or principally by myself, in collaboration with others as acknowledged and indicated in the thesis appropriately.

Name: **Blessings Msango Kapumba**

Signed: 

Date: 30/07/2023

**Abstract**

**Introduction**: The provision of ancillary care is increasingly becoming recognised as an ethical requirement in healthcare-related research across the globe. This does, however, raise complex ethical concerns when research is conducted in resource-constrained settings where participants may have additional healthcare needs that fall outside the scope of the research and are not provided for by the local healthcare system. Despite growing calls for the provision of ancillary care to study participants during medical research, there remains a noticeable gap in ethics guidelines for medical researchers in resource-constrained settings. I aim to address this evidence gap by examining the existing ethical and policy guidance, current practices, research stakeholders' perspectives on the provision of ancillary care in medical research, and the ethical and social implications of this in the global south.

**Methods**: First, I conducted a systematic review and meta-synthesis of research published between 2004 and 2020 to understand the practices relating to ancillary care during medical research in East and Southern Africa. A database search was conducted, and all the papers included (24 out of 4,710) were appraised for methodological quality and assessed to see if they reported on ancillary care provision to study participants. Next, I undertook a chronological discourse analysis of research guidance documents. For this, 34 documents outlining international ethical guidelines and policy were reviewed to explore the evolution of language referring to ancillary care and the way it has been used in different documents. Finally, I gathered primary data from research stakeholders in Malawi on their experiences of and views on ancillary care. I conducted a qualitative methods study between September 2021 and June 2022 in Malawi, gathering data, through in-depth interviews, on the experiences of 45 research stakeholders (including researchers, research ethics committee members, health officials, researcher funders and study participants) and their perspectives of ancillary care. I also explored research stakeholders' views on the impact of ancillary care in medical research conducted in resource-constrained settings.

**Results**: The systematic review and meta-synthesis showed that approaches to the provision of ancillary care in health-related research are not standardised, and ethics guidance is not consistent. In the discourse analysis, I found varied interpretations of ancillary care language, leading to diverse applications in practice due to the absence of explicit definitions in international ethics guidelines. In the qualitative in-depth interview study in Malawi, all stakeholders perceived the significant role of ancillary care in promoting participants' well-being and viewed it as a way for researchers to demonstrate reciprocity. Still, they were concerned about the absence of ethical guidance to support it. There was a suggestion that consideration of ancillary care could be possible on a case-by-case basis but that most of the support from research projects should be directed towards strengthening the public health system, emphasising public good above personal benefit. Funding for the research was also recognised as a limiting factor for ancillary care, owing to the potential conflict between meeting study demands and treating participants' additional health conditions.

**Conclusion**: My findings provide evidence that the practice of ancillary care provision in health-related research in resource-constrained settings is limited by the absence of guidelines for researchers regarding what ancillary care to provide and how to provide it. The study identifies key principles to consider when addressing ancillary care, emphasizing the urgent need to establish formal ethical frameworks that safeguard the well-being of research participants. Through the application of constructivist and interpretivist epistemological approaches, this research promotes culturally sensitive and contextually grounded ethical practices, enhancing research integrity in the global south. The implications of this study call for increased awareness and collaboration among researchers, institutions, and funders to ensure equitable and ethically responsible research conduct, ultimately improving ancillary care practices and participant welfare in RCS. Furthermore, the study provides insights that could inform future strategies for engaging international and local research ethics and regulatory bodies in developing specific

guidelines for the provision of ancillary care in these settings. Future research might investigate the question of whether ancillary care should prioritise individual participants over public benefit.

**Contents**

**Acknowledgements**

I am grateful to God for the gift of life, good health, and a spirit of persistence that has made it possible for me to complete my PhD.

This research was made possible by the participation of various research stakeholders, both within Malawi and internationally. Thanks to them all for agreeing to be interviewed and sacrificing their limited time to participate in this research. I appreciate the views they shared during our discussions and the fact they gave consent for me to share the findings globally.

A special thank you to colleagues and friends at the Malawi-Liverpool Wellcome Trust Clinical Research Programme, especially the social science team and the PhD students group. You provided a happy atmosphere for me to work in, much fun and laughter, and excellent minds to bounce ideas off. The Clinical Research Support Unit team at Malawi-Liverpool Wellcome Trust Clinical Research Programme provided me with all the necessary information and guidance for sourcing the documents that I used for this study, as well as supporting the ethics approval process. Thank you for the support and guidance that you provided during the data collection process and throughout the research period.

I wish to acknowledge with gratitude the support from my supervisors, Prof. Janet Seeley and Dr Nicola Desmond; they made my PhD journey an exciting learning experience. Janet and Nicola, thank you for your encouragement and guidance during this attempt to research ancillary care ethics in health-related research conducted in the global south. Thank you for always making time for me and thank you for the important insights that challenged me to think differently and dig deeper into my analysis. Thank you for the feedback that has always made me reflect on how my analysis and findings might be received by a non-social-science audience. I am grateful to you for your thorough review of all my papers and for always providing detailed feedback. Janet, thank you for always checking up on me when I go silent for some days; I have always felt that I was in safe hands. I learned a lot during my time under the supervision of both of you, and I appreciate your being part of this journey. I am also

grateful to my Advisory Panel – Prof. Michael Parker, Dr Jantina De Vries, Dr Katherine Littler, Prof. Moffat Nyirenda, and Dr Deborah Nyirenda – for their support, advice, and insights, and for their enthusiasm for my PhD project. Thank you!

I am grateful to the Global Health Bioethics Network, funded by Wellcome Trust, for meeting all the costs of my PhD (tuition fees, travel expenses, field costs, and stipend). The team also provided me with an opportunity to receive feedback on my PhD project in each year of my studies through the summer schools and conferences they organised.

I also wish to acknowledge Isabel Tucker for proofreading my thesis. Thank you, Isabel, for proofreading my thesis. You highlighted areas with obvious mistakes that I couldn't see.

Finally, I would like to thank my family. My parents, brothers, and sisters have been steadfastly supportive of my work and decision to move far away from home for part of this period, and they have always encouraged me to be curious, to explore, and to learn. My parents-in-law and my sister in-law Golda Rapozo have been inspirational and unbelievably encouraging over the last three years as regards my work, my research, and my life generally. My partner, Pempho, could not have been more supportive, endlessly encouraging me and enabling me to continue my PhD after the birth of our son by working part time. And finally, I'd like to offer my thanks to Micah, our son, for giving me tight deadlines and for the utter joy you have brought.

**Abbreviations**

| | |
|---|---|
| CIOMS | Council for International Organizations of Medical Sciences |
| COMREC | College of Medicine Research Ethics Committee |
| LMICs | low-and-middle-income countries |
| MLW | Malawi-Liverpool Wellcome Programme |
| NCD | non-communicable disease |
| NHSRC | National Health Sciences Research Committee |
| QECH | Queen Elizabeth Central Hospital |
| RCS | resource-constrained settings |
| REC | Research Ethics Committee |

## Chapter 1. Introduction

In the two decades since Belsky and Richardson (2004) conceptualised ancillary care, there has been a growing interest in the topic, but there is still a relative paucity of academic work that addresses how it might be implemented in contexts with limited resources. In particular, questions about its practicalities have received little or no attention in health-related research conducted in the global south. Understanding how ancillary care is provided in resource-constrained settings (RCS) will aid the design of evidence-based policies, guidelines or frameworks that promote ethical practice in research. Practice in this area must be guided by ethical principles to enhance study participants' protection, rights, and well-being (Beauchamp and Childress, 2001) with an understanding of the social context in which the principles are applied. Applying ethical principles such as respect for persons, beneficence and justice sets clear ethical responsibilities for researchers concerning how participants may benefit from the provision of ancillary care in settings with limited health care. Operationalising these ethical principles requires researchers and research institutions to identify, analyse and respond to potential ethical issues (Blackmer, 2010) that may come with ancillary care, including examining the ethical guidance for and exploring research stakeholder's perspectives on ancillary care for studies conducted in RCS. In this thesis, I adopt a sociological perspective to comprehensively explore and understand the ethical framework or framing pertaining to ancillary care. Through this sociological lens, I aim to gain deeper insights into the complexities of ancillary care ethics and its implications for research participants and healthcare practices. By considering the broader social context, this thesis contributes to a more nuanced and contextually grounded understanding of the ethical dimensions of ancillary care in the field of health-related research. This thesis explores current practices, existing ethics guidance, and research stakeholder perspectives on ancillary care in health-related research, as well as the ethical and social implications for research conducted in the global south. The study was designed to shed light on the researcher’s response to the ancillary care needs of study participants and the impact that it has on the ethical conduct of health-related research in RCS.

In 2004, Belsky and Richardson first set out the role of ancillary care ethics in health-related research, emphasising that their efforts cover both clinical and public health research ethics (Belsky and Richardson, 2004). The primary purpose of providing ancillary care is to ensure the well-being and safety of research participants. This can include diagnosing and treating medical conditions, managing symptoms, providing counselling or mental health services, or offering referrals to appropriate healthcare providers. In Belsky and Richardson's (2004) initial definition of ancillary care, such care was described as "care which is not required to make a study scientifically valid, to ensure a trial's safety, or to redress research injuries" ( pg. 1494) and "care not required by sound science, safe trial conduct, morally optional promises, or redressing subject injury" (Belsky and Richardson, 2004 pg. 26). Richardson (2012 pg. 2-3) refined their definition of ancillary care as "medical care that the research subjects need but that is not required to make a study scientifically valid, to ensure a study's safe, or to redress research injuries". In health-related studies, participants may receive ancillary care when unforeseen health diagnoses arise or when existing health conditions require attention. In applying such a definition, the context of the study is seen to have a major influence on how the researcher make considerations to respond to the participant's demands for ancillary care. In the context of research conducted in situations of need, ancillary care has a unique position for the numerous health issues that individuals (volunteer research participants) face in these contexts (Belsky and Richardson, 2004). There are several examples of the ancillary healthcare needs of study participants in RCS. Belsky and Richardson (2004) provide the example of researchers investigating a new treatment for tuberculosis in a setting with limited resources, like Malawi, and discovering that some patients/participants are HIV-positive - do they have an obligation to provide antiretroviral medication? Is the researcher's responsibility limited to just informing the participant that they have another illness (HIV) and guiding them towards medical care and treatment, or does it extend to providing (or covering the cost of) HIV management, including antiretroviral medication (Nuffield Council on Bioethics, 2002)? On the other hand, does the concept of ancillary care defined by Belsky and Richardson (2004) include consideration for non-physical health, such as addressing the mental health

problems identified for a participant during research? These are some of the questions that raise complex ethical concerns regarding the ancillary care obligations of researchers towards their participants when research is conducted in RCS (Participants in the 2006 Georgetown University Workshop, 2008, CIOMS, 2017).

Particularly, the obligation to provide ancillary care to study participants in RCS is argued most forcefully because many people there live in poverty and have no health insurance, while the populations also bear a disproportionate share of the global disease burden, including conditions such as HIV/AIDS, tuberculosis, and malaria, as well as non-communicable diseases. In addition, many people in RCS lack access to basic medical care services, owing to a lack of resources or limited availability of such services within their settings (UNICEF and WHO, 2013, Lignou, 2011). As a result, medical researchers conducting their research in these RCS may expect to encounter a variety of unmet health needs among their research participants that may demand health care ancillary to the condition under study (Miller et al., 2008). The guidelines set out by the CIOMS (2002) include in Guideline 21 the observation that "*while sponsors are generally not obliged to provide healthcare services beyond what is required for their research, it is morally praiseworthy to do so*" ( pg. 82). The challenge, however, is that it is often unclear what that recommendation means, and the scope and practicalities of ancillary care in RCS remain unexplored. Furthermore, although a number of guidelines, including those of the CIOMS (2016) and Declaration of Helsinki (World Medical Association, 2013), refer to the issue of ancillary care, none of them provide explicit analysis of and guidance on the topic (Kapumba et al., 2022).

During the stakeholder discussions that took place at the Participants in the 2006 Georgetown University Workshop (2008) and the 2012 workshop on ancillary care in central francophone Africa (Tshikala et al., 2012), it was strongly recommended that medical researchers and their sponsors from high-income nations or global north conducting research in low-and-middle-income countries (LMICs) consider providing ancillary care to their study participants.

Stakeholders in these workshops highlighted the notion that researchers in RCS should recognise the needs of their participants and take some responsibility for providing ancillary care. Moreover, these discussions also point to the many anticipated healthcare challenges that participants or the general population experience in RCS. On the other hand, there is limited research on the practicalities of the provision of ancillary care when research is conducted in RCS. Most of the long-standing empirical and theoretical work on ethical issues raised by ancillary care has been directed at establishing whether medical researchers and their sponsors regard it as a moral obligation to enhance the health of their research participants. While the emphasis on understanding the moral responsibility of researchers is significant, it may be insufficient to understand the practical ethical complexities of ancillary care comprehensively.

The ancillary care obligation in health-related research is best represented by the partial-entrustment model and the whole-person model (Belsky and Richardson, 2004, Richardson, 2007, Dickert and Wendler, 2009), both of which justify for the existence of special ancillary care duties for researchers (and sponsors) that are above and beyond the general duties of rescue (McKie and Richardson, 2003). According to the partial-entrustment model, special ancillary care duties are derived from a morally significant feature of the researcher–participant relationship: the participants entrust some aspects of their health to researchers. On the other hand, the whole-person model considers such duties to be based on the moral significance of the researcher–participant relationship as a whole (Richardson, 2007, Dickert and Wendler, 2009, Bridget et al., 2013). As a means of clearly defining the content of the duties supported by the two models, Merritt et al. (2010) and Merritt (2011) developed a two-step framework to facilitate the identification of baseline ancillary care obligations derived from the duty of rescue. However, having the normative models is insufficient to ensure that ancillary care obligations are met in health-related research. Understanding the practices is essential for informing debate and designing appropriate guidelines for the consideration of ancillary care in health-related research conducted in RCS (Participants in the 2006

Georgetown University Workshop, 2008). The need to promote the provision of ancillary care as a means of protecting research participants in any human subject related research and build fair and effective partnerships between researchers and their participants is essential for ensuring the ethical delivery of high-quality research.

Given the importance that ancillary care may have for participants who may have or present with additional health needs (positive ancillary care needs), and given their limited options for medical care, it is essential to understand the practices and experiences of research stakeholders regarding ancillary care in Malawi, as well as their perspectives on it, since Malawi is one setting with limited healthcare capacity. My analysis sheds light on several crucial aspects of ancillary care in health-related research, offering empirical evidence that brings attention to additional ethical issues related to limitations in current practices. Moreover, my work contributes to the discourse on enhancing ethical practices in research by advocating for the inclusion and careful consideration of ancillary care in RCS. However, applying ethical standards in health research in RCS can be particularly challenging because of unmet health, economic and social welfare needs; thus, attention must be paid to the social context in which the standards are applied. Additionally, it is necessary to understand what specific research ethics guidance is available on the consideration of ancillary care. This study will contribute an essential step towards narrowing the knowledge gap in this setting.

**Research objectives**

The thesis aims to achieve the following four main objectives:

1. To describe the provision and explore the practices relating to ancillary care in health-related research in east and southern Africa over the last decade.
2. To examine the practical features that have underpinned the evolution of the topic of ancillary care in health-related research ethics guidance documents.
3. To investigate the experiences and perspectives of research stakeholders on the process, practice, and expectations of research participants regarding the provision of ancillary care.

4. To determine how the values and practices beyond perceived ancillary care obligations of medical researchers may need to be balanced in decisions about study demands and ethical requirements.

**Study structure**

This study involved three phases: first, the systematic review and meta-synthesis, which involved a review of published research papers to establish what has been reported regarding ancillary care. The second phase involved documenting the chronology of how the text that describes ancillary care in ethics guidance and policy documents has changed over time. The stakeholder engagement phase, which is the main focus of this thesis, involved interviews with key research stakeholders involved in conducting health-related research in Malawi. The primary objective of the stakeholder engagement phase was to examine research stakeholder perceptions and experiences of ancillary care in biomedical research projects in Malawi.

**Thesis Outline**

This thesis includes three academic papers, each of which constitutes a separate chapter (Chapters 5, 6 and 7). As detailed in the research paper cover sheets, the papers presented in Chapters 5 and 6 have been published. Furthermore, the paper presented in Chapter 7 has been submitted, reviewers have provided feedback, and the responses to the reviewers' comments have been resubmitted to the journal. I include a short introductory overview before each of the papers, outlining the rationale for the paper and linking it to the other papers and to the rest of the thesis to facilitate the coherence of the body of work. This thesis contains five additional chapters: introduction, literature review, study setting, methodology, and discussion.

**Chapter 1** introduces the topic and gives the rationale for the research and an overview of the aims and structure of the thesis.

**Chapter 2** provides a background on ancillary care and outlines the forms of ancillary care in

health-related research, the ethical justification for the provision of ancillary care, and some potential ethical issues associated with the provision of ancillary care, with a particular focus on RCS. The conceptual framework that informed this study is also presented.

**Chapter 3** describes the overall methodology used for the study and includes the overall study design; a description of the study location; descriptions of the systematic review and the discourse analysis; an overview of the qualitative in-depth interview data collection methods; and an outline of the ethical considerations during the conduct of the study. The specific methods applicable to other chapters are described in the respective chapters.

In **Chapter 4,** I outline Malawi and its health system, as well as the location where this study was conducted and from which my findings are derived. This chapter provides background information on the healthcare constraints in Malawi, the research and research ethics context, and the link between those factors and the need for ancillary care in health-related research.

**Chapter 5** is written as a paper and presents a systematic review and meta-synthesis of ancillary care practices in health-related research in east and southern Africa. This chapter reports findings suggesting that some researchers consider providing ancillary care to their study participants even though the practice does not adhere to any recognised standards. The provision of care and support to study participants during health-related research extends to people who are not participating in the research, such as siblings. It also includes the provision of non-medical support, such as clothes and food. The findings from this study revealed the lack of guidance for ancillary care, which is what informed my decision to conduct a discourse analysis of guidance documents.

**Chapter 6** is written as a paper and presents the results of the chronological discourse analysis of ancillary care in ethics guidance documents. It examines both international and local (Malawian) ethics guidance documents, as well as policy documents from the research funding organisations and the Malawi Ministry of Health. This chapter reports findings suggesting that guidance for ancillary care in ethics guidance documents is not made explicit.

**Chapter 7** describes the perspectives of research stakeholders on the provision of ancillary care in the context of the global south, using Malawi as a case study. It draws on the qualitative data collected from key research stakeholders, including study participants, researchers, Research Ethics Committee (REC) members, and Ministry of Health officials, on their experiences and on their views on the researcher's obligation to provide ancillary care to their study participants during health-related research. All stakeholders thought that ancillary care had potential benefits for individuals who volunteer to participate in research. However, some thought that providing support to strengthen the health system in general would benefit a greater majority.

**Chapter 8** concludes the thesis with a discussion of the overall findings from each research paper. The chapter uses the conceptual framework I developed by drawing on existing literature and integrates the findings from different sources in order to draw conclusions and recommendations on the practicalities of the provision of ancillary care during health-related research in the global south, including setting ethics principles for ancillary care provision in RCS. In this chapter, I also present the strengths and limitations of the PhD research and finally end with the conclusions of the thesis.

The appendices provided at the end of this thesis include ethical approvals, informed consent forms, data collection tools, and other work that has been disseminated, such as posters and slides presented at international conferences.

**Role of the candidate**

I came up with the overall concept, formulated the research questions, and designed all the studies presented in this thesis, in collaboration with my supervisors, Janet Seeley and Nicola Desmond. For the qualitative research study with the key research stakeholders, I developed the study tools, sought ethical approval, recruited the participants, and led all the data generation processes. The qualitative in-depth interview study contributes the majority of the fieldwork-generated data to this thesis.

I conceptualised and conducted the entire analysis with the support of my supervisors and co-authors. I have written the entire thesis, including all papers and related material. I am the primary author of every paper presented in this thesis.

## Chapter 2. Literature review

### Introduction

This chapter outlines the conceptual and theoretical underpinnings that inform this thesis. It begins with a discussion about the global discourse on ancillary care in health-related research and how this has been framed, the contributions of the models that have been used to justify the ethics of ancillary care consideration, and how those contributions have been applied in health-related research globally. I then narrow down to draw on this literature to understand the application of ancillary care in RCS. This is linked to a debate about the ethics and social implications of providing ancillary care in settings with limited resources, such as Malawi, while considering how this may be limited by the social and structural context. I draw on these debates, in this thesis, by investigating researchers' responses to the ancillary care needs of their participants, where research is conducted in RCS. Lastly, I introduce the theoretical framework developed from this literature review to inform the development and theoretical framing of this research.

### Provision of care in health-related research

The ethics of health-related research, as well as the ethics of any health-related research that involve human subject participation, require that researchers must regard the interests and safety of their participants as paramount (ICH - GCP Guidelines, 1996, World Medical Association, 2013, CIOMS, 2017). On the basis of this long-standing tradition in health-related research, it is generally acknowledged that medical researchers and funders have a responsibility to provide for the health needs of research participants. However, these health needs must be related primarily to the study; for example, immediate adverse events related to study procedures (CIOMS, 2016) including medication side effects, injury, psychological harm or trauma. This raises ethical issues when research participants have additional healthcare needs besides those related to the condition under study. For instance, a research team identifying malnutrition in children recruited for a malaria study. When the required ancillary care is beyond the scope of the study, how do researchers respond to or resolve

such needs? What ethical principles govern the researcher's decisions?

From an ethical perspective, health-related research should evolve from a position of paternalistic beneficence to one where the principle of nonmaleficence and patient welfare is foregrounded (Sacristán, 2015). While this may seem not to be a problem in settings where resources are available or access to medical care is not a challenge, in RCS, it is very likely that many participants experience additional healthcare needs outside the scope of the research, which may not be provided for by the local healthcare system. This forms the basis for arguments that medical researchers have some obligation to provide care for the ancillary health needs of their research participants. Principles 8 and 9 of the Declaration of Helsinki, as revised in 2013, state respectively that *"while the primary purpose of medical research is to generate new knowledge, the goal can never overshadow the rights and interests of individual research participants", and that "physician-researchers must promote and safeguard the health of their research participants"* (World Medical Association (2013). Such recommendations do not, however, define what kind of health needs medical researchers should concentrate on or the extent to which care can be provided. I agree with the comment made by a stakeholder at the Participants in the 2006 Georgetown University Workshop (2008) that this guidance could be construed in two ways: either as suggesting that there is no moral need to provide ancillary care, or as merely noting that the moral commitment belongs to someone other than the study team.

In recent years, policymakers and scholars concerned with research ethics have declared a new ethical imperative: that researchers should consider responding to the ancillary care needs of their study participants during health-related research. Research participants often need this kind of care because researchers might make incidental diagnoses during their investigations or discover unmet health needs resulting from the limited availability of and access to healthcare services. In the case where additional healthcare needs are identified among study participants in high-income settings or well-resourced settings, participants could be referred to medical practitioners or hospitals that would provide the care needed.

Clear communication, collaboration with healthcare providers, and oversight from ethics committees can help ensure that participants receive appropriate medical attention when needed in higher-income settings (Emanuel et al., 2004). However, in RCS, where most people do not have access to healthcare, participants with incidental diagnoses may not be able to access the healthcare they need unless it is provided for them by the research team. This is so because sometimes, even if they do get referred, the services are not available at the facility they are getting referred to. These ancillary care obligations on the part of medical researchers are crucial for supporting research participants with health needs that may emerge during study procedures. As such, Richardson (2012) regarded ancillary care as an ideal moral obligation which is carried out by all individuals (in this case, researchers, sponsors, funders and the healthcare system), or special duties explicitly fulfilled towards their study participants by researchers.

Over the past decade, there has been increasing global discourse on the ethics of ancillary care provision to research participants, with rising concerns about how that care is provided, including in RCS. Moreover, Richardson (2012) claims that despite the empirical evidence demonstrating the significance of ancillary care obligations, the current ethics framework for health-related research conducted with human subjects and all guidelines that apply to it do not explicitly address the issue of ancillary care. The Nuffield Council on Bioethics (2002) contends that providing care during health-related research is a distinct and essential way global health researchers can fulfil their ethical obligations towards their participants and the communities where they conduct their research. Building on earlier studies (Belsky and Richardson, 2004, Merritt et al., 2010, Bridget et al., 2013, Jacobson et al., 2016), there has been a rapid increase in the number of institutions that support the provision of ancillary care (Krubiner et al., 2015). Guideline 6 of the international ethical guidelines set out by the CIOMS (2016), supports the provision of ancillary care with studies conducted in LMICs.

> *"…, researchers and sponsors must make adequate provisions for addressing participants' health needs during research and, if necessary, for the transition of*

*participants to care when the research is concluded. The obligation to care for participants' health needs is influenced, among other things, by the extent to which participants need assistance and established effective care is available locally. When participants' health needs during and after research cannot be met by the local health infrastructure or the participant's pre-existing health insurance, the researcher and sponsor must make prior arrangements for adequate care for participants with local health authorities, members of the communities from which persons are drawn, or nongovernmental organizations such as health advocacy groups"* (CIOMS, 2016 pg. 21).

Such international guidelines identify the researchers' primary obligations to consider research participants' rights, safety, and well-being above the interests of science and society. However, a statement in the commentary to the same guideline 6, while supporting what is stated in the guideline, clearly indicates that sponsors are not obligated to provide ancillary care but advise for a referral (CIOMS, 2016). Such statements clearly show a gap in research ethics guidelines regarding ancillary care, similar to what Krubiner and colleagues reported on the landscape of ancillary care generally, *"the preponderance of institutions taking no position on ancillary care represents a clear policy gap"* (Krubiner et al., 2015 pg. 18). Similarly, owing to these gaps in ethical guidance on ancillary care, I also examine the present guidelines for ancillary care in Malawi as a case study for RCS.

On the other hand, since most health-related research carried out in RCS is funded by international organisations (Nuffield Council on Bioethics, 2002), researchers conducting their studies in these settings may be subject to restrictions that limit the demands put on research, including for the need to provide ancillary care for research participants (Richardson, 2012, Philpott et al., 2010). For example, the existing National Institutes of Health policies actually restrict the use of funds to provide care that is not required for scientific validity or participant safety, limiting the researcher's ability to provide ancillary care directly (Philpott et al., 2010). These restrictions pose severe challenges for medical

researchers who wish to consider providing ancillary care to their participants in RCS. Despite these restrictions, Krubiner et al. (2015) reported that a significant number of sponsors recognise the need for ancillary care in their guidance documents. For example, the Wellcome Trust has a policy that permits researchers to meet the ancillary care needs of their participants on condition that certain ethical conditions (such as no "undue influence") are satisfied (Wellcome Trust, 2010). Nevertheless, there is limited information on the practical application of this policy for health-related research conducted in RCS.

**Moral justification of ancillary care obligations**

The ethics of whether researchers have ancillary care duties towards their participants have been established by many scholars, using justifications such as the theory of justice (Hooper, 2010), entrustment (Richardson, 2012), and rescue (Rulli and Millum, 2016). In addition, the concept of ancillary care obligations is grounded on assumptions that draw on assessments of urgency, the researcher's fiduciary duty to participants, the capacity of the local healthcare infrastructure, and the capacity of the research infrastructure (Belsky and Richardson, 2004, Hyder and Merritt, 2009, Merritt et al., 2010, Bright and Nelson, 2012, Jacobson et al., 2016). These scholars have most often cited the general duty of justice, rescue, and partial entrustment as substantive models that support the notion of ancillary care obligations on the part of a medical researcher. It is widely argued, however, that these substantive models have both philosophical and practical challenges that constrain their use to justify the provision of ancillary care during the conduct of research, particularly in RCS. I next consider these substantive models as applied to ancillary care in health-related research conducted in RCS.

***Ancillary care for healthcare justice***

Enabling healthcare access entails supporting individuals in acquiring suitable healthcare resources for the purpose of enhancing their well-being. Access encompasses multiple facets that necessitate assessment across various dimensions. While service availability is a prerequisite for access, barriers such as affordability, physical accessibility, and acceptability

significantly influence utilization. Attaining equitable access involves acknowledging diverse perspectives, health requirements, and societal contexts, and demands the consideration of equity dimensions in relation to service availability, utilization, and outcomes (Gulliford et al., 2002). Global healthcare injustices encompass systemic disparities and inequities in access to healthcare services and resources across different regions and populations worldwide. These injustices raise significant ethical concerns within the realm of global health research, particularly where research is conducted in RCS. Recognising the disparities in access to healthcare between ow- and middle-income countries and high-income countries sheds light on the larger inequities in allocating healthcare resources and developing healthcare infrastructure. By acknowledging and addressing these ethical dimensions, for example, through the consideration to provide ancillary care, researchers can contribute to mitigating these injustices.

The principle of health justice is a critical ethical concept in research involving human subjects and is founded on values (United States - NCPHS of Biomedical and Behavioral Research, 1978, CIOMS, 2002). Overall, healthcare is recognised globally for its importance for the quality of life of individuals, as a right or a public good (United Nations, 1948). Grossly inadequate access to healthcare is considered a violation of human rights and, thus, an injustice in itself. Ancillary care discussions delve into issues of justice and fairness. They consider how the provision of ancillary care can contribute to addressing health disparities and promoting equitable access to healthcare, particularly for disadvantaged populations involved in research. Acknowledging the need for ancillary care emphasizes the presence of health disparities between LMICs and high-income countries. It underscores the inequitable access to healthcare resources, infrastructure, and services, which are frequently more constrained in LMIC settings. This discrepancy brings attention to wider global health inequities and the imperative to take measures to tackle them. By ensuring that participants' healthcare needs are met during and beyond the research process, ancillary care promotes equity, fairness, and the recognition of participants' inherent worth. It contributes to reducing

health disparities, particularly among disadvantaged populations, and helps foster a more ethical and inclusive approach to global health research.

In health-related research, the “duty of justice” may relate to the “moral obligation” of researchers to provide ancillary care for their research participants. This is especially the case when research is conducted in settings where it is anticipated that most participants may have additional healthcare needs beyond the scope of the study. The researchers may demonstrate fairness by providing care to their participants; for example, by ensuring that research participants are as well treated for their additional healthcare needs and not just focusing on research.

The duty of justice to provide ancillary care during health-related research is also supported by Ruger’s health capability paradigm (Ruger (2010), which requires researchers to treat their participants fairly. This paradigm justifies ancillary care provision through the idea that everyone has to efficiently minimise limitations in the health capabilities of individuals or others. In the case of RCS, where local healthcare systems are unable to ensure the capacity of their populations’ health, medical researchers have to bring a basic level of health to individuals who volunteer to participate in their research, to meet this obligation (Ruger, 2010, Pratt and Loff, 2014). According to the principle of justice, the provision of ancillary care is a prerequisite for medical researchers and sponsors to provide a reasonable plan for their participants’ unmet health needs in RCS.

The Nuffield Council on Bioethics (2002) strongly recommends that medical researchers respect each participant by committing themselves to considering their interests while involving them in research. By doing that, medical researchers demonstrate concern about the healthcare needs of their participants and help reduce disparities and promote equality in global health (Benatar, 2000, Bridget et al., 2013, Pratt and Loff, 2015). The current ethical guidelines for international research, such as those set out by the CIOMS (2000 and 2016), also promote justice within the researcher–participant relationship and describe what is

required of sponsors and researchers to promote the general well-being of the participants and their communities (CIOMS, 2017). Richardson (2012) also notes that while it is not up to medical researchers or sponsors to remedy global injustices in the provision of healthcare, they do encounter many who suffer as a result of such injustices, and they have certain obligations to help mitigate this suffering if they have the ability to do so. The main question that drives this argument is, however, that when international medical researchers want to promote global health justice through their research, how efficiently or fairly do they respond to the health needs of the research participants while still fulfilling their primary obligation, namely, to generate ethical generalisable knowledge and fulfil their obligations towards study funders?

***Ancillary care as a duty to rescue***

A second dominant pillar of ancillary care obligations is the duty to rescue, which in medical ethics is concerned with protecting others from potential risks, irrespective of the opportunity costs (Jonsen, cited in Lubbe, 2019). McKie and Richardson (2003) and Smith (1990) have all described the duty to rescue in healthcare as the necessity to save known individuals from facing avoidable health risks without giving too much thought to the cost of doing so or as an effort to avoid serious harm to someone when the cost of rescue attempts is minimal. Similarly, in line with Hadorn (1991), medical researchers cannot ignore their research participants when they realise that the lives of the latter are at risk and rescue measures are available. In such circumstances, it demonstrates a callous disregard by the researcher for human life and a lack of compassion for those suffering from illnesses (Lubbe, 2017, Rulli and Millum, 2016). For example, medical researchers working in RCS may have a rescue obligation to provide ferrous sulphate (a supplement to treat iron deficiency anaemia) to participants who experience iron deficiency (anaemia) symptoms, even when their study is on malaria. Doing so costs little for the researcher and addresses a critical need.

Given the health challenges in RCS, it is more likely that the majority of research participants have significant unmet health needs that they can be rescued from at minimal cost and

without depleting the resources meant for the study. In this respect, in this study, I will attempt to address questions regarding the practices used as part of ancillary care provision in RCS, and the extent of such care: how do researchers determine the scope of ancillary care fairly and reasonably, at a minimal cost? If researchers in these settings recognise the obligation to provide care as a duty to rescue for such ancillary conditions, what do they do?

***Partial entrustment***

The third model is partial entrustment, which is concerned with the trust established between researchers and their participants. Trust is essential to the proper functioning and continued success of health-related research (Alberts and Shine, 1994). Smirnoff and colleagues defined trust in clinical or health-related research as the belief by the study participant that his/her interests are considered before the interests of the study or the researcher (Smirnoff et al., 2018). Smirnoff et al.'s definition would be reflective of Wright's (2010) view, that a trustworthy researcher acknowledges the value of the trust that the participant vests in them and uses this to rationally decide how to act. Trustworthiness, as described by Kerasidou (2017), refers to the manifestation of characteristics exhibited by the trustee (in this case, the researcher), reflecting their positive intentions and "good will" towards the trustor (the study participant). When it comes to providing ancillary care, the researcher's trustworthiness can be demonstrated by recognizing and appreciating the trust placed in them to assist study participants with ancillary care requirements. As emphasised by O'Neill (2002), since trust is a voluntary aspect that cannot be compelled, the only means of building trust between researchers and study participants is by enhancing trustworthiness. Researchers aiming to enhance their trustworthiness, rather than merely creating an impression of trustworthiness, can do so by actively addressing the ancillary care needs of their participants. This involves recognizing the vulnerability inherent in the trusting relationship and taking appropriate steps to acknowledge and meet those needs. If one can rely on a researcher or research institution to act as expected, then one should be able to trust them as individuals, as well (Wright, 2010).

Without trust in research, voluntary participation would be impossible, and health-related

research could not continue, thus depriving the public of potential benefits. The role of trust in health-related research and the application to ancillary care was set out by (Belsky and Richardson, 2004) and Richardson (2012) on the basis of the premise that research participants entrust certain (but not all) aspects of their health to researchers. In this regard, Richardson defends the provision of ancillary care as a way of influencing the trust that participants develop in the researchers. Belsky and Richardson (2004) present a model incorporating factors that strengthen the determination of the researchers' responsibilities as far as ancillary care is concerned, including the degree of vulnerability and dependency of participants and the depth of the relationship. Similarly, a Cochrane review (McKinstry et al., 2006) describes the main aspects of trust as the partnership notion, the voluntary response to a set of expectations, the study participant vulnerability and study-related risks, and the belief that is embedded in the hope that others will have concern for your interests.

Another significant aspect that influences entrustment is the process of informed consent, as described by Richardson (2012). The relationship between researchers, their institutions and research participants is often described as a consent-based relationship, which depends on reasonable expectations among study participants and the proven capacity of the researchers. Informed consent is a crucial aspect of ancillary care in health-related research because it signifies trustworthiness of researchers towards their participants (World Medical Association, 2013). Participants should be informed about the potential for ancillary care, including the scope, limitations, and potential risks associated with it. Informed consent discussions should address the balance between the research objectives and the provision of ancillary care, ensuring that participants understand the potential impact on their participation. When the participant consents to participate in a study, a relationship is established, and the terms of the relationship between the researcher and the participant are defined. In this process participants feel confident that researchers will uphold ethical standards, protect their rights, and act in their best interests (National Academies of Sciences, Engineering, and Medicine, 2018, p. 82). The partial-entrustment model sees the special

responsibility for ancillary care resulting from this process, even if it comes to light while carrying out study procedures. According to this principle, the provision of ancillary care is expected and is regarded as one way of building the trust of research participants in researchers. The fact that participants implicitly but inevitably entrust some aspects of their health to the researchers reflects the importance of providing care for their ancillary needs. Kerasidou (2017) emphasises the point that because research participants depend on researchers to act in line with their expectations, it is necessary for researchers to retain this role and provide care as anticipated.

**Ethical issues relating to ancillary care in RCS**

Carrying out health-related research in RCS poses additional ethical challenges because study participants and communities may be especially vulnerable to poverty-related exploitation. They are more likely to be illiterate, to lack resources and to have poor access to good-quality education and healthcare. Furthermore, they will probably have no experience of or knowledge about research (Grady, 2006). In this section, I describe the ethical issues related to the provision of ancillary care in health-related research conducted in RCS.

***The risk of therapeutic misconception***

Researchers and ethicists have long been concerned about the expectations for direct medical benefit expressed by participants in early phase clinical trials (Jansen, 2011). Earlier research on this topic contemplated the possibility that participants misunderstand the purpose of clinical research or are misinformed about the likelihood that they will receive medical benefits from these trials (Horng and Grady, 2003). Recent attention, however, has shifted to the possibility that participants in these trials are merely expressing optimism or hope (Jansen, 2011). The expression of hope for medical care in clinical research refers to the positive expectation or desire for beneficial healthcare outcomes through participation in research studies. It reflects the optimistic outlook of individuals who hope to receive effective treatments, improved health outcomes, or potential medical advancements as a result of their involvement in clinical research (Miller and Rosenstein, 2003). Therapeutic optimism entails

an optimistic perspective regarding the potential positive results of a therapeutic intervention, while on the contrary, therapeutic misconception pertains to a miscomprehension or misinterpretation of the fundamental nature and objectives of clinical research (Appelbaum et al., 2004). According to Appelbaum et al. (2004), therapeutic misconceptions pose an ethical problem in RCS because of the failure on the part of research participants to differentiate the goals of research intervention from those of ordinary care, which seriously undermines informed consent. Dunn et al. (2006) also note that when subjects incorrectly attribute a predominantly therapeutic purpose to research procedures, the concepts of risk and/or benefit are likely to be misunderstood. While medical researchers may reject their participants' therapeutic misconceptions during research because they are concerned with strengthening the scientific validity of their study, participants may still think that researchers are best positioned to help them meet their health needs. However, there is some discussion in African bioethics about when "therapeutic misconception" is an expression of the expectation of a reciprocal relationship, where taking care of the (limited) health needs of research participants can be seen as a reasonable way of acknowledging participants' help to researchers (Gyekye, 2011).

Another critical factor for developing an ethical framework for ancillary care in research, especially in RCS, is an understanding of what motivates individuals to participate in health-related research. Mfutso-Bengo et al. (2008) report that some people would choose to participate in research projects as the only way of accessing quality healthcare services. Research participants in RCS may join the study because they think it is their last hope for an untreatable disease (Belsky and Richardson, 2004, Henderson et al., 2007, Mfutso-Bengo et al., 2008). Some scholars have suggested that the provision of ancillary care may distort informed consent by promoting a therapeutic misconception (Haire and Ogundokun, 2014) because the research participant expects that researchers will automatically help them with any health needs as a result of their commitment to the research study and the trust they have put in them. Similarly, the Nuffield Council on Bioethics (2002) notes that research

participants in settings with limited resources also expect that researchers will feel concerned about their health status or diagnosis.

***Risk of undue inducement***

The principle of “undue inducement” applies when the incentives (financial or non-financial) offered to participants are so attractive that they may encourage people to participate in a research project against their best interests and thereby risk suffering serious harm (Emanuel, 2005). Because of their likely low socio-economic status, unmet health needs, and lack of access to quality healthcare facilities, participants in RCS may be more susceptible to undue inducement. Consequently, according to Grant and Sugarman (2004), if the participant is particularly vulnerable, inducement that would ordinarily be acceptable may become undue. The provision of ancillary care in RCS can potentially pose a risk of undue inducement due to several factors specific to these settings. Some of these factors may include:

- Limited access to healthcare - RCS often lack adequate healthcare infrastructure and services, resulting in limited access to essential medical care (Kruk et al., 2018). In such contexts, the provision of ancillary care within a research study may be seen as a unique opportunity to receive medical attention that is otherwise scarce or unaffordable. This perception of limited access can create a heightened reliance on the ancillary care provided, potentially influencing participants' decisions to enrol or continue in the research study.
- Vulnerability and desperation - individuals in RCS may face significant health challenges and socio-economic disadvantages (Russell, 2004, McIntyre et al., 2006). The provision of ancillary care can tap into their vulnerability and desperation for healthcare, making them more susceptible to undue influence. Participants may feel compelled to participate or remain in the research solely for the ancillary care, even if they may not fully understand the research objectives or appreciate the associated risks and benefits.
- Perceived benefits as compensation - in RCS, the provision of ancillary care may be seen as a form of compensation or tangible benefit for participants' involvement in the research study. Participants may view the ancillary care as a necessary resource to address their

healthcare needs, which could inadvertently lead to the perception of a quid pro quo arrangement. This perception of a direct exchange between research participation and ancillary care can undermine the voluntary nature of informed consent and introduce the risk of undue inducement.

- Influence of power dynamics - power imbalances and unequal relationships between researchers and participants can be more pronounced in RCS. Participants may feel obliged to comply with the expectations of researchers or community leaders who may have authority or control over the provision of ancillary care (Tindana et al., 2011). This power dynamic can further increase the risk of participants feeling coerced or unduly influenced to participate in research against their own best interests. For example, in rural communities, the local senior community members hold significant influence and play a vital role in decision-making. Recognising the potential benefits of participating in research studies, particularly those involving healthcare interventions, the senior community members may advocate for increased research participation among community members, solely to sustain the limited community healthcare. The influence exerted by the senior community members may compromise the voluntary decision-making process of individuals and potentially overshadow their personal autonomy.

Haire and Ogundokun (2014) state that participants may regard the provision of ancillary care as of excessive value (access to better healthcare persuades them to participate in health research). Emanuel and colleagues (2016) support this argument by stating that inducement does not only have to be monetary. Some participants choose to participate in health-related research for non-financial reasons, precisely because of access to ancillary healthcare benefits (Stunkel and Grady, 2011), and such participants could be regarded as being unduly influenced. The guidelines set out by the CIOMS (2016), however, clearly state that, even though the provision of ancillary care may persuade people in RCS to enrol, it should not be considered an undue inducement. Even with this, many scholars have argued that the extended position of ancillary care may unacceptably exaggerate the incentives to potential

study volunteers (Participants in the 2006 Georgetown University Workshop, 2008). One of the motivations for conducting this research in Malawi, where a considerable proportion of participants in health-related research are likely to have unmet ancillary healthcare needs, is the ongoing discussion regarding what constitutes undue inducement.

***Risk of exploitation of vulnerable populations***

Resnik (2003) and Emanuel et al. (2014) define exploitation as when an individual, for their own benefit, takes unfair advantage of another person, or harms, disrespects, or acts unjustly toward them in a particular relationship or transaction. In 2005, Jason Lott described an individual's vulnerability when participating in health-related research if they are unable to give informed consent or are more susceptible to exploitation (Lott, 2005). Individual participants in all health-related research can be vulnerable to exploitation and harm. Current ethical guidelines for international research promote justice within the researcher–participant relationship and describe what is required of sponsors and researchers to prevent the exploitation of trial participants (Nuffield Council on Bioethics, 2002, El Setouhy et al., 2004, Pratt and Loff, 2011, CIOMS, 2016). Participants in RCS may face increased risks of exploitation because of poverty and limited access to healthcare, and because they have little experience and understanding of research. According to de Melo-Martín and Ho (2008), this provides a sound reason for researchers to protect subjects from exploitation and undue harm while ensuring that they as researchers achieve their research objectives.

International medical researchers working in RCS are required to have a good understanding of the socio-economic and political milieu that frames the context in which they conduct their studies and that greatly influences the health of their research participants (Benatar, 2000, Cash, 2006). This includes understanding factors that impinge on participants' abilities to access standard healthcare services. In health-related research, one of the most widely cited absolute criteria for assessing whether or not a study is, in reality, exploitative is the failure of the researchers to provide participants with sufficient information to enable them to give valid consent (Macklin, 2004). Often exploitation of individuals participating in research occurs because researchers may seem to have more power, experience, and control than their

participants (Emanuel et al., 2014, Gilson, 2006). There are concerns over participant exploitation when international researchers or researchers from the global north go to RCS to do their research (Kim et al., 2017), mainly because the majority of individuals who participate in research in these settings have different forms of vulnerabilities that relate to healthcare (Emanuel et al., 2014).

In this study, I will describe whether providing ancillary care could be exploitative, as medical researchers may seem to benefit from taking advantage of vulnerable research participants in RCS by offering additional incentives. However, there are also important questions about whether it is exploitative or not to provide ancillary care.

**Forms of ancillary care**

Ancillary care provided to research participants can be of different forms and related to different purposes, times, and contexts where the research is conducted. While some forms of ancillary care, which researchers recognise, maybe reasonably easy to implement, others are costly and require substantial expertise and finance. Even where specialised medical care is freely available, there can be many ways in which researchers could at least help participants to get access to it; for example, by facilitating access to ancillary care for their participants. For example, Barsdorf and colleagues (2010) explored the value of assisted referral with staff members and patients at rural primary care clinics in KwaZulu-Natal, South Africa. In many settings, an assisted referral may act as an incentive, for example by assisting the recipient to circumvent long queues with direct referral cards for antiretroviral treatment initiation in HIV intervention trials.

***Diagnostic practices and screening***

Screening research participants for their ancillary care needs may include activities researchers perform when recruiting participants to their studies. For example, researchers may include screening services that are not part of their research but part of the process of examining an individual as part of recruitment considerations. Medical researchers may discover through this process other problems besides the condition under investigation; these

are ancillary-care needs – ancillary to the condition under investigation. Diagnostic ancillary care may include supporting the local healthcare system to provide laboratory testing of samples, as well as radiology, genetic testing, and more. Another example would be medical researchers testing their participants for diabetes in a study of pregnant women during antenatal visits.

***Referral***

Merritt and colleagues (2015) note a researcher's responsibility to facilitate ancillary care through referral as an ethical issue. They cite a systematic review by Krubiner et al. (2015), which found that 23 institutions in RCS (about half of those they studied) explicitly took a position on the responsibility of researchers to provide ancillary care – half of these organisations recommended that ancillary care be provided through local healthcare services. With the referral, the researchers can both convey that the care is needed and provide some detailed medical information that may help with its provision. The responsibilities of local medical hosts are then to provide expertise, medical resources, and access. Richardson (2012) notes that participants who show up with ancillary-care needs may require only a referral to the appropriate specialist. In some other cases (in RCS), participants with ancillary-care needs may not have any source of care other than whatever the research teams provide.

A country's public healthcare system holds the primary responsibility or obligation to promote health capabilities and reduce any shortfall in their population's health. However, in contexts where the public system is overburdened, any plans to provide ancillary care to research participants may impose ethically inappropriate burdens on the healthcare system and those who participate in research. The report published by the National Bioethics Advisory Commission (2001) indicates that extreme poverty, inadequate primary healthcare resources, and difficulties in accessing, or an inability to access, basic and essential health services pose a unique challenge to conducting health-related research in LMICs. While worried about neglecting people with significant health needs who have nowhere else to seek

healthcare services, participants in a workshop on ancillary care in central francophone Africa were equally concerned about the excessive burden that ancillary care can constitute for health researchers in RCS (Tshikala et al., 2012). Owing to the extent and complexity of these health needs in RCS, Tshikala et al. (2012) suggest integrating ancillary care into the local healthcare system. Participants in a stakeholder engagement workshop on research ethics in central francophone Africa suggested that "*when specific ancillary care needs can be clearly anticipated, researchers should collaborate with local communities to create or bolster existing services to meet those needs, and the costs of those services should be reflected in the research budget*" (Tshikala et al., 2012). However, even though this may seem to be a good idea, there are still concerns about the sustainability of the provision of ancillary care for chronic conditions when the study closes. Since this might be the greatest challenge in many RCS, appropriate arrangements with collaborating local partners or with the local health system are needed for where referrals can be made (Bridget et al., 2013). Medical researchers need to make a proper plan for ancillary care referrals by partnering with other organisations that share their interests. It is ethically unacceptable to tell participants that the researchers provide all the necessary measures for screening but will not make provision for the treatment needed or any supportive care for the advanced condition.

***Therapy or treatment***

Therapeutic ancillary care involves medical researchers providing treatment to their research participants that is not within the scope of the study. In contrast to referring participants for any ancillary care, this involves researchers, where necessary, providing direct care to their participants. During the design phase of the study, researchers may consult with communities where the study will be conducted to find out what the ancillary health needs of their potential participants might be. This care is provided as one means of addressing participants' ancillary care needs and also of supporting the local health system, notably in RCS, where services are not available. Therapeutic care may range from providing treatment for specific conditions in a participant to arranging rehabilitation, as well as including physical or occupational therapy.

**Study conceptual framework**

When considering what is important in ancillary care, it is critical to address the principles of justice and trust between researchers and their subjects. On the other hand, special consideration must be given to issues regarding the exploitation of vulnerable populations in health-related research undertaken in RCS. My focus on ancillary care practices in RCS brings these concepts to the fore, as most studies in this domain use these models, at least to tackle the issue of understanding the limitations imposed by wider issues on the moral obligation to provide ancillary care. Richardson (2012) emphasises that these concepts are critical for moral reasons, and medical researchers should provide ancillary care to their participants. While there can be concerns that providing healthcare outside the study is not moral, the practice cannot be ignored in the context of the RCS (Belsky and Richardson, 2004). Taking an ethical approach is about achieving a common purpose and perspective in health-related research practice, as well as introducing institutional procedures which drive decisions that are considerate and respectful of individuals and a range of perspectives.

To understand the ethical complexities of ancillary care provision in RCS, I developed a conceptual framework (Figure 1) that delineates how justice, trust, exploitation of vulnerable populations, and use of the different systems of influence might affect the provision of ancillary care. The framework is based on an understanding of the interplay of these systems. The four systems identified as influencing the ethical practice of ancillary care in Malawi and RCS more generally are research funding agencies, researchers, the healthcare system context, and the research ethics and regulatory guidance.

Research funders support research that addresses important societal challenges and may advocate explicitly to promote responsible research and innovative practices. However, funding does not necessarily extend to ancillary care needs. It is important to note that the funding responsibility for ancillary care can be complex and may vary depending on individual circumstances, regional healthcare policies and expectations, and the specific services required (Council for International Organisations of Medical Sciences, 2017). The main

question I explore, however, is whether they have or include plans for ancillary care as recognised in different contexts. How much do they plan for the support they provide towards ancillary care to all the research that is conducted in RCS for the promotion of healthcare justice while at the same time ensuring participants are not exploited? Another critical issue considered is concern that resources meant to achieve research objectives could be depleted. Still, one would argue for the inclusion of a special budget intended to cover the anticipated or incidental ancillary care needs of the study participants. To promote health justice and show responsibility for individuals who volunteer to participate in health-related research, and to avoid exploitation, ancillary care support from research funders is critical.

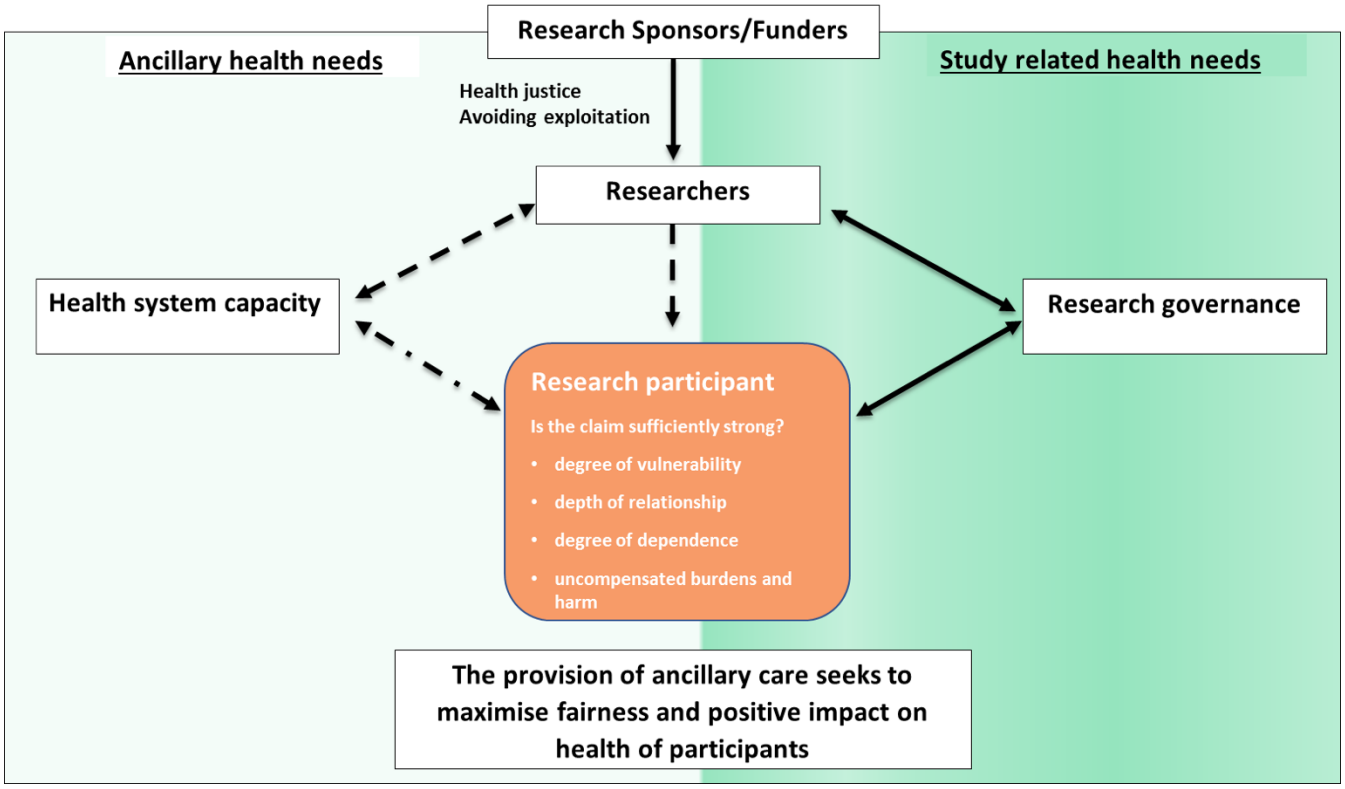
On the other hand, as research investigators and researchers gain a better understanding of the context in which research is conducted, they must ensure that appropriate ancillary care plans are included in their protocols. Through consultation with the local healthcare system and research regulatory authorities when designing research projects, researchers can learn what ancillary healthcare needs their participants might have. The consultation with the community, in particular, helps them gain an in-depth understanding of individual and community health needs. As reflected in this framework, the trust established between researchers and participating communities and individuals is another critical factor that influences researchers' ancillary care duties towards their participants. Research participants expect to gain more benefit from research than just participation (Miller and Weijer, 2006). In addition, researchers' capacities (resources and expertise) are important when considering what additional support can be provided to meet the participants' ancillary health needs.

Another important support system for ancillary care is the research ethics and regulatory bodies that are concerned with the safety and welfare of research participants. The ethics bodies put in place guiding principles and standards on how medical researchers can protect their participants from study-related harm. All medical researchers follow guidance from these bodies, so they play an essential role in guiding decisions around ancillary care. They safeguard the fair conduct of health-related research and ensure that research participants

are not exploited in the process. Similarly, on the other hand, the local healthcare system has an obligation to provide healthcare services to individuals according to their health needs. In order to achieve that, they must have the capacity to provide for all the health needs of the population, whether an individual is involved in research or not. In this framework, however, the broader question is: how does the provision of ancillary care impact on the healthcare system in terms of gains or burdens or workload of staff? Does the local healthcare system have the capacity (resources and expertise) to provide the care necessary or to meet the unmet health needs? Do research participants have access to standard medical services within their setting or community?

All the systems, as described above, have a common goal that points to the individual research participant, who is central to all the ancillary care practices in this framework. Apart from the health needs related to the medical condition being researched, a research participant in RCS may have a strong claim for healthcare for their ancillary needs. The participant, to some extent, expects that the local healthcare system will address their health needs, and being involved in research, they also hope to be supported by the researchers (Mtunthama et al., 2008, Mfutso-Bengo et al., 2008). The participant's expectation of ancillary care may be based on factors such as the disease or condition they are suffering from, their socio-economic status, their vulnerability, the trust they have in researchers, the duration of the participant–researcher relationship, their access to healthcare services, and their degree of dependency on the research team for healthcare.

Figure 1: A conceptual framework for




Given the importance of justice, trust, and the exploitation of vulnerable populations to influence ancillary care decisions, one of the objectives of this thesis is to gain an understanding of the ethical and social challenges faced by research stakeholders in Malawi, so as to maximise the impact of this understanding on research ethics in RCS. The components of this framework are used throughout this thesis to demonstrate its application and address the current gaps in ancillary care in health-related research.

In line with this framework, I explored the links between participants' additional healthcare needs, ethical guidance for ancillary care provision, and the perspectives of research stakeholders on the ethics of ancillary care provision in Malawi. Through the systematic review and the discourse analysis, I identified different models and theories that are used by researchers or in health-related research to justify the provision of ancillary care; for example, the theories of justice and beneficence. In addition, while conducting the discourse analysis, I came across a description that made use of key terms like "protection of the participants' well-being" and "morally praiseworthy" as things that reflect the researcher's ethical obligation

to take into consideration the provision of ancillary care to the participants. The qualitative data from interviews with research stakeholders addressed the link between ethical considerations regarding ancillary care and the impact that ancillary care may have on the study participants and society, the research, and the health system. I identified challenges both within the health system, which limited the services provided, and coming from the funder, who imposed restrictions on the research funding that limited researchers' ability to plan for and provide ancillary care.

**Chapter summary**

In this chapter, I have outlined the framing of ancillary care as an emerging ethics concept that guides the conduct of health-related research globally but is of particular relevance where research is conducted in RCS. I have also provided a description of the conceptual framework for the study, which is informed by the models described within the chapter.

## Chapter 3. Study setting

### Introduction

In this chapter, I introduce Malawi as one of the RCS in the global south, with a focus on its health and socio-economic characteristics, which shape the research gap and the need to consider ancillary care for participants during health-related research. I also describe the research landscape, including institutions that conduct health-related research in Malawi, particularly focusing on the Malawi Liverpool Wellcome Programme.

### The context

Malawi is a landlocked country in southeast Africa that shares borders with Mozambique, Tanzania, and Zambia. The population was estimated to be 17,563,749 in 2018, up from 13,029,498 in 2008, with an average annual growth rate of 2.9% (National Statistical Office, 2019). Based on this present growth rate, the population is projected to double by 2042. At least 84% of the population is projected to live in rural areas, compared to 16% in urban centres. From 2013 to 2030, Malawi is projected to enjoy an average annual urban population growth rate of 4.2%, resulting in urbanisation. According to World Bank (2022a), the life expectancy for both sexes in Malawi is 65 years. In 2021, the per capita gross domestic product of Malawi was predicted to be 642.7 USD. Agriculture, forestry, and fisheries account for 28% of the country's gross domestic product, although the majority of the population lives below the poverty line. Estimates place informal work and formal employment at 89% and 11%, respectively. The estimated mean and median monthly incomes for the overall economically active population were USD 114 and USD 37, respectively, showing a significant disparity. Development aid remains crucial to the economy and contributes an average of 62% of overall financing in the health sector (World Bank, 2022b). Malawi's population is suffering disproportionately from severe and persistent poverty, according to the 2017 Integrated Household Survey (National Statistical Office, 2017).

### The healthcare system in Malawi

Health services in Malawi are provided principally by the Ministry of Health via a three-tiered

system (primary, secondary, and tertiary), although the number of private not-for-profit providers (for example, mostly institutions owned by religious groups) and private for-profit providers have been increasing (Munthali et al., 2014). These different levels are linked to each other through an established referral system. Primary- and secondary-level care falls under district councils. The Director of Health and Social Services is the head of the district healthcare system and reports to the District Commissioner, who is the Controlling Officer of public institutions at the district level. The public sector includes all health facilities under the Ministry of Health; district, town, or city councils; the Ministry of Defence; the Ministry of Internal Affairs and Public Security (Police and Prisons); and the Ministry of Natural Resources, Energy and Mining (Government of Malawi Ministry of Health, 2017). Public provision of healthcare is enshrined in the constitution, which states that the State is obliged "*to provide adequate health care, commensurate with the health needs of Malawian society and international standards of health care*" (Ministry of Justice, 2006 pg. 2-3). To achieve its goal of providing healthcare, the government has decentralised healthcare services and seeks to deliver health services close to the people. Health services in the public sector (public facilities) and in private facilities contracted through the Service Level Agreement (Government of Malawi Ministry of Health, 2017) included in the essential healthcare package are provided free of charge at the point of use. The major religious provider is the Christian Health Association of Malawi, which provides approximately 29% of all health services in Malawi (Malawi Ministry of Health and ICF International, 2014). Most private and private-not-for-profit providers charge user fees for their services.

Primary-level healthcare services, which typically include health services offered in health centres (facilities) and community hospitals in rural areas, are the first point of contact in the health system for patients. Health surveillance assistants provide these services comprising promotive and preventative healthcare. Community hospitals offer outpatient and inpatient care as well as minor surgical procedures. District hospitals and similar facilities run by the Christian Health Association of Malawi offer a secondary level of care. Healthcare facilities at

this level provide referral services to patients from health centres and community hospitals, as well as outpatient and inpatient services to local communities. The central hospitals provide tertiary care. Ideally, they provide specialised healthcare and referral services to patients from district hospitals within their region.

In line with the objective of delivering universal healthcare, one of the major areas of focus for the health system is the scale-up of community health interventions that have shown high impact. The government is also focusing on strengthening the referral systems between the different levels of care (Malawi Ministry of Health, 2017). Through the referral system, patients should ideally seek care first from the lower-level facilities that are closest to them and only be referred to higher-level facilities for services not available at the lower level. However, this referral system often does not work. Consequently, owing to the absence of a functional gate-keeping system, approximately 70% of the services provided are either primary or secondary services (Government of Malawi Ministry of Health, 2017).

**Availability of and access to healthcare**

Colonialism shaped the way healthcare services are made available and accessible to the general population (Tilley, 2016). It had a profound impact on healthcare systems in sub-Saharan Africa. When European powers colonised various African countries from the late 19th century to the mid-20th century, they introduced their own systems of governance, including healthcare structures that served their interests. However, these systems often neglected the needs of the local populations and focused primarily on serving the colonial powers (Stilson, 2019). In terms of access to health care, colonial powers typically established healthcare infrastructure in urban areas, serving colonial administrators, military personnel, and settlers. Access to healthcare for local African populations was limited, particularly in rural areas (Azevedo and Azevedo, 2017). Even after the end of direct colonisation, the legacies of colonialism continue to shape power dynamics and healthcare systems in African countries and other RCS (Tilley, 2016). Post-colonial governments often inherited healthcare structures that were ill-equipped to meet the needs of their populations.

Additionally, the privileging of biomedical approaches established during colonialism still influences healthcare policies and decision-making, often disregarding local understandings of disease causation and indigenous healing practices (Tilley, 2016). However, there are now calls for decolonisation of healthcare in African countries and other developing nations (Ong'era et al., 2021). The decolonization of healthcare in Africa refers to the efforts made to address the historical injustices and imbalances created by colonial rule and to establish healthcare systems that are responsive to the needs and aspirations of African populations. It involves dismantling structures, practices, and ideologies rooted in colonial rule and promoting indigenous knowledge, cultural practices, and self-determination in healthcare delivery (Barcham, 2022).

While the healthcare system is impacted by several challenges, the Government of Malawi strives to align the provision of healthcare services with the United Nations' agenda of ensuring that all people have access to effective health services (including prevention, promotion, treatment, rehabilitation, and palliative care) of sufficient quality while ensuring that the use of these services does not place the user in a position of financial hardship (WHO, 2021). However, universal access to healthcare remains unattainable, especially in rural regions, owing to a lack of healthcare personnel, a lack of basic health-facility infrastructure, and inadequate funding for health. Recent studies indicate that human resource shortages at public facilities and delays in drug supply continue to expose households and individuals to considerable out-of-pocket spending when they seek care, and in the process limit access to healthcare services (Government of Malawi Ministry of Health, 2017, Bowie and Mwase, 2011, Mueller et al., 2011). In addition, the network of public healthcare services does not, by the government's definition of physical access (within an 8-km radius of a public health facility) fall within the recommended distance; this indicates that there is still a significant proportion of the population that is underserved, especially those residing in the rural and hard-to-reach areas (Government of Malawi Ministry of Health, 2017).

Therefore, either private institutions provide services, or they are unavailable. In some

contexts, the essential health package is only on paper; in practice, such services are not available. In general, access to basic healthcare services, including screening or diagnostics and treatment, is limited. Msokwa (2021) identified several factors that contribute to the limited access to healthcare services in Malawi, including a lack of or unavailability of services, drugs, and medical equipment, long travel distances to the nearest health facility, and a shortage of healthcare workers in public health facilities. For instance, owing to a lack of resources (drugs) at medical facilities, patients may occasionally be sent home or instructed to purchase their medication from private pharmacies.

Given the limited availability of and access to healthcare services, those who volunteer to participate in health-related research may have increased expectations that they will receive some form of medical care from the researchers conducting the study. Because the majority of RCS face similar challenges, it is reasonable to anticipate that researchers will identify unmet healthcare needs among their participants which call for ancillary care provision.

**Disease burden**

Malawi, just like many other RCS continues to have a high disease burden, including HIV/AIDS, respiratory infections, malaria, diarrhoeal diseases, and perinatal conditions, notwithstanding advances made over the past decade in the provision of healthcare services. In addition, while Malawi continues to strive to reduce its communicable disease burden, it is now faced with an increase in non-communicable diseases and the double burden that this brings (Government of Malawi Ministry of Health, 2017). Insufficient information exists regarding the patterns, trends, and determinants of multimorbidity in Malawi and other low and middle-income countries (LMICs), despite its increasing prevalence. However, a recent study conducted by Price et al. (2018) revealed a significant occurrence of overweight and obesity (24%), hypertension (14%), and diabetes (3%) among both rural and urban men and women. Similarly, a systematic review conducted by Spencer et al. (2023) found that the highest prevalence of multimorbidity among medical admissions in sub-Saharan Africa was associated with HIV infection (36.4%), followed by hypertension (24.7%), diabetes (11.9%),

heart failure (8.2%), chronic kidney disease (7.7%), and stroke (6.8%). Masiye et al. (2018) and Price et al. (2018) reported that a high proportion of this burden falls on patients under 40 years of age, and the Ministry of Health increasingly recognises the importance of care delivery systems for non-communicable diseases.

Since 2004, the Government of Malawi has been committed to providing accessible and affordable healthcare to all its citizens through what is known as an Essential Health Package, which includes cost-effective interventions that are provided to Malawians completely free of charge at the point of use. The primary objective of the Essential Health Package has been to reduce the disease burden by offering interventions that are both effective and cost-efficient in combating the top diseases and conditions in terms of disease burden, with a focus on ensuring equity (Government of Malawi Ministry of Health, 2017, Ochalek et al., 2018). While all these efforts are intended to address the high double burden of disease, ensuring access to healthcare services remains a challenge, as mentioned above. The major contributing factors to the failure to achieve the objectives of the Essential Health Package include a lack of resources in public health facilities and inadequate funding for health services, which have been largely dependent on donor aid (Government of Malawi Ministry of Health, 2017, Health Policy Project, 2016).

**Health research in Malawi**

Health research in Malawi continues to grow and inform policy and the delivery of healthcare services. Nevertheless, a high proportion of all the health research conducted in Malawi is externally driven, with very little operational and basic health research influenced by the local academic community. While efforts are being made to align health-related research with national health priorities included in the Health Sector Strategic Plan, most of the externally funded research does not align with the national health priorities (Government of Malawi Ministry of Health, 2017, African Institute for Developement Policy, 2016). It is possible that the misalignment is the result of funding organisations prioritising projects in accordance with the areas in which they believe they have a comparative advantage rather than in accordance

with national research interests (Ali et al., 2006). Ali et al. (2006) highlighted that even though the majority of international funding organisations have a stated “country focus” and many have a strategy or process for engaging with country priorities when making finance available for health research in a country, they rarely systematically consider country needs. Many gaps also exist in the management and sharing of research results at the local level, owing to a lack of documentation systems that support the sharing of research reports and data which could inform decision-making.

***Health-related research at the Malawi-Liverpool Wellcome Programme***

The Malawi-Liverpool Wellcome Programme (MLW) is a Wellcome-Trust-funded programme that conducts research that focuses on the prevention both of death and of the transmission of infection. Since its inception in 1995, MLW has built strong research links with various stakeholders, including communities in Blantyre (where MLW is based) and other districts in southern Malawi. MLW conducts several large-scale clinical and community-based intervention research studies, including studies on HIV, tuberculosis, malaria, respiratory conditions, and non-communicable diseases. For the long term, MLW has established rural field sites to improve rural–urban disparities in access to healthcare, support individual health centres, and enable coordination of all studies through an approval system routed through the district health office as well as the local ethics committee.

This study was conducted at MLW. Blantyre, where I am based, is a major urban centre located in the south of Malawi. Just like any other district in Malawi, it is divided into non-overlapping geographical areas, each serviced by locally resident community health workers known as health surveillance assistants, who are employed by Ministry of Health and serve as a link between health facilities and communities. Given this landscape of healthcare and research systems, it is likely that the majority of individuals who participate in health-related research have ancillary care needs. No recent studies have described the practices of ancillary care during health-related research in Malawi. It is important to understand practices relating to ancillary care during health-related research to inform the development of

guidelines that are data-led or data prompted. The aim is to provide a cohesive framework for the provision of ancillary care to participants in research in this setting through a series of studies, as reported in Chapters 5, 6, and 7.

**The role of research regulatory authorities and ethics committees**

The RECs and national research regulatory boards are mandated to safeguard the rights and welfare of study participants by ensuring that ethical issues in the conduct of research are addressed and that researchers follow ethical principles and guidelines scrupulously. RECs in Malawi, such as the National Health Sciences Research Ethics Committee, the Malawi University of Science and Technology Research Ethics Committee, and the College of Medicine Research Ethics Committee, in addition to the National Commission for Science and Technology, which is the national regulatory board (mandated to promote and regulate the conduct of research in Malawi), have all adopted policies, guidelines, and procedures that protect participants' interests and welfare. Despite previous appeals for ancillary care during health-related research, particularly in research conducted in the global south, these guidelines and policies are silent on ancillary care guidance for medical researchers (Participants in the 2006 Georgetown University Workshop, 2008, Richardson, 2012, Tshikala et al., 2012). As a result of this gap in ancillary care guidance, this study was motivated to explore the existing ethical and policy guidance, current practices, and the perspectives of research stakeholders on the provision of ancillary care in health-related research, as well as its ethical and social implications in the global south. Specifically, the study sought to examine the perspectives of research stakeholders on the ethical and social implications of providing ancillary care in health-related research in developing countries.

**Chapter summary**

In this chapter, I have described the context in which the study was conducted and linked that to the numerous anticipated healthcare challenges people face that may demand that researchers consider providing ancillary care. I have also described health research in Malawi and the positionality of the Malawi-Liverpool Wellcome Trust Clinical Research Programme.

## Chapter 4. Methodology

### Introduction

This chapter outlines the overall study design of this thesis, details the study designs used, and describes the methods for each of the three components of the study, namely the systematic review and meta-synthesis, the discourse analysis, and the qualitative in-depth interview data collection and management. It gives an overview of general analytical methods used in this thesis, although further details of specific analyses are detailed in each chapter. Lastly, this chapter outlines the ethical considerations undertaken in order to implement the activities of this study.

### Study design

Qualitative approaches were used in all three components of this PhD research. The use of qualitative approaches was appropriate in this study because they provide substantive answers to the research questions by providing detailed descriptions of complex phenomena, tracking unique or unexpected events, and illuminating the experience and interpretation of events by actors with widely differing stakes and roles (Sofaer, 1999). Thus, the three qualitative approaches used in this study were chosen to address the evidence gap on practices of ancillary care in the global south. My research consisted of three studies that were conducted in a specific sequence. I began with a systematic review and meta-synthesis to understand current practices relating to ancillary care, followed by a chronological discourse analysis to examine the practical features that have underpinned the evolution of ancillary care over time. Both initial studies involved secondary research methods, using data sources that are already available in the public domain. While the synthesis provided valuable insights, it also revealed the need for more in-depth exploration of the subject matter from the perspective of those directly involved in research processes. Therefore, building upon the findings of the first two studies, I conducted an empirical research study to delve deeper into the experiences of research stakeholders and gain a comprehensive understanding of their perspectives on the provision of ancillary care during health-related research. Through this

primary data collection, I aimed to gather firsthand accounts and contextual insights from research stakeholders, such as healthcare providers, researchers, and participants, to enrich the existing knowledge and gain a deeper understanding of their experiences and perspectives regarding ancillary care. This approach allowed me to capture the intricacies, nuances, and potential ethical considerations that might have been inadequately addressed in previous research, enhancing the robustness and relevance of the findings and contributing to the advancement of knowledge in the field of ethics in health-related research. For each objective, a specific method best suited to answer the research question was chosen, as outlined below.

**Epistemological approach**

The underlying philosophy of the qualitative approaches adopted in this thesis was that of constructivism and interpretivism (Denzin and Lincoln, 2018). Constructivists question the notion that knowledge is an inherent entity existing independently in the world, which can be acquired through objective means (Thorogood and Green, 2018, Creswell and Poth, 2016). Instead, they argue that all information is subject to interpretation by the researcher or learner, highlighting the active role of individuals in constructing knowledge and understanding.

Conducting the systematic review and meta-synthesis allowed me to synthesize existing literature on ancillary care practices in the region, acknowledging that the meaning and significance of ancillary care vary across different research contexts and cultural settings. The constructivist approach guided me to view ancillary care as a multifaceted and context-specific concept, understanding that its interpretation is influenced by diverse factors such as healthcare infrastructure, cultural norms, and historical legacies. In the chronological discourse analysis of ancillary care provision in guidance documents for research conduct in the global south, I applied an interpretivist lens to examine how the concept of ancillary care has evolved over time within ethical guidelines and policies. This approach enabled me to critically analyse the language, values, and power dynamics embedded in these documents. I recognized that the ethical guidance on ancillary care is not value-neutral but reflects

broader socio-political contexts and assumptions about research participants' rights and welfare. By adopting an interpretivist perspective, I highlighted the importance of critically engaging with ethical frameworks and understanding how they shape ancillary care practices in research conducted in the global south.

In conducting qualitative interviews to explore participants' views and experiences on the practices and ethics of ancillary care in health-related research, both constructivist and interpretivist epistemological principles were utilised. Firstly, I recognized the subjective nature of participants' knowledge and understanding, acknowledging that their views on ancillary care are constructed based on their individual interpretations and experiences. The interviews were designed to create a space for participants to actively engage in the construction of meaning, allowing them to share their perspectives and provide in-depth insights into their experiences. The research also emphasized the importance of context, understanding that participants' views are shaped by their social and cultural contexts, as well as the specific setting of health-related research. Language and discourse analysis were employed to explore how participants talked about and made sense of ancillary care, highlighting the influence of language in constructing their understandings. Additionally, the research involved reflexivity, where I was also critically reflecting on my own biases and assumptions, and considering how these may influence the interpretation of participants' views.

In contrast to positivism, which seeks universal laws and objective knowledge, the constructivist and interpretivist approaches in this study acknowledge the subjectivity and contextuality of knowledge about ancillary care. Positivism relies on quantitative data and seeks to establish causal relationships, which may not be suitable for capturing the rich and subjective experiences that qualitative research aims to explore. Similarly, post-positivism (Creswell and Poth, 2016), while acknowledging the role of subjectivity, still seeks generalizable knowledge and may overlook the contextual and interpretive aspects emphasized by the constructivist approach. Instead of aiming for generalizability, I embraced

the uniqueness of each context and study, recognizing that the findings would be context-bound and contingent on the participants' perspectives. Moreover, the constructivist and interpretivist approaches in this study stood in contrast to critical theory, which focuses on critiquing power structures and advocating for social change. While acknowledging the influence of power dynamics on research ethics, the primary emphasis in this study was on understanding the lived experiences and perspectives of research stakeholders to inform ethical considerations in ancillary care practices.

**Objective 1:** To describe the provision of and understand the practices relating to ancillary care in East and Southern Africa or resource-constrained settings.

The systematic review and meta-synthesis were used as they provided the best way to synthesise available evidence. They allow the gathering of the available evidence from primary studies, which is important for understanding what is known about the problem and drawing the findings together (Seers, 2015). Thus, in this study, combined with meta-synthesis (Erwin et al., 2011, Lachal et al., 2017), I was able to review all the evidence available from East and Southern Africa on ancillary care practices in health-related research, and this informed the next phase of my research, particularly analysing the language used to describe ancillary care over time in research ethics guidelines and documentation.

**Objective 2:** To examine the practical features that have underpinned the evolution of ancillary care in health-related research ethics guidance documents.

Discourse analysis was used as it provides an interpretive method of analysing texts (Arribas-Ayllon and Walkerdine, 2008). In this study, I analysed how the language that characterises ancillary care in ethics guidance documents has changed over time, providing a chronology of discourses around care provision to study participants, and how this has influenced the development of research ethics guidelines. The lack of explicit language to describe ancillary care in guidance documents informed the types of questions to ask research stakeholders in a qualitative interview study.

**Objective 3:** To explore the experiences of research stakeholders, as well as their perspectives on the provision of ancillary care during health-related research.

Qualitative in-depth interview methods were chosen to allow exploration of the experiences and the perspectives of research stakeholders on ancillary care provision in health-related research conducted in Malawi. The qualitative data were generated around the experiences and perceptions of key research stakeholders involved in health-related research in Malawi. In-depth interviews were used to delve deeper into research stakeholders' views regarding the implications of providing ancillary care during health-related research in settings with limited resources.

**Systematic review and meta-synthesis**

I conducted a mixed-methods synthesis by integrating quantitative, qualitative, and mixed-methods evidence or data from primary studies and/or systematic reviews. This approach to evidence synthesis helps us understand how complexity impacts interventions (ancillary care) in specific contexts. In addition, the use of both qualitative and quantitative evidence in systematic reviews is recognised and recommended. Researchers note that in order for policymakers and managers to make informed decisions regarding policy and organisational change, they require access to evidence from many sources, which mixed-methods systematic reviews can give (Noblit and Hare, 1988, Dixon-Woods et al., 2005, Mays et al., 2005). Diverse methodologies and strategies exist for performing mixed-methods synthesis. Sandelowski et al. (2006) provide an outline of three primary research designs for conducting it. These include separately synthesising qualitative and quantitative data followed by a combined analysis of the findings; an integrated framework in which both qualitative and quantitative data are synthesised together; and a contingent framework in which synthesis is performed sequentially with the following synthesis topic/question derived from the previous one.

In line with my study objectives, the synthesis was conducted to synthesise evidence on ancillary care practices during health-related research in east and southern Africa as a focus

area representing the context of RCS. I intentionally conducted separate searches specifically targeting Malawi and South Africa in addition to the general search on East and South Africa to ensure I did not miss papers. The reason for this approach was twofold: Firstly, Malawi served as the primary case study throughout my PhD research, hence my interest in reviewing papers specifically related to this country. Secondly, I conducted a targeted search for articles from South Africa because of the abundance of research from this country and to explore whether any variations exist in the reporting of ancillary care provision within the context of a comparatively improved healthcare system in that country. I selected studies published within the last decade (from 2004 onwards) to ensure that the findings of the studies aligned with the understanding and conceptualisation of the role of ancillary care in health-related research that emerged in 2004 (Belsky and Richardson, 2004). The mixed-methods synthesis was mainly informed by the type of studies included, as described by Harden and Thomas (2010). The process of the synthesis involved two main stages. First, the idea of ancillary care was extracted from individual studies. The second step was to develop a new interpretation that combined the various elements extracted from different studies into a coherent viewpoint. The interpretation of this synthesis was that medical researchers provide ancillary care without following any standards or guidance, and the main drive for doing that is just a desire to help others when they are in need. The findings have implications for policy and practice in RCS. The systematic review and meta-synthesis methods are described in depth in Chapter 4.

**Discourse analysis of ethics guidance documents**

I conducted a chronological discourse analysis to uncover the motivation behind the text in research ethics guidance documents that relate to the description of ancillary care. Chronological discourse analysis is an analytical approach that focuses on examining how individuals construct narratives or communicate information in a sequential and time-ordered manner (Fairclough, 2013). This approach seeks to understand how individuals organize and present their discourse in a temporal framework, emphasizing the linguistic and structural

devices used to establish chronology and coherence. In this study, I was interested to understand changes in the language used to describe ancillary care over time. Fairclough describes discourse analysis as a particular way of constructing a particular (domain of) social practice, and genre is a way of using language which corresponds to the nature of the social practice that is being engaged in (Fairclough, 2013). Discourse constitutes society and culture. That means every instance of language use makes its own contribution to reproducing and transforming society and culture, including relations of power (Fairclough et al., 1997). According to Fairclough et al. (1997) discourse does ideological work because ideologies are often produced through discourses. To understand how ideologies are produced, it is not enough to analyse text; the discourse practice (how the texts are interpreted and received and what social effect they have) must also be considered (Fairclough et al., 1997).

In line with this description, I used discourse analysis to examine the different features that characterise ancillary care and the changes in language over time. This discourse attempts to move beyond textual analysis to the critical analysis of the visible practices of text interpretation and its use. It is well highlighted that in most health-related research, researchers and sponsors critically focus on the protection of their participants. What is missing, however, is what that means and involves when research is done in RCS. In order to achieve the objectives of this study, I conducted an in-depth analysis of 34 (6 national and 28 international) research ethics policies and guidelines, exploring their descriptions of and normative justifications for ancillary care, as well as their implications of ancillary care in RCS. The process started with the identification of the ethics guidance documents and was followed by data extraction using identified key phrases used to describe ancillary care. The documents used in this study were from both local and international institutions. If the document is updated and has multiple versions, I use all the versions of the documents to track how the language has changed. For example, for the Declaration of Helsinki, I used three versions, starting with the initial version developed in 1964. I used this process for all

guidance and policy documents. The interpretation of the discourses on ancillary care in guidance documents is that it lacks clarity. Further details of the procedures I used to conduct the discourse analysis are presented in Chapter 5.

**Qualitative data**

***Introduction***

The overarching purpose of this component of the study was to get an in-depth understanding of the actual experiences of research stakeholders, as well as their perspectives on the provision of ancillary care. I aimed to explore this during health-related research conducted in Malawi, and I wanted to understand their perspectives on the ethics and social implications of the provision of ancillary care. In particular, I wanted to understand the plans that researchers have to address the ancillary care needs of their participants, as well as the responses of researchers to incidental findings during health-related research. A lot has been reported suggesting that researchers should take some responsibility, particularly in genomic research (Meacham et al., 2010, Wolf et al., 2012), but there is a lack of information to provide as examples of ancillary care in Malawi and in RCS in general. Moreover, I wanted to explore the standpoint of different research stakeholders, including those from research funding organisations, on how they perceive the considerations for ancillary care in health-related research conducted in RCS.

I conducted qualitative in-depth interviews with key research stakeholders, including the researchers at MLW, REC members, participants in health-related research conducted at MLW, health officials from the Ministry of Health, and officials from a research funding organisation. The sampling framework was designed to gain insights from diverse stakeholders with different functions, table 1. All the key research stakeholders were selected purposively, using a criteria included in table 1. In addition to the in-depth interviews, I also held informal conversations with researchers and some stakeholders from public hospitals regarding their views on ancillary care. That data from the informal conversations was not included in the final analysis, but it helped to refine the topic guide.

Stakeholders from funding partner organisations were critical to this study since they fund many projects in Malawi and RCS in general. Therefore, their voice and views on ancillary care are key. However, although many officials from these organisations were approached for an interview, I only managed to interview one official from a funding organisation. I did not receive responses to the enquiry from four organisations, while officials from two funding organisations indicated that they did not have any information on their approach to ancillary care, so I declined the interview.

***Study instruments and interview process***

I used a standardised open-ended interview approach as described by Patton (2002). This meant that I prepared a set of open-ended questions for each group of interviewees (*Appendix 1*). The interview guides were developed on the basis of the study objectives and the themes identified during the literature review. While these topic guides were not an "exact prescription" of the questions that I discussed, they provided a roadmap for the discussion (Arthur and Nazroo, 2003). I asked the questions, and depending on the answers given, I probed further. Having these guides helped ensure that I covered all the relevant themes, while the flexibility to probe further allowed me to explore any emerging ones. I developed the initial guides. My supervisor then reviewed the guides and provided suggestions on how to improve the questions and add other questions. I then conducted "pilot" interviews using the guides to assess the language, the content, and my interviewing skills. I used all this feedback from the pilot interview to refine the questions and my interviewing skills for the subsequent interviews.

Table 1: Participants included in the study

| Participant characteristic | Criteria for Selection and Inclusion |
|---|---|
| Research teams (investigators, frontline research staff) | • They have experience in research planning, participant recruitment, participant reactions to health research, and their own opinions on planning and responding to ancillary care needs during research. |

| | |
|---|---|
| | • They have information on ethical issues encountered regarding the provision of additional health care while conducting research activities in different settings. |
| Research funders (grants officers including from Wellcome Trust, NIHR) | • They provide funding to different research projects conducted in RCS including in Malawi.<br>• They determine the funding structure of the research projects and provide direction on the use of the funds.<br>• They have plans or considerations for the provision of support towards ancillary care demands as presented in individual research projects conducted in RCS. |
| Ministry of Health officials (research unit officer and district health office) | • They have views and information on health facilities' capacity to respond to ancillary care demands of individuals who participate in health-related research and the overall impact on the health system.<br>• Views on their perceptions of the researcher's ancillary care responsibilities will also be explored. |
| Malawi research ethics committee members and ethics regulatory authorities | • They provide an understanding of ethical norms and guidelines for ancillary care and ethical conduct of health-related research in Malawi.<br>• They are involved in reviewing and approving research studies.<br>• They provide guidance on how research may respond to the ancillary care needed by their study participants. |
| Research participants (selected from ongoing studies) | • They have experience participating in different research projects conducted in Malawi.<br>• They provide information on their views and experiences on how researchers respond to their ancillary care needs and their perceptions of researchers' obligations on ancillary care. |

Interviews were conducted either face-to-face at an arranged venue (in the facility setting for participants in other studies and office for other stakeholders) or virtually through Zoom, Microsoft Teams, or a phone call. All the participants gave consent for the interview to be audio-recorded, while I was also taking a few handwritten notes, particularly as a way of keeping track of the areas I needed to explore further during the interview or logging interesting observations such as body language. All research participants who were interviewed face-to-face, including those who were already participating in other studies, provided their written informed consent. All individuals who participated in interviews virtually through Zoom, Microsoft Teams, or a phone call provided verbal consent. The verbal consent approach was incorporated into the protocol as a COVID-19 preventive measure and was approved by both RECs. In addition, some participants requested verbal consent since they wanted a virtual interview, whereas, for others, it was the only option available; for instance, for participants from research funding organisations or principal investigators and REC members who had travelled outside Malawi for other assignments. The interviews lasted approximately 20–45 minutes. Interviews were conducted in English, or in Chichewa (local language) if the participant was not comfortable with English. Participants were also allowed to respond to questions in whichever language they were most comfortable with, but this was limited to English and Chichewa. I am fluent in both English and Chichewa. All interviews conducted in the local language (Chichewa) were translated into English, and I consistently shared these translated versions with my supervisors during the analysis phase.

Throughout the duration of this study, I maintained a research diary in which I recorded my experiences, observations, and other points of clarification. I also made a note of any novel thoughts and insights that surfaced during the interviews I conducted and considered them for further investigation during later interviews.

***Data management and analysis***

Qualitative data were transcribed verbatim and typed out in Microsoft Word. I transcribed all the audio-recorded interviews and translated those that were done in Chichewa. Because I

conducted all the interviews, I was quite familiar with the content. Nevertheless, I did multiple readings of all the transcripts to ensure that they were accurate and consistent with the recordings. Once I had checked the transcripts, I imported them into NVivo for Mac software that I used for coding.

The analysis continued during fieldwork. I used a thematic analysis approach (Braun and Clarke, 2006) to systematically analyse the data and derive meaningful insights. Using this approach, I identified recurring patterns, themes, and concepts within the data related to the provision and impact of ancillary care in health-related research conducted in RCS. Employing an iterative approach (Northcutt and McCoy, 2004), I continuously identified emerging themes that required further exploration or clarification through subsequent data collection. To manage the thematic coding process, I utilised NVivo (Q.S.R. International Pty Ltd, 2022) to organize and analyze the data. The coding was structured around broad themes, such as consideration of ancillary care and ethical concerns related to ancillary care, while also incorporating inductively derived sub-themes, including levels of obligation regarding ancillary care. This comprehensive approach enabled a thorough and systematic analysis of the data, contributing to a more nuanced understanding of ancillary care in the context of health-related research in RCS. To begin with, I developed a coding framework and shared it with my supervisors. We had a discussion about it, and they guided me through and suggested some changes to the final coding framework, which I later used to code all the transcripts. While coding, I noted down any emerging new ideas and concepts from the data not categorised previously. I then gave them new themes and codes (inductive). To improve the reliability of coding and ensure that I was not over-interpreting (or under-interpreting) information, my supervisor reviewed some coded transcripts at random. We had a discussion on the coded transcripts, and they provided input during the data analysis phase. With this input, I updated the coding framework as necessary and made changes to the analysis to reflect the suggestions from my supervisors.

Once data were coded, I then sorted them and grouped materials with similar codes together.

I then synthesised the data through critical reading and summarised the contents through a framework matrix chart consisting of each major theme, sub-categories and relevant data from each participant (Arthur and Nazroo, 2003). From these charts, I then made interpretations and summarised the findings for a write-up of the paper presented in Chapter 7.

**Reflexivity**

During this entire process of collecting data and analysing it, I was cognizant of the fact that my identity and experience might affect how I collect, view, and interpret the data. For instance, being a social scientist and also an upcoming bioethicist, I had predetermined ideas of how the stakeholders might perceive ancillary care in Malawi. These ideas were influenced by the responses we got from stakeholders of a similar type on a study that I conducted at MLW before starting this PhD (Kapumba et al., 2020). In order to address this, I did not take on the role of an ethicist or bioethicist during the interview. I tried to balance my role of being a researcher and ethical point of view. I avoided asking stakeholders questions that would make it seem as if I fully supported ancillary care, which allowed me to get the views of the stakeholders instead.

While I understand that my fieldwork was necessarily affected by COVID-19 in some ways, and potential participants could not be communicated with in person, it proved difficult to communicate solely via email. This led to delays in the implementation of study activities which directly impacted on the progress on my studies. Most of the stakeholders also kept on rescheduling the interviews, and some did not indicate their availability for interviews, even though I made several attempts to obtain further details. I felt that power dynamics played a role, particularly with those who held senior positions; some were indicating to me that they were very busy. All this delayed the data collection. Despite all this, I managed to get at least some responses from all the groups of the research stakeholders that I had purposively selected. I also was supported by my supervisors and advisors, who facilitated my approaches to some of the senior officials involved in my study.

The COVID-19 pandemic presented significant challenges not only in terms of its impact on the study but also in conducting research activities. With restrictions on face-to-face interviews and interactions with participants, several measures were implemented to ensure safety. Adapting to these circumstances, changes were made in the approach to data collection. To safeguard both myself and the potential study participants, I diligently adhered to the guidelines and procedures set forth by the Government and the research institution (MLW) to mitigate the risk of COVID-19 transmission during research participation. Furthermore, MLW developed a Crisis Standard Operating Procedure (SOP) that provided comprehensive information on ensuring the safety of both research participants and researchers throughout the research process. These measures were crucial in protecting the well-being of all involved parties and upholding ethical considerations during these challenging times.

It is notable, however, that my background was not a real drawback during the process, as it also provided some advantages. Knowing the healthcare system well and also the officials in the research institutions meant that I knew the gaps that existed and was, therefore, in a better position to explore these with my interviewees.

**Ethical considerations**

Ethical approval for this research was obtained prior to the commencement of the study from the institutional ethics review committees of the College of Medicine Research Ethics Committee in Malawi (*Appendix 5*) and the London School of Hygiene and Tropical Medicine (*Appendix 6*). Permission to conduct the study was obtained from the relevant country authorities, including the District Health and Social Services for Chikwawa and Blantyre district hospitals (*Appendix 3 & 4*), and from MLW principal investigators. The MLW directors also provided a letter of support allowing the study to be conducted at MLW (*Appendix 2*). The approaches undertaken in this research were in accordance with the ethical guidelines of the Association for Social Anthropologists of the UK the Commonwealth (2011) and the World Medical Association (2013). In my capacity as a researcher, I ensured that I acted in

accordance with the principles outlined in these ethical guidelines throughout the process of preparing for, conducting, and reporting on the research. Throughout the course of my research, I approached ethics as a relational process, which required me to maintain an open mind and be attentive to the diverse range of individuals and situations I encountered.

This was a qualitative in-depth interview study; therefore, the participants were exposed to minimal danger or risk. However, the interactions I had with research stakeholders, particularly participants who were also involved in other projects at MLW, may have created some confidentiality-related ethical concerns. Therefore, I was mindful of their circumstances.

All participants gave written or verbal informed consent prior to being interviewed. A study information sheet and informed consent form were first read to them before they consented. I made sure that all of the individuals who took part in the study were aware that their participation was entirely voluntary and that they would not be penalised in any way if they chose not to answer certain questions, refused to take part in the study, or withdrew from the study at any point during its duration. I made sure that those who were taking part in other studies understood that the purpose of my research was to learn about their perspectives on the provision of ancillary care during health-related research in Malawi and to find out what their experiences of this provision were like. More broadly, I ensured that participants understood that my research aimed to contribute to improved ethics and policy guidance for ancillary care that would potentially benefit people participating in health-related research in RCS.

Confidentiality of all participants was maintained throughout the study. For the face-to-face interviews, consent processes and interviews were carried out at an agreed venue for the study participants who were participating in other studies and some REC members, health officials and principal investigators. This was the MLW offices for the principal investigators, the district health offices for the health officials, and the offices of Kamuzu University of Health Sciences for the REC members. Interviews with study participants participating in other

studies were done at the study sites. I met the costs associated with travel to the venue for the interview for all interviewees.

Participant anonymity was maintained by ensuring that in place of personal identifiers such as names, a code was used on the study instruments. I ensured that participants were informed that their identities would be safeguarded by the use of identification numbers or pseudonyms in transcriptions and all future references to interview proceedings, including written accounts. Participants had the opportunity to ask questions and discuss the study's specifics with me, and they were allowed to ask further questions at any moment during or after the study's interviews. During the consent process, I made it clear that participants had the right to withdraw from or discontinue their involvement in the study at any time, in which case their data would not be utilised. I asked permission for interviews to be audio-recorded and assured them that the interview notes, transcripts, and audio-recorded files were stored in a locked cabinet and only I had access to study records and any identifying information. Data in the study laptop, as well as NVivo data, were encrypted and password protected. The names of any individual mentioned during the interviews were anonymised during transcription. These data will be archived in a secure server at The London School of Hygiene and Tropical Medicine in anonymised form for ten years after the completion of the study, in accordance with the London School of Hygiene and Tropical Medicine data storage policy.

## Chapter 5. Ancillary care practices in East and Southern Africa

### Introduction

This chapter addresses Objective 1, to describe the provision of and explore the practices regarding ancillary care in health-related research in East and Southern Africa over the last decade. It presents findings from a systematic review and a meta-synthesis of the practices associated with ancillary care provided during health-related research in East and Southern Africa that was published in peer-reviewed journal *Wellcome Open Research* (Kapumba et al., 2021). In this paper, I used thematic content analysis (Clarke and Braun, 2021, Ford, 2004, Neuendorf, 2017) as a methodological approach to analyse and synthesise the findings from the included studies. By systematically examining the textual data, such as from the study methods, results, and discussion sections, I identified recurring themes and concepts related to the provision of ancillary care. Through a rigorous process of coding and categorisation, I organised and synthesised these themes to generate comprehensive findings and interpretations. Thematic content analysis allowed me to explore different approaches to the provision of ancillary care across the studies, facilitating a holistic understanding of the practices in this area. This systematic and transparent approach enabled the extraction of meaningful insights and the generation of new knowledge. Current practices associated with ancillary care in health-related research indicate that researchers take ancillary care for their participants into account. However, a lack of explicit documentation of the care delivered, especially in clinical trials and other clinical studies, restricts our knowledge about it. In addition, there is a lack of a standard approach to the provision of ancillary care, as some care recorded as ancillary care, such as providing clothing or phone credit, does not meet the criteria of ancillary care. This suggests that medical researchers undertaking health-related research in RCS must be provided with explicit guidance for ancillary care.

### Research paper

The research paper cover sheet is presented below, followed by the paper itself.

London School of Hygiene & Tropical Medicine
Keppel Street, London WC1E 7HT

T: +44 (0)20 7299 4646
F: +44 (0)20 7299 4656
www.lshtm.ac.uk

# RESEARCH PAPER COVER SHEET

**Please note that a cover sheet must be completed for each research paper included within a thesis.**

## SECTION A – Student Details

| | | | |
|---|---|---|---|
| **Student ID Number** | 418617 | **Title** | Mr |
| **First Name(s)** | Blessings Msango | | |
| **Surname/Family Name** | Kapumba | | |
| **Thesis Title** | Understanding Ancillary Care in the Global South: Examining Practice, current Ethical Guidance, and Stakeholder Perspectives in Malawi | | |
| **Primary Supervisor** | Prof. Janet Seeley | | |

**If the Research Paper has previously been published please complete Section B, if not please move to Section C.**

## SECTION B – Paper already published

| | | | |
|---|---|---|---|
| Where was the work published? | Wellcome Open Research | | |
| When was the work published? | 29/06/2021 | | |
| If the work was published prior to registration for your research degree, give a brief rationale for its inclusion | Not applicable | | |
| Have you retained the copyright for the work?* | **Yes** | Was the work subject to academic peer review? | **Yes** |

*If yes, please attach evidence of retention. If no, or if the work is being included in its published format, please attach evidence of permission from the copyright holder (publisher or other author) to include this work.

## SECTION C – Prepared for publication, but not yet published

| | |
|---|---|
| Where is the work intended to be published? | |
| Please list the paper's authors in the intended authorship order: | |

| | |
|---|---|
| Stage of publication | Choose an item. |

**SECTION D – Multi-authored work**

| | |
|---|---|
| For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary) | |

**SECTION E**

| | |
|---|---|
| **Student Signature** | [redacted] |
| **Date** | 21/02/2023 |

| | |
|---|---|
| **Supervisor Signature** | [redacted] |
| **Date** | 23/02/2023 |

SYSTEMATIC REVIEW

# What do we know about ancillary care practices in East and Southern Africa? A systematic review and meta-synthesis [version 1; peer review: 1 approved]

Blessings M. Kapumba [1,2], Nicola Desmond [3], Janet Seeley [1]

[1]Global Health and Development, London School of Hygiene & Tropical Medicine, London, WC1E 7HT, UK
[2]Community Engagement and Bioethics, Malawi-Liverpool Wellcome Trust, Blantyre, BT3, Malawi
[3]International Public Health, Liverpool School of Tropical Medicine, Liverpool, L3 5QA, UK

**v1** **First published:** 29 Jun 2021, **6**:164
https://doi.org/10.12688/wellcomeopenres.16858.1
**Latest published:** 29 Jun 2021, **6**:164
https://doi.org/10.12688/wellcomeopenres.16858.1

## Abstract

**Background:** Despite growing calls for the provision of ancillary care to study participants during medical research, there remains a noticeable gap in ethical guidelines for medical researchers in resource-constrained settings (RCS). We reviewed recent studies to determine the extent to which ancillary care is provided in East and Southern Africa and to examine the ethical justifications researchers provide to support their views on ancillary care obligations.

**Methods**: A systematic search for qualitative and mixed methods studies on ancillary care was conducted across MEDLINE, Embase, African Wide Information, PubMed, CINAHL Plus, and Scopus. The National Institutes of Health (NIH) Department of Bioethics and H3 Africa websites and Google Scholar were further searched. Studies conducted in East and Southern Africa between 2004 and 2020, as well as those that reported on ancillary care provided to study participants were included. All studies included in this review were evaluated for methodological quality as well as bias risk. NVivo version 12 was used for thematic analysis.

**Results**: Overall, 4,710 articles were identified by the initial search. After the data extraction and quality assessment, 24 articles were included. Key areas presented include ancillary care approaches and the themes of researcher motivation for providing ancillary care and expectations of participants in medical research. The review shows that while some international researchers do provide ancillary care to their study participants, approaches are not standardised without consistent guidelines for ethical practice for ancillary care. We found limited empirical studies in RCS that report on ancillary care, hence findings in this review are based on single studies rather than a collection of multiple studies.

**Conclusions**: This paper emphasizes the value of establishing ethics guidelines for medical researchers in RCS who consider provision of ancillary care to their participants, and the need to account for these ethical guidelines in medical research.

## Keywords

Ancillary Care Practices, Medical Research, Meta-Synthesis, Research Participants, Resource Constrained Settings, East and Southern Africa

**Open Peer Review**

**Approval Status** ✓

| | 1 |
|---|---|
| **version 1** 29 Jun 2021 | ✓ view |

1. **Dorcas Mwikali Kamuya**, KEMRI-Wellcome Trust Research Programme, Kilifi, Kenya

Any reports and responses or comments on the article can be found at the end of the article.

**Corresponding author:** Blessings M. Kapumba (bkapumba@mlw.mw)

**Author roles: Kapumba BM**: Conceptualization, Data Curation, Formal Analysis, Methodology, Resources, Writing – Original Draft Preparation, Writing – Review & Editing; **Desmond N**: Conceptualization, Methodology, Resources, Supervision, Validation, Writing – Review & Editing; **Seeley J**: Conceptualization, Funding Acquisition, Methodology, Resources, Supervision, Validation, Writing – Review & Editing

**Competing interests:** No competing interests were disclosed.

**Grant information:** This work was supported by the Wellcome Trust [096527, https://doi.org/10.35802/096527; a Strategic Award to the Global Health Bioethics Network, administered by the London School of Hygiene and Tropical Medicine]. The funding body had no role in the design of the study and collection, analysis, and interpretation of data and in writing of the manuscript.
*The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.*



**How to cite this article:** Kapumba BM, Desmond N and Seeley J. **What do we know about ancillary care practices in East and Southern Africa? A systematic review and meta-synthesis [version 1; peer review: 1 approved]** Wellcome Open Research 2021, **6**:164 https://doi.org/10.12688/wellcomeopenres.16858.1

**First published:** 29 Jun 2021, **6**:164 https://doi.org/10.12688/wellcomeopenres.16858.1

## Abbreviations

RCS: Resource-constrained settings; LMICs: Low-and-Middle-Income Countries; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; JBI-QARI: Joanna Briggs Institute Qualitative Assessment and Review Instrument; AMSTAR: A MeaSurement Tool to Assess Systematic Reviews

## Introduction

Providing care and support to study participants during medical research that is not in pursuit of the research scientific objectives, to prevent study-related harms, or address study-related injuries presents ethical challenges worldwide[1]. There remains a noticeable gap in research guidelines addressing medical researchers' obligations to provide additional or ancillary care in resource-constrained settings (RCS). Without clear guid- ance, how can and do researchers navigate and respond to the broader needs of ancillary care in RCS? The ethical impera- tive for provision of ancillary care during medical research has been documented and recommendations for the provision of such care are incorporated in ethical guidance such as the Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization (WHO) and the Nuffield Council on Bioethics. These respectively state:

> *"when participants' health needs during and after research cannot be met by local health infrastructure or the participant's pre-existing health insurance, the researcher and sponsor must make prior arrangement for adequate care for participants with local health authorities, members of the communities from which persons are drawn, or nongovernmental organisations such as health advocacy groups"*[2].

> *"…during research, participants may develop an entirely unrelated condition. In some circumstances, it may be relatively easy for researchers to treat the condition or refer participants to a local health centre where treatment can be provided"*[3].

Despite the existence of such guidance and extensive discussion in the ethics literature[4], how this care can be achieved in practice, particularly across populations that vary politi- cally, socially, and culturally is a matter for debate. This debate is heightened in RCS, where individuals who volunteer to participate in research may have several unmet health needs. Participants in low- and middle-income countries (LMICs) often live in poverty, suffer disproportionately from high dis- ease burdens, such as HIV, tuberculosis, and malaria, and are often limited to sub-standard health care systems[5]. Even while health care services can be available within the local health care system, people are concerned about such services because of quality and costs[6,7]. Existing limitations in accessibility and affordability of health care services are compounded by ongoing structural inequalities in health access, education, and socioeconomic status, leading to poor health outcomes. These underlying and overlapping structural issues may influence research participation amongst those most in need in order for them to access effective health care provided as a compo- nent of research. Recognising these structural concerns in RCS, researchers encounter a variety of unmet health needs among their research participants, many of whom will require medical care ancillary to the study[8]. For example, a study on malaria may uncover other comorbidities like HIV or other infec- tious disease other than the condition under study. Despite recognition that additional health needs commonly arise amongst research participants, there is a lack of evidence as to how researchers actually respond when conducting research in RCS as well as questions as to their obligations to provide such care.

There is some evidence regarding the ethics of ancillary care in research conducted in developing countries[4,9,10]. Some recent studies have reported on the obligations of medical researchers to provide ancillary care to their participants[11–13]. While recognising these ethical obligations of ancillary care in medical research, researchers have argued that provision of ancillary care could unduly influence[4,14,15] or could be a form of structural coercion to participants[16–18] and also as one way of exploitation of vulnerable populations[19–21]. The chal- lenge, however, is that while much research has been con- ducted on the ethics of ancillary care in the context of medical research, there is a lack of clarity of what ancillary care means and the concept remains insufficiently unpacked to guide medi- cal research in RCS. Our focus in this paper is on this paucity of information on approaches to and applications of ancillary care provision in East and Southern Africa.

Using a mixed methods approach, including systematic review and meta-synthesis, we looked for evidence of information on ancillary care provision or provision of care to study participants during research. We carried out a review of stud- ies conducted in East and Southern Africa, where structural ine- qualities are particularly salient, that reported some ancillary care or the need to provide ancillary care to study participants. We seek to answer the question: "what are the current practices of and factors that influence the provision of ancillary care dur- ing medical research in east and southern Africa?" Specifically, we aimed to ascertain the current evidence on the extent of pro- vision of ancillary care in East and Southern Africa and to explore the ethical justifications researchers provide to support their views on ancillary care obligations.

## Methods

A systematic search was conducted to synthesise published articles and researchers that have recently worked on medical research that involved the provision of care and support to study participants in East and Southern Africa were contacted in an attempt to obtain their published articles if not available online. This review included qualitative empirical studies, systematic reviews, and theoretical articles describing the ethics of ancillary care. The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA)[22,23] guide- lines were followed. Since this study utilised a secondary syn- thesis of data, which is already in the public domain, ethical approvals, and consent to participate were not necessary.

### Search strategy

A comprehensive electronic search strategy was conducted to identify all relevant published studies where the primary focus was to highlight the provision of care to study participants by medical researchers, the variety of forms of care provided,

and the ethical basis justifying care provision. The search cov- ered the period between June 2004 and November 2020 to ensure that the studies' findings reflected the role of ancillary care in medical research established in 2004[1] and reflect key information pertaining to current practices of ancillary care in RCS. Six databases were searched in November 2020. The ini- tial search was conducted using a combination of index terms and text-based queries in Ovid MEDLINE. We used this as a primary search strategy to identify text words contained in the title and abstract as well as classify the appropriate MeSH terms to be used (Table 1).

The next step used identified keywords and index terms in five electronic databases: Embase via Ovid® host, African Wide Information via EBSCO host, PubMed, CINAHL Plus, and Scopus, Table 2. A search string involving relevant key words and possible variations was constructed based on the domain (medical and behavioural research in RCS) and practices (provi- sion of ancillary care to study participants). The search strat- egy was readjusted several times for comprehensive and updated retrieval. The National Institutes of Health (NIH) Department of Bioethics, Human Heredity and Health in Africa (H3 Africa) and Google Scholar websites were added to the search. The reference lists of all studies potentially eligible for inclusion were screened to elicit additional relevant articles. If the full-text article was not available online, one attempt was made to con- tact the author, and if no response was received the article was excluded.

### Study selection and eligibility criteria

The database search was initially conducted against a broad inclusion criterion by the first reviewer (BK) and was focused on the title and abstract of the articles. All articles identified to be potentially eligible for inclusion in this study were obtained in full texts. BK then conducted full-text article screening to identify studies that met the following inclusion criteria:

- Qualitative empirical study, systematic review or theoretical article
- *Published between June 2004 and November 2020*
- *Related to the domain of medical research involving human subjects conducted in East and Southern Africa*
- *Providing narratives on the ethics of ancillary care provision and experiences in RCS*

**Table 1. Systematic review MEDLINE full search strategy.**

| | |
|---|---|
| **Database: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) <1946 to November 23, 2020>** | |
| **Ancillary care** | |
| 1 | ancillary.mp. |
| 2 | additional.mp. |
| 3 | practice*.mp. |
| 4 | care.mp. |
| 5 | service*.mp. |
| 6 | exp "Delivery of Health Care"/ |
| 7 | (additional adj5 care).mp. |
| 8 | (additional adj5 service*).mp. |
| 9 | (additional adj5 practice*).mp. |
| 10 | Ancillary Care, Research/ |
| **Forms of ancillary care** | |
| 1 | treat*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] |
| 2 | (referral* or refer or referred).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] |
| 3 | "Referral and Consultation"/ |
| 4 | (consulted or consultation* or consult?).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] |
| 5 | insurance. mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] |

| | |
|---|---|
| **Ethics of ancillary care** | |
| 1 | ethic*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] |
| 2 | exp Ethics/ |
| 3 | moral*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] |
| 4 | social.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] |
| 5 | obligation*.mp [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] |
| 6 | responsib*.mp [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] |
| 7 | dut*.mp [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] |
| **Behavioral and medical research** | |
| 1 | (medical or health-related or biomedical).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] |
| 2 | (behavioral or social).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] |
| 3 | researche*,mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] |
| 4 | (clinical trials or observation* studies or cohort studies).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] |
| **East and Southern Africa** | |
| 1 | LMIC/ |
| 2 | south africa*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] |
| 3 | South Africa/ |
| 4 | malawi*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] |
| 5 | Malawi/ |
| 6 | east* africa*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] |
| 7 | exp Africa, Eastern/ |
| 8 | exp Africa, Southern/ |
| 9 | southern africa*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] |

**Table 2. Summary of the search strategy used for the review.**

| 1. | Type of literature | Source |
|---|---|---|
| a | Published materials | MEDLINE |
| | | EMBASE |
| | | African Wide Information |
| | | PubMed |
| | | CINAHL Plus |
| | | Scopus |
| b | Grey Literature | Google Scholar |
| | | NIH – the department of Bioethics |
| | | H3 Africa |
| **2.** | **Search Terms** | |
| | | ancillary OR additional AND care OR treatment OR services |
| | | obligation OR responsibilities OR duties AND researcher |
| | | behavioural OR medical OR health related AND research OR studies |
| | | LMIC OR sub-Saharan Africa OR southern Africa OR east Africa OR Malawi |
| | | ethics |

- *Reporting ancillary care practices, including the provi- sion of standard of care to research participants additional to study related care. Clinical trials, observational studies, and prospective cohort studies that report on provision of ancillary care as part of the trial, either formally or informally were eligible.*

Studies were excluded if they were published prior to 2004 and not in English; if they documented or reported provi- sion of care or support to study participants as part of the study; if conducted in high-resource settings; if they were opinion or commentary papers and workshop or meeting reports; and if there was no clear statement on the study setting.

### Quality appraisal

Methodological rigor was achieved through three independ- ent reviewers (BK, ND and JS) critically appraising the meth- odological quality of the included studies. All potentially eligible studies were appraised and scored for methodological quality according to the Joanna Briggs Institute critical appraisal checklist for qualitative studies (JBI-QARI)[24,25]. Compared to other commonly used tools, the domains examined in this tool have been found to be more coherent and sensitive to assess- ment of quality, Table 3. The quality assessment was used not as a basis to exclude studies but rather to: (1) ascertain the relative contribution of each study to the overall synthesis and (2) assess the methodological rigour of each study as part of a proc- ess of assessing confidence in the review findings as well as to assess risk of bias[26,27].

The JBI-QARI 10 questions were applied to each individual paper and an aggregate score was calculated (Table 4). For systematic reviews and theoretical studies, we applied the AMSTAR 2 (a measurement tool to assess systematic reviews)[28] checklist based on the 16 items (Table 5 and Table 6).

Any disagreements that arose between reviewers were resolved through discussion with at least one other member of the research team. Team meetings were used to achieve a shared and consistent approach in operationalising the domains in the tools and inclusion of studies.

### Data extraction

Details of each of the included papers were imported into a 2016 Microsoft Excel® (Microsoft Corporation, Redmond, WA, USA) file and duplicate articles were removed. Data extrac- tion of study characteristics was primarily undertaken by one reviewer (BK); however, a second and third reviewer (ND and JS) randomly selected papers and double-checked the extractions for accuracy. In addition, the team had regular meet- ings to discuss any uncertainties, to ensure consistency of the approach and to agree definitions.

Portable Document Format files of all the included papers were then imported into NVivo 12 (QSR International, Warrington, UK) software and the "methods and results" sections were coded and analysed. If relevant information was located in other parts of the papers (for example, the background or discus- sion sections), these were also coded. Each relevant full-text

**Table 3. Critical appraisal checklist for qualitative studies.** Y=yes, N=no, U=unclear/unsure, P=partially.

| Question | | Y | N | U | P |
|---|---|---|---|---|---|
| **1.** | Is there congruity between the stated philosophical perspective and the research methodology? | ☐ | ☐ | ☐ | ☐ |
| **2.** | Is there congruity between the research methodology and the research question or objectives? | ☐ | ☐ | ☐ | ☐ |
| **3.** | Is there congruity between the research methodology and the methods used to collect data? | ☐ | ☐ | ☐ | ☐ |
| **4.** | Is there congruity between the research methodology and the representation and analysis of data? | ☐ | ☐ | ☐ | ☐ |
| **5.** | Is there congruity between the research methodology and the interpretation of results? | ☐ | ☐ | ☐ | ☐ |
| **6.** | Is there a statement locating the researcher culturally or theoretically? | ☐ | ☐ | ☐ | ☐ |
| **7.** | Is the influence of the researcher on the research, and vice- versa, addressed? | ☐ | ☐ | ☐ | ☐ |
| **8.** | Are participants, and their voices, adequately represented? | ☐ | ☐ | ☐ | ☐ |
| **9.** | Is the research ethical according to current criteria or, for recent studies, and is there evidence of ethical approval by an appropriate body? | ☐ | ☐ | ☐ | ☐ |
| **10.** | Do the conclusions drawn in the research report flow from the analysis, or interpretation, of the data? | ☐ | ☐ | ☐ | ☐ |

**Table 4. JB-QARI quality assessment score.**

| Study | Question | | | | | | | | | | Score | Quality band | Richness: thick or thin | Publication type | Relevance: high, medium or low |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | | | | | |
| Barsdorf *et al.*, 2010 | Y | Y | Y | Y | Y | N | P | Y | Y | Y | 8.5 | high | thick | journal | high |
| Chou *et al.*, 2007 | Y | Y | Y | Y | Y | P | Y | U | U | P | 8 | high | thick | journal | high |
| Devries *et al.*, 2015 | Y | U | Y | U | Y | N | Y | U | Y | N | 7 | high | thick | journal | high |
| Essack *et al.*, 2010 | Y | P | Y | N | U | P | U | U | Y | N | 5.5 | low | thin | journal | low |
| Gooding *et al.*, 2018 | Y | Y | P | U | U | Y | N | Y | P | N | 6 | medium | thick | journal | medium |
| Kamuya *et al.*, 2013 | Y | P | Y | Y | Y | P | Y | U | Y | P | 8 | high | thick | journal | high |
| Kamuya *et al.*, 2014 | Y | N | Y | P | P | Y | P | Y | Y | U | 7 | high | thick | journal | high |
| Lairumbi *et al.*, 2012 | Y | Y | Y | N | Y | N | Y | N | Y | N | 6 | medium | thick | journal | medium |
| Mfutso-Bengo *et al.*, 2008 | Y | Y | Y | U | Y | P | P | U | Y | N | 7 | high | thick | journal | high |
| Mfutso-Bengo *et al.*, 2015 | Y | Y | Y | Y | P | U | U | U | Y | N | 7.5 | high | thick | journal | medium |
| Mtunthama *et al.*, 2008 | Y | P | Y | Y | Y | P | Y | U | Y | P | 8 | high | thick | journal | high |
| Nkosi *et al.*, 2020 | Y | Y | Y | Y | Y | Y | U | U | Y | P | 8.5 | high | thick | journal | high |
| Pratt and Hyder, 2018 | Y | Y | Y | P | P | Y | P | U | N | N | 6 | medium | thin | journal | low |
| Ramjee *et al.*, 2010 | Y | U | Y | U | Y | N | Y | U | Y | U | 7.5 | high | thick | journal | high |
| Sullivan *et al.*, 2020 | Y | Y | Y | Y | Y | U | U | U | Y | Y | 8.5 | high | thick | journal | high |
| Vreeman *et al.*, 2012 | Y | Y | Y | N | U | P | Y | Y | Y | Y | 8 | High | thick | journal | high |
| Ward *et al.*, 2018 | Y | U | Y | U | Y | Y | N | Y | Y | N | 7 | high | thick | journal | medium |

Key: Y=yes, N=no, U=unclear/unsure, P=partial

**Note:** The questions refer to those in the JBI-QARI, *Table 3*

**Table 5. AMSTAR 2 - a critical appraisal tool for systematic reviews.** Y=yes, P=partially, N=no, NA=not applicable, PICO=population, intervention, comparator group, outcome.

| Question | | Y | P | N | NA |
|---|---|---|---|---|---|
| 1 | Did the research questions and inclusion criteria for the review include the components of PICO? | ☐ | ☐ | ☐ | ☐ |
| 2 | Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol? | ☐ | ☐ | ☐ | ☐ |
| 3 | Did the review authors explain their selection of the study designs for inclusion in the review? | ☐ | ☐ | ☐ | ☐ |
| 4 | Did the review authors use a comprehensive literature search strategy? | ☐ | ☐ | ☐ | ☐ |
| 5 | Did the review authors perform study selection in duplicate? | ☐ | ☐ | ☐ | ☐ |
| 6 | Did the review authors perform data extraction in duplicate? | ☐ | ☐ | ☐ | ☐ |
| 7 | Did the review authors provide a list of excluded studies and justify the exclusions? | ☐ | ☐ | ☐ | ☐ |
| 8 | Did the review authors describe the included studies in adequate detail? | ☐ | ☐ | ☐ | ☐ |
| 9 | Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review? | ☐ | ☐ | ☐ | ☐ |
| 10 | Did the review authors report on the sources of funding for the studies included in the review? | ☐ | ☐ | ☐ | ☐ |
| 11 | If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results? | ☐ | ☐ | ☐ | ☐ |
| 12 | If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis? | ☐ | ☐ | ☐ | ☐ |
| 13 | Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review? | ☐ | ☐ | ☐ | ☐ |
| 14 | Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review? | ☐ | ☐ | ☐ | ☐ |
| 15 | If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review? | ☐ | ☐ | ☐ | ☐ |
| 16 | Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review? | ☐ | ☐ | ☐ | ☐ |

**Table 6. AMSTAR 2 quality assessment score.** P=partially.

| Study | Question & inclusion | Protocol | Study design | Search strategy | Study selection | Data extraction | Exclusion reasons | Inclusion details | Assess risk of bias | Funding source | Analysis method | Risk of bias on analysis | Risk of bias | Discuss heterogeneity | Publication bias | Conflict of interest |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Chilengi, 2009** | P | P | Yes | No | No | No | No | No | No | No | No | N/A | N/A | Yes | Yes | Yes |
| **Cohen et al., 2009** | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | N/A | N/A | Yes | Yes | Yes |
| **Embleton et al., 2015** | P | P | Yes | No | No | No | No | No | No | Yes | No | N/A | N/A | Yes | Yes | Yes |
| **Ngongo et al., 2012** | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | N/A | N/A | Yes | Yes | Yes |
| **Oduwo and Edwards, 2014** | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | N/A | N/A | Yes | Yes | Yes |
| **Richards and Helmchen, 2013** | P | P | Yes | No | No | No | No | No | No | No | No | N/A | N/A | Yes | Yes | Yes |
| **Stunkel and Grady, 2011** | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | N/A | N/A | Yes | Yes | Yes |

paper was analysed, and key details were recorded including year of publication, country in which the study was conducted, methods used, the phenomenon of interest, and target popu- lation. Furthermore, note was made of funding sources and any potential conflict of interest. Only qualitative data were extracted, whatever the type of research method used (qualitative or systematic reviews).

### Data synthesis

The review followed the principles of a thematic synthesis approach as described by Thomas *et al.*[29,30]. This process involved the aggregation of findings and categories to generate a set of synthesised statements that represented aggregation through categorisation of findings related in meaning by all the three reviewers (BK, ND, and JS). We followed the three stages outlined in thematic synthesis theory: (i) coding text from the methods, findings, and discussion sections of the included studies line-by-line; (ii) organising free codes into related areas to structure descriptive themes to capture meaning; and (iii) developing analytical themes[31]. The themes for synthesis were predefined from the research questions that guided the cod- ing, and then additional themes emerged as the data was exam- ined. The outcome of coding was verified and discussed by BK with ND and JS to check for clarity, consistency and understanding. Each study was read several times to ensure that all texts relating to provision of care or support to study participants were integrated. The concepts were examined for similarities and differences and grouped together based on shared meanings to create new codes, and then organised into a set of descriptive themes[32].

## Results

The electronic search across all databases yielded a total of 4,710 references of which 3,469 unique articles remained after removal of duplicates, Figure 1. All 3,469 were screened by title and abstract. A total of 3,379 articles that did not meet the

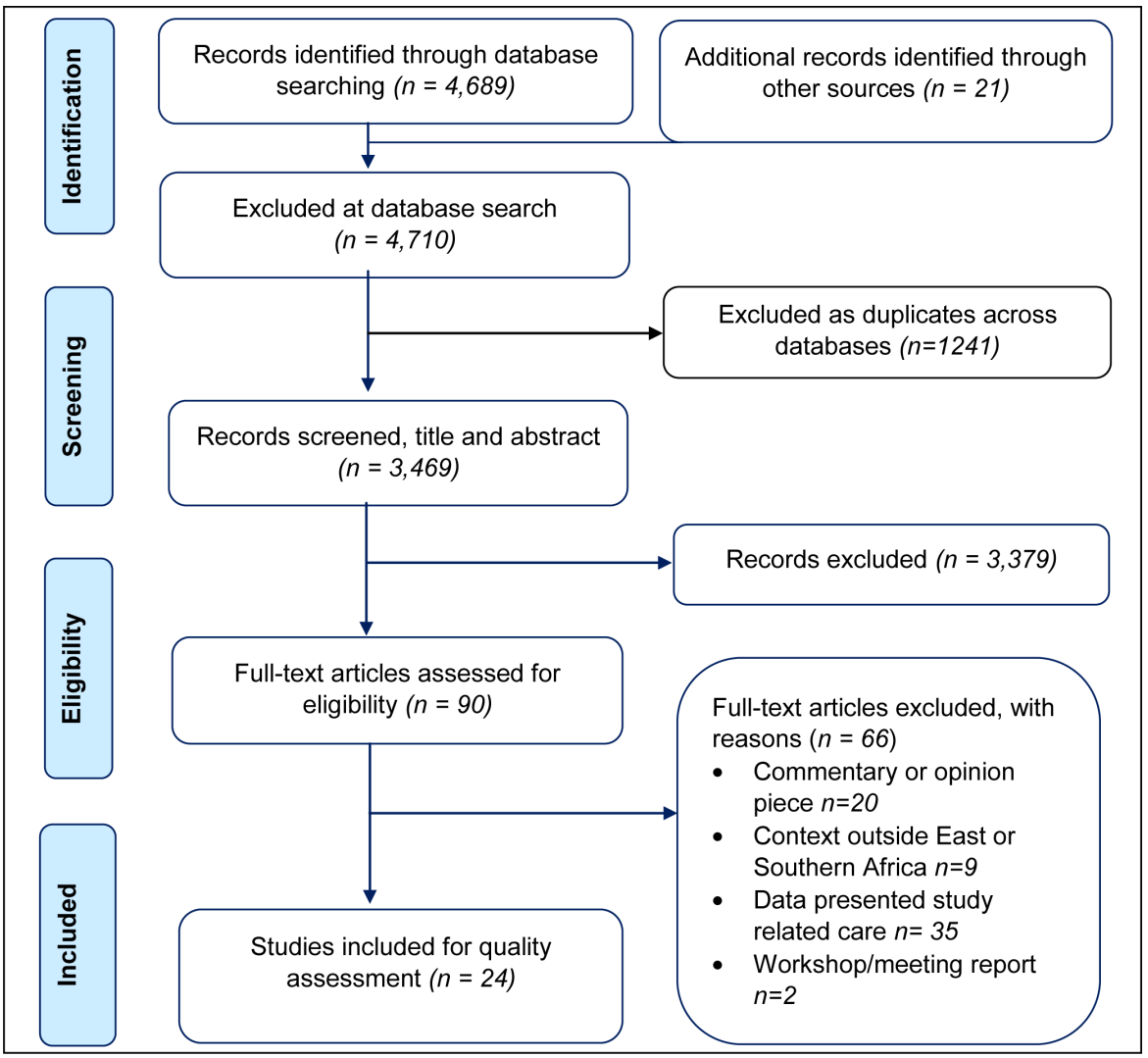



**Figure 1. Prisma flow diagram – identification of relevant studies.**

inclusion criteria were removed during screening. Of the 90 full-text articles screened, 66 were excluded: 20 were opin- ion or commentary papers, 9 were conducted outside East and Southern Africa, 35 reported provision of care that was related to the study (not ancillary), and 2 were workshop or meet- ing reports. The remaining 24 articles met the inclusion criteria and were included in the quality assessment.

### Characteristics of included studies

All of the studies reported in the review were conducted in East and Southern African settings: Kenya (*n=6*)[33–38], Uganda (*n=2*)[39,40], Malawi (*n=5*)[41–45], South Africa (*n=4*)[46–49], Tanzania (*n=1*)[50], one study (*n=1*)[51] was conducted at mul- tiple research centres of East and Southern Africa and those that focused on RCS in general (*n=5*)[52–56]. In total, 16 studies were qualitative, four were systematic reviews, three were theoretical and one quantitative. Only qualitative data was extracted from the quantitative study and used in the analysis. Although the search criteria focused on studies published from June 2004 to November 2020, 85% of the studies were pub- lished since 2010, reflecting a more contemporary context. This was expected given the fact that the concept of ancillary care in medical research has been increasingly recognised as a complex ethical challenge particularly where medical research is conducted in RCS. The included studies are summarised in Table 7.

### Key themes

The studies focused on different approaches to ancillary care provision (direct medical care, referral, non-medical support); researcher motivation for providing ancillary care (inadequate health care options, lack of available and accessible basic medical services, constraints in resources, vulnerability due to socio-economic inequalities); and participation for purpose (gaining access to medical care and support, ancillary care alternative for standard care offered by the local health care system, better medical care). A theme matrix of the included studies is summarised in Table 8.

### Approaches to ancillary care provision

In total, 14 studies conducted in Kenya (*n=5*)[33,34,36–38], Malawi (*n=3*)[41,44,45], South Africa (n=3)[46–48], Uganda (*n=2*)[39,40], and East and Southern Africa research centres (*n=1*)[51] were explicit in mentioning the care and support provided to study participants additional to the study related care. Three main approaches are reported in the included studies that researchers use to address health needs of their participants identified dur- ing the conduct of research. The type of ancillary care reported in these studies ranged from provision of medical care by the research team or partners to assisting with referral services for participants to access additional care (Table 9).

***Direct medical care.*** Studies that reported researchers pro- vided health care according to the needs of participants made available access to free medical treatment, screening and diagnostic services and other services such as counselling.

Some studies reported that participants felt that they get better medical services when they join to participate in medical research.

Two studies reported the provision of ancillary care being extended to non-research participating individuals includ- ing partners of volunteers, ineligible to participate volunteers following screening, and former volunteers[47,51].

***Referral.*** Referral was common for those participating in medi- cal research to access healthcare services from partners or local health care service providers if not provided for by researchers. Referral was described to support participating individual access to specialised services or services not pro- vided locally such as diagnostic and screening services or met the healthcare costs incurred by participants only during the study[33,38,40,46,51].

***Non-medical support.*** While most of the studies reported the provision of health or medical care to meet participants' needs, there was a range of studies that mentioned non-health related support, and some studies provided both including for exam- ple provision for the tuition for children of parents participating in a study or the provision of water and sanitation in households and communities where research was conducted[34,36,39,42].

### Researcher's motivation for providing ancillary care

Researcher motivations for providing ancillary care referred to researchers' justifications for meeting a particular additional need requiring either health care or support services. Ten studies explicitly mentioned the reasons researchers took a decision to consider providing care and support for their participants' ancillary health needs[33,35,36,40,46,47,50–52,54].

Increased vulnerabilities due to the lower socio-economic sta- tus of most participants in RCS was a frequently cited reason for ancillary care provision[33,36,54], justified because individuals failed to afford the costs for access to routine or basic medi- cal care and treatment such as antiretroviral treatment[35]. Other studies reported poor and resource-constrained health care demanding for additional mechanisms to address participants needs[36,40,50,51].

### Participation for purpose

Evidence that individuals volunteer to participate in medical research to accrue benefits was reported in ten studies[34,35,39,40,42,44,46–48,52]. Although participation is voluntary in medical research, participants expect researchers to be clear about the benefits whether directly or indirectly adding to their study responsibilities. Participants expectations on benefits from participating in medical research were reported across the majority of the studies. Perceived benefits expected by participants were dominated by the opportunity to access better quality care unavailable in the local health care system[38,42,44,45,50,55].

**Table 7. Characteristics of included studies.**

| Author & year | Study aim | Methods | Description of participants | Funding |
|---|---|---|---|---|
| Barsdorf ***et al***., 2010<br>South Africa | To explore a South African community's perceptions of who should provide what to HVT participants and explore respondents' perceptions of how and why this should be done | Qualitative (interviews) | 29 respondents - adult men and women working at or attending five primary health care clinics in two rural areas in KwaZulu- Natal where HVT preparation activities have been carried out | International AIDS Vaccine Initiative (IAVI); US NIH funded HIV Vaccine Trials Network (HVTN) and FIT Biotech. |
| Embleton ***et al***., 2015<br>Kenya | To describe the processes of adapting ethical guidelines for SCCY's specific vulnerabilities in LMIC | Theoretical study | 446 SCCY included across the three studies based in Eldoret. | Eunice Kennedy Shriver National Institute of Child Health and Human Development |
| Richards and Helmchen, 2013<br>RCS | To highlight two previously underappreciated facets of ancillary care adoption and develop plausible solutions to reduce the unintended and overlooked adverse consequences from mandating the provision of ancillary care in developing countries | Theoretical study | | Details not available |
| Chou ***et al***., 2007<br>Uganda | To estimate the cost of identification, reporting, treatment, and follow-up of AEs in a perinatal HIV clinical trial in a developing country setting and to establish the relative cost for components of the AE reporting and management system | Quantitative – (cost evaluation) | | HIV Prevention Trials Network and sponsored by the NIH, and US Department of Health and Human Services, under Cooperative Agreement |
| Pratt and Hyder, 2018<br>RCS | To identify how HSR funding schemes are designed to incentivise research that contributes to better health systems for the worst-off | Qualitative – (Semi-structured in-depth interviews) | - Grants officers working for 11 funders and organisations that support HSR in LMICs regarding their largest HSR funding scheme<br>- 10 women and six men were interviewed about nine HSR funding schemes | Australian NHMRC Early Career Sidney Sax Public Health Overseas Fellowship |
| Ngongo ***et al***., 2012<br>East and Southern Africa | To determine what services are currently provided by IAVI-sponsored RCs, identify gaps and challenges in service provision, and whether sponsors and RCs can agree on standards of care despite the differences in national and regional contexts | Systematic review | | USAID |
| Ward ***et al***., 2018<br>Tanzania & Ghana | To address the ethical issues raised by the provision of health care during the conduct of a long-standing PMVT in resource constrained settings | Qualitative – (key informant, semi-structured interview) | - clinical and research team members from four separate research centres in Ghana and Tanzania<br>- wider partners of the PMVT were also included as respondents: respective government bodies, ethics review committees, health care system representatives, and international partners | GlaxoSmithKline Biologicals SA (GSK) and the PATH/MVI) in partnership with Malaria Clinical Trials Alliance (MCTA) |
| Chilengi, 2009<br>RCS | To address from an ethical perspective, the moral obligations that the various stakeholders in biomedical research inevitably inherit by virtue of being in their state either as research participants themselves, researchers and their institutions, sponsors of the research, data safety monitoring boards, community advisory boards, regulatory authorities or committees that review and approve the research | Theoretical study | | Details not available |



Wellcome Open Research 2021, 6:164 Last updated: 01 DEC 2022

| Author & year | Study aim | Methods | Description of participants | Funding |
|---|---|---|---|---|
| **Kamuya *et al*., 2013 Kenya** | To explore how social relations between one group of fieldworkers and participants, and associated practical and ethical dilemmas, evolved and shifted over the course of the study | Qualitative (interviews and observations) | Fieldworkers | KEMRI-Wellcome Trust (Strategic Award and fellowship to SM) |
| **Ramjee *et al*., 2010 South Africa** | To describe the methods used to conduct HIV prevention trials in KwaZulu Natal, South Africa, with a focus on strategies developed to ensure good data quality, completion of the trial within an ethical framework, and partnerships developed with participants, the broader community and other health care providers | Qualitative approaches | Consultation and information sessions held with community stakeholders and political and traditional leaders as part of the community-entry process, prior to development of the CRS | The Bill and Melinda Gates Foundation, USAID, UK DfID and the MRC, the US NIH |
| **Lairumbi *et al*., 2012 Kenya** | To explore the views of stakeholders involved in health-related research regarding these forms of benefit sharing in a developing world context | Qualitative (in-depth interviews) | 52 respondents drawn from institutions involved in global health research in Kenya | Wellcome Trust Biomedical Ethics PhD Studentship awarded to Lairumbi |
| **Devries *et al*., 2015 Uganda** | To describe how current research guidelines and best practice for conducting research with children may be applied to survey research, and to explore tensions between recommended best practices and real-life challenges encountered during data collection. | Qualitative (interviews with trial participants) | - 23 children who had been referred and who had received some sort of help from a protection agent, another 7 children who had been referred and who also had requested counselling after the survey, and a further 10 who had been referred for violence but did not request counselling and did not receive any support from a community agency.<br>-The children attended different schools in Luwero.<br>-22 were girls and 18 were boys, and most were aged 12-14 years. | Hewlett Foundation, UK- MRC, DfID and the Wellcome Trust, and Unicef Uganda. |

Wellcome Open Research 2021, 6:164 Last updated: 01 DEC 2022

| Author & year | Study aim | Methods | Description of participants | Funding |
|---|---|---|---|---|
| **Mtunthama *et al*., 2008**<br><br>**Malawi** | To determine the usefulness of our subject recruitment information, the reasons for subject's participation in the research and the complication rates of our programme | Qualitative (interviews with trial volunteers) | A total of 100 volunteers (36 women; 64 men) participated in the audit in 2004. Nine subjects had been patients in the hospital, while the others were either employees, relatives of patients. Volunteers ranged from 20 to 57 years of age (mean 33.9 yrs). | Wellcome Trust of Great Britain |
| **Nkosi *et al*.,**<br><br>**2020 South**<br><br>**Africa** | To describe how research staff and intervention implementing partners responded to these needs, the challenges they faced in responding and the insights they shared for improving ancillary care planning in LMICs | Qualitative (interviews) | - 77 participants<br>1) participants from the research case study<br>2) ethics committee, PE officers and CAB members<br>3) community stakeholders | Wellcome Centre award<br>- Wellcome Trust & MRC Newton Fund Collaborative Award |
| **Stunkel and Grady, 2011**<br><br>**RCS** | To examine, classify and compare empirical studies which measure self-reported motivations, reasons for participation, and/or decision-making processes for healthy volunteers participating in drug studies and other clinical research not intended to offer direct health benefits | Systematic review | | NIH Clinical Center Department of Bioethics |
| **Mfutso-Bengo *et al*., 2015**<br><br>**Malawi** | To fill a gap in the literature by contributing to the understanding of factors that motivate research participants to give their consent to participate in biomedical research in Malawi | Qualitative – (focus group discussion) | One hundred eighty-two research participants took part in 18 FGDs. Most of the participants were women and had attended at least primary school. | The Wellcome Trust |

| Author & year | Study aim | Methods | Description of participants | Funding |
|---|---|---|---|---|
| **Vreeman *et al*., 2012**<br><br>**Kenya** | To evaluate the community's perspectives on research, informed consent, and use of the baraza within the research process to engage families in western Kenya | Qualitative using mabaraza (similar to focus groups) | - 108 total participants<br>- male and female Orphaned and separated children (vulnerable), chiefs, caregivers and members of the general public from selected communities | Multiple international funding organisation including NICHD, NIMH and USAID-AMPATH Partnership as part of the President's Emergency Plan for AIDS Relief (PEPFAR) |
| **Cohen *et al*., 2009**<br><br>**RCS** | To determine the extent to which recently registered clinical trials report the use of standard of care and post-trial obligations in trial registries, and whether trial characteristics vary according to setting | Systematic review | | Details not available |
| **Gooding *et al*., 2018**<br><br>**Malawi** | To deepen understanding of the acceptability of research to potential participants, and to suggest directions for future assessment of acceptable trial design | Qualitative – (interviews) | - Parents in 41 households invited to enrol their children, including parents who enrolled their child (21), who withdrew (9), and who did not participate (11).<br>- Most interviews involved the main carer (usually the mother), but in some cases a wife and husband were interviewed together because both wanted to be interviewed. | Research Project Cooperation Agreement between the University of Liverpool and the Centre for Disease Control: Epidemiology, Prevention and Treatment of Influenza and Other Respiratory Infections |
| **Essack *et al*., 2010**<br><br>**South Africa** | To identify and explore the ethical concerns of various stakeholders through an open-ended, in-depth interview approach | Qualitative – (open-ended, in-depth interview approach) | Stakeholder groups involved were Community Advisory Boards (CABs) at sites; site staff (including site principal investigators, medical officers and vaccine educators); media personnel that have reported on HVTs; civil society representatives (including human rights, gender and child groups); government representatives; Research Ethics Committee (REC) members who had reviewed HVT protocols; and HVT sponsors. | South African AIDS Vaccine Initiative |
| **Oduwo and Edwards, 2014**<br><br>**Kenya** | To determine whether cluster trials in Kenya are used artificially to delay or limit children's access to treatment, or designed and implemented to avoid obligations for children's right to health | Systematic revies | Focused on clinical trials conducted in Kenya between 2003 and 2014 | Wellcome Trust |
| **Kamuya *et al*., 2014**<br><br>**Kenya** | To explore nature of interactions between fieldworkers and research participants in community-based studies, the challenges that fieldworkers faced, and if and how these challenges were resolved | Qualitative – (in-depth interviews) | 42 fieldworkers, 4 researchers, and 40 study participants | Wellcome Trust strategic award |
| **Mfutso-Bengo *et al*., 2008**<br><br>**Malawi** | To understand participants' perceptions, understanding and attitudes towards health research | Qualitative – (focus group discussion) | - 18 focus group discussions<br>- 23 male and 159 female<br>- 30 rural and 11 from urban | The Wellcome Trust, UK |
| **Sullivan *et al*., 2020**<br><br>**Malawi** | To elicit the views of Malawian women on factors influencing women's interest in participating in a HIV prevention clinical trial that involves initiating PrEP while pregnant. | Qualitative – (semi-structured interviews) | 35 reproductive-aged women at risk for HIV in but HIV-negative | National Institute of Allergy and Infectious Diseases of the NIH |



Wellcome Open Research 2021, 6:164 Last updated: 01 DEC 2022

**Table 8. Theme matrix of the included studies.**

| Author & year | Themes | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Approaches to ancillary care | | | Researcher motivation for providing ancillary care | | | Participation for purpose | | |
| | 1 | 2 | 3 | 1 | 2 | 3 | 1 | 2 | 3 |
| **Barsdorf *et al*., 2010** | | x | | x | | | | | |
| **Embleton *et al*., 2015** | | x | | | | x | | | |
| **Richards and Helmchen, 2013** | | | | | | x | | | |
| **Chou *et al*., 2007** | x | | x | | | | x | x | |
| **Pratt and Hyder, 2018** | | | | | x | | | | |
| **Ngongo *et al*., 2012** | x | x | | x | | | | | |
| **Ward *et al*., 2018** | | | | x | x | | | x | |
| **Chilengi, 2009** | | | | | | x | | | |
| **Kamuya *et al*., 2013** | x | | x | | | | | | |
| **Ramjee *et al*., 2010** | x | x | | x | | | | | |
| **Lairumbi *et al*., 2012** | | | | | | x | x | x | x |
| **Devries *et al*., 2015** | x | x | | x | x | x | | | |
| **Mtunthama *et al*., 2008** | x | | | | | | | x | x |
| **Nkosi *et al*., 2020** | | x | | | x | x | | | |
| **Stunkel and Grady, 2011** | | | | | | | x | | |
| **Mfutso-Bengo *et al*., 2015** | | | | x | x | | | | x |
| **Vreeman *et al*., 2012** | x | | x | x | | x | | | |
| **Cohen *et al*., 2009** | | | | | x | | | | |
| **Gooding *et al*., 2018** | | | | | | | x | | |
| **Essack *et al*., 2010** | | | | | x | | | x | |
| **Oduwo and Edwards, 2014** | x | | | x | | | | | |
| **Kamuya *et al*., 2014** | x | | | | | | | | X |
| **Mfutso-Bengo *et al*., 2008** | x | | | | | | x | | X |
| **Sullivan *et al*., 2020** | x | | | | | | | x | X |
| **Key** | 1 = direct medical care<br>2 = referral<br>3 = non-medical support | | | 1 = inadequate health care options<br>2 = constrained resources<br>3 = vulnerability due to socio-economic inequalities | | | 1 = gain access to care and support<br>2 = alternative for standard care<br>3 = better medical care | | |

Gaining access to better medical care and support was reported as one of the direct benefits that most participants expected. Additional direct benefits included researchers providing direct health care for any problem presented or found in their participants, but not as a direct result of participation[39,40,42,44,46,52]. Some studies reported participants expectations beyond direct medical care provided by the study, such as for food items, cell phone airtime, and baby clothes[34,36,47,48]. Others thought that participants considered provision of ancillary care as an alterna- tive for standard care offered by the local health care system[39], for example, participants thinking that effective drugs are always available in medical research clinics[42] and that any researcher

**Table 9. Approaches to ancillary care provided to study participants.**

| Author | Context | Study-purpose | Form of ancillary care |
|---|---|---|---|
| Vreeman *et al.*, 2012 | Kenya - Uasin Gishu county of western Kenya | To evaluate the community's perspectives on research, informed consent, and use of the baraza within the research process to engage families in western Kenya | **Health related care**<br>- Primary health care services<br>- Access to free treatment (ART)<br>- Nutrition support services<br>- Psychosocial support<br><br>**Social support**<br>- support with tuition for children<br>- provide water sources<br>- economic development training |
| Oduwo and Edwards, 2014 | Kenya – Only trials conducted in Kenya were eligible for review. | To determine whether cluster trials in Kenya are used artificially to delay or limit children's access to treatment, or designed and implemented to avoid obligations for children's right to health | **Health related care**<br>- any needed care equivalent to the local standard of care |
| Barsdorf *et al.*,, 2010 | South Africa - primary health care clinics in rural areas in KwaZulu-Natal | To explore a South African community's perceptions of who should provide what to HVT participants and explore respondents' perceptions of how and why this should be done | **Health related care**<br>- Assisting with referral to access ART |
| Embleton *et al.*, 2015 | Kenya | To describe the processes of adapting ethical guidelines for SCCY's specific vulnerabilities in LMIC. | **Health related care**<br>- Assisting study participants with referral for specialised health care services |
| Ngongo *et al.*, 2012 | East and Southern Africa - Research centres within the IAVI collaborative network in sub-Saharan Africa<br>- Eastern and Southern Africa | To determine what services are currently provided by IAVI-sponsored RCs, identify gaps and challenges in service provision, and whether sponsors and RCs can agree on standards of care despite the differences in national and regional contexts | **Health related care**<br>- Provided counselling<br>- Provided CD4 count services to volunteers<br>- Assisting study participants with referral for ART<br>- Management or treatment of STIs<br>- Provided male condoms, FP services, information, education and counselling on Adult male Circumcision<br>- paying service costs for volunteers<br>- Ancillary care extended to non-trial volunteers (STIs and CD4 count) including partners of volunteers, screen outs, and former volunteers |
| Kamuya *et al.*, 2013 | Kenya | To explore how social relations between one group of fieldworkers and participants, and associated practical and ethical dilemmas, evolved and shifted over the course of the study | **Health related care**<br>- Free medical care for all common illnesses during study period<br><br>**Social support**<br>- two chairs for each participating household,<br>- sweets for children and minors,<br>- educational materials to school going children,<br>- in-kind token to each household at end of study |



Wellcome Open Research 2021, 6:164 Last updated: 01 DEC 2022

| Author | Context | Study-purpose | Form of ancillary care |
|---|---|---|---|
| Ramjee *et al.,* 2010 | South Africa - The HPRU set up clinical research sites (CRS) in several communities in the greater Durban area and one site in a rural area | To describe the methods used to conduct HIV prevention trials in KwaZulu Natal, South Africa, with a focus on strategies developed to ensure good data quality, completion of the trial within an ethical framework, and partnerships developed with participants, the broader community and other health care providers | **Health related care**<br>- Provided HIV prevention, treatment, and care education to communities where Clinical Research Sites (CRSs) are based<br>- Provided Pap smears to women of 18-50 years old<br>- Referral of participants to health care partners<br>- Provided STI screening with support from partners<br>- Provided oral and injectable hormonal contraception at clinic sites |
| Devries *et al.,* 2015 | Uganda - Luwero in Uganda | To describe how current research guidelines and best practice for conducting research with children may be applied to survey research, and to explore tensions between recommended best practices and real-life challenges encountered during data collection. | **Health related care**<br>- Offered counselling to children (participants)<br>- referral of participants urgently if they required immediate intervention<br>- attending to children's health and emotional needs |
| Mtunthama *et al.,* 2008 | Malawi - Queen Elizabeth Central Hospital, Blantyre, Malawi | To determine the usefulness of our subject recruitment information, the reasons for subject's participation in the research and the complication rates of our programme. | **Health related care**<br>- provided free medical care to study participants for all their health problems |
| Nkosi *et al.,* 2020 | South Africa - PIPSA of the Africa Health Research Institute (AHRI), KwaZulu-Natal, South Africa. | To describe how research staff and intervention implementing partners responded to these needs, the challenges they faced in responding and the insights they shared for improving ancillary care planning in LMICs | **Social support**<br>- Referral for social and welfare services<br>- Facilitate access to social grants |
| Chou *et al.,* 2007 | Uganda, Kampala. The Makerere University-Johns Hopkins University Research Collaboration (MU-JHU | To estimate the cost of identification, reporting, treatment, and follow-up of AEs in a perinatal HIV clinical trial in a developing country setting and to establish the relative cost for components of the AE reporting and management system | **Health related care**<br>- provide prescribed medications without charge to study participants<br>- paying expenses billed to the study by pharmacies<br>**Social support**<br>- paying expenses for meals for participants visiting the research clinic<br>- financial assistance for hospitalised patients |
| Kamuya *et al.,* 2014 | Kenya - The KEMRI-Wellcome Trust Research Programme (KEMRI-WT in Kilifi on the Kenyan Coast. | To explore nature of interactions between fieldworkers and research participants in community-based studies, the challenges that fieldworkers faced, and if and how these challenges were resolved | **Health related care**<br>- provided all needed health care to study participants and household members<br>- assisting with referral costs of participants for other common illnesses<br>- free medical care for all common illnesses during the study |
| Mfutso-Bengo *et al.,* 2008 | Malawi – in the rural and urban health centre setting within Blantyre. | To understand participants' perceptions, understanding and attitudes towards health research | **Health related care**<br>- free medical treatment for conditions unrelated to the study |
| Sullivan *et al.,* 2020 | Malawi - Lilongwe | To elicit the views of Malawian women on factors influencing women's interest in participating in a HIV prevention clinical trial that involves initiating PrEP while pregnant. | **Health related care**<br>- access to high quality care including treatment unavailable in the local healthcare system<br>- access to diagnostic services |



Wellcome Open Research 2021, 6:164 Last updated: 01 DEC 2022

is mistakenly considered as a doctor who would provide care for any health problem[34].

## Discussion

This study describes the practices of ancillary care provision to study participants in medical research in East and South- ern Africa. The results show that reporting on care and support provided for the ancillary health needs of study participants in RCS remains low, despite growing calls for its implementation in medical research[9,57–59]. For researchers conducting medical research in RCS to consider planning for ancillary care, as recommended in international ethical guidelines, the existing evidence-base is currently insufficient to guide best practice. For example, in the commentary to guideline 6 of the CIOMS it states that "*while sponsors are generally not obliged to provide healthcare services beyond what is required for their research, it is morally admirable to do so*"[2], but as *universal* guidelines how relevant are they to contexts with underlying poverty or structural inequalities in health care access? Should ancillary care be considered as unethical when it is really a need among participants and communities in RCS? Because it is difficult to establish whether medical research- ers care about participants' ancillary care needs, it was hard to explore the rationale for decisions on provision of ancil- lary care, particularly in clinical trials and observational stud- ies. According to Haire[60], it could be that the possible reasons why medical researchers fail to provide ancillary care to their participants include funders' or sponsors' stringent rules over research funds. The systematic review and meta-synthesis undertaken here points toward some key considerations in relation to optimising the evidence on the ethics of ancillary care in research especially where it is conducted in RCS.

The findings of this study, consistent with the findings of other studies conducted in RCS, reveal that given the numerous health challenges faced by individual volunteers who partici- pate in medical research, it may be obvious that researchers bear some responsibilities (not all) for the well-being of their participants[61]. The evidence has shown that participants in research conducted in RCS are likely to be socioeconomi- cally vulnerable and face particular barriers to access healthcare services[62]. This inequality in health care access presents medi- cal researchers in RCS with a need to provide or consider ancil- lary care for their participants as a direct benefit. The possible levels of ancillary care reported in the findings of this review are similar to what Dickert and Wandler[58] suggested which include: providing diagnostic information, making referrals for care, providing treatment, or paying for treatment. Ancillary needs of participants were documented in at least some of the included studies in this review, and researchers' responsive- ness to them was reported as justification for the provision of additional care. A cross-cutting theme in our synthesis was the tension between what researchers can provide as ancillary care for participants' unmet health needs and the obligations linked to ethics of conducting medical research. However, it has proven difficult to establish strict rules as to what levels of ancillary care is universally required of researchers working in RCS[13,58].

While some contend that the provision of ancillary care can be perceived as either structural coercion or undue inducement for study participants or communities because of the health- care disparities in RCS[16,18,63], we argue that applying ethical guidelines makes this a requirement. Applying the concepts of coercion and undue influence are inadequate in determining whether or not ancillary care is unethical in medical research. We agree with JA Fisher[16] in asserting that these terms (coer- cion and undue influence) only serve as a rational approach to ethics, one that ignores the social and economic contexts of research and instead places those domains outside the needs of participants. When considering the arguments advanced by others on medical researchers' obligations, we contend that it is ethical for researchers to demonstrate responsiveness to the ancillary needs of individual participants or communities by offering care or support if they have the capacity to do so[13]. Both L Belsky and HS Richardson[1] and MW Merritt[11] have also suggested that the duty to address the health needs of study participants must be well anticipated and planned for dur- ing the planning of research studies, and funds specifically budgeted to provide ancillary care. In this review, however, it is unclear to what extent authors of the included studies included plans to provide for the ancillary health needs. That said, there are key questions concerning the impact this has on ethical research practice in RCS.

Notwithstanding the concerns that different authors raise about ancillary care, the findings support the theory that the ancil- lary care model has the potential to promote individual's participation i n medical research[1]. Careful consideration of what participants expect from participating in medical research, as reported in the included studies, ancillary care can only be regarded as a benefit for individual volunteers to participate[35,42,47,50]. Although most of the included studies that reported ancillary care provision to study participants did not mention any ethical conflicts encountered, Lairumbi and colleagues[35] suggested that since ancillary care conflates the benefits in research participation to those of clinical care – it may lead to errors in ethical judgement. While identifying varia- tions in ancillary care practices across studies can indicate ways to strengthen medical research design, there is a debate over how much ancillary care is needed to be ethical[48], and how to make standardised research design responsive when approaches from different studies vary.

In order to develop and maintain trust and commitment of par- ticipants to the research, findings in this review revealed that researchers felt the need to demonstrate an understanding of participant health needs and be responsive to them[46,51,52,54]. Special consideration on strategies that can improve con- ceptualisation of ancillary care are recommended to balance study related demands with ethical conduct of research and ancillary care obligations. Furthermore, medical research should be conducted with proper clinical and ethical oversight, and participants should be treated in a way that minimizes risks and maximises (feasible) benefits to their well-being.

Additionally, our findings highlight the importance of research- ers seeking a balance between taking into consideration the

immense health burdens their participants face, while also ensuring that study regulations are upheld. Providing ancillary care in medical research is a critical issue to consider in RCS, but whereas provision of any care unrelated to the study may appear to be in question, this study reveals that such care is often critical. It must be noted that if additional care is given to participants through the study, would it qualify as reciprocity? In that specific case, who defines what benefit is in the context of RCS? If the community defines school fees as a benefit to them and researchers give it to them, should that be considered unethical?

This review is not without limitations. As discussed above, the provision of ancillary care is inconsistently reported in most of the biomedical research studies (observational or clinical trials). Moreover, due to limited reporting of ancillary care in biomedical research in RCS, we were unable to relate provision of ancillary care with guidelines from funding institu- tions. Also, because of the limited research in this area, some of the results presented within this review are based on single studies rather than the compilation of several studies. To aid clar- ity when presenting a description of the results of this review, we have summarised the volume of evidence supporting key themes drawn, Table 8.

## Conclusion

This systematic review and meta-synthesis aimed to understand the current practices of ancillary care provision by research- ers conducting medical research in East and Southern Africa. While several studies have documented ancillary care being an ethical obligation for researchers conducting medical research in RCS, this, to our knowledge, is the first systematic review and meta-synthesis to assess the reporting of practices in East and Southern Africa. Understanding these current prac- tices could help steer guidelines in the direction that meets the broader needs of ancillary care ethics in medical research. This review has shown that, factors influencing ancillary care decisions, participants expectation from participating in medical research, and the ethical basis of conducting medical research in settings coupled with competing health challenges may explain the current practices of ancillary care in RCS. While the specifics of the issues that researchers face are likely to vary depending on the type of research and the context in which that research is being conducted, we recommend that appro- priate ancillary care is also a key requirement to strengthen research practice and for the long-term sustainability of research programmes in RCS. The ethical challenges that must be addressed in medical research in RCS, such as those related to making provisions for ancillary care to study participants during research, are rarely clearly described. We highlight the importance of developing adaptable ethics guidelines for medi- cal researchers in RCS to consider provision of ancillary care to their participants, and the need for these ethical guide- lines to be accounted for in the conduct of medical research that aim to enhance quality of life in this population.

## Data availability

All data underlying the results are available as part of the article and no additional source data are required.

### Reporting guidelines

Figshare: PRISMA Checklist for "What do we know about ancillary care practices in East and Southern Africa? A systematic review and meta-synthesis." https://doi.org/10.6084/m9.figshare.14703426.v1[23].



### Acknowledgements

We thank Deborah Nyirenda (Malawi-Liverpool Wellcome Trust Clinical Research Programme) for her help with addi- tional articles included in this review and for reviewing the draft manuscript.

## References

1. Belsky L, Richardson HS: **Medical researchers' ancillary clinical care responsibilities.** *BMJ.* 2004; **328**(7454): 1494–1496.
PubMed Abstract | Publisher Full Text | Free Full Text

2. Council for International Organizations of Medical Sciences: **International ethical guidelines for health-related research involving humans.** *International ethical guidelines for health-related research involving humans.* 2017.
Reference Source

3. McMillan JR, Conlon C, Nuffield Council on Bioethics: **The ethics of research related to health care in developing countries.** *J Med Ethics.* 2004; **30**(2): 204–206.
PubMed Abstract | Publisher Full Text | Free Full Text

4. Haire BG, Ogundokun O: **Ethics of ancillary care in clinical trials in low income countries: a Nigerian case study.** *Afr J Reprod Health.* 2014; **18**(3 Spec No): 135–142.
PubMed Abstract

5. UNICEF, World Health Organization: **Health in the post-2015 development agenda: need for a social determinants of health approach: joint statement of the UN Platform on Social Determinants of Health**. In: *Health in the post-2015 development agenda: need for a social determinants of health approach: joint statement of the UN Platform on Social Determinants of Health.* edn.; 2013: 18–18.
Reference Source

6. Adindu A: **Assessing and assuring quality of health care in Africa.** *African Journal of Medical Sciences.* 2010; **3**(1): 31–36.
Reference Source

7. Eide AH, Mannan H, Khogali M, *et al.*: **Perceived barriers for accessing health services among individuals with disability in four African countries.** *PLoS One.* 2015; **10**(5): e0125915.
PubMed Abstract | Publisher Full Text | Free Full Text

8. Miller FG, Mello MM, Joffe S: **Incidental findings in human subjects research: what do investigators owe research participants?** *J Law Med Ethics.* 2008; **36**(2): 271–9, 211.
PubMed Abstract | Publisher Full Text | Free Full Text

9. Richardson HS: **Moral entanglements: the ancillary-care obligations of**

**medical researchers.** Oxford University Press. 2012.
Publisher Full Text

10. Krubiner CB, Syed RH, Merritt MW: **Health researcher's ancillary-care responsibilities in low-resource settings: The landscape of institutional guidance.** *IRB.* 2015; **37**(3): 12–19.
PubMed Abstract

11. Merritt MW: **Health Researchers' Ancillary Care Obligations in Low-Resource Settings How Can We Tell What Is Morally Required?** *Kennedy Inst Ethics J.* 2011; **21**(4): 311–47.
PubMed Abstract | Publisher Full Text | Free Full Text

12. Rulli T, Millum J: **Rescuing the duty to rescue.** *J Med Ethics.* 2016; **42**(4): 260–264.
PubMed Abstract | Publisher Full Text

13. MacKay D, Rulli T: **The Duty to Rescue and Investigators' Obligations.** *Kennedy Inst Ethics J.* 2017; **27**(1): 71–105.
PubMed Abstract | Publisher Full Text

14. Grant RW, Sugarman J: **Ethics in human subjects research: do incentives matter?** *J Med Philos.* 2004; **29**(6): 717–738.
PubMed Abstract | Publisher Full Text

15. Emanuel EJ: **Undue inducement: nonsense on stilts?** *Am J Bioeth.* 2005; **5**(5): 9–13; discussion W18–11, W17.
PubMed Abstract | Publisher Full Text

16. Fisher JA: **Expanding the frame of "voluntariness" in informed consent: structural coercion and the power of social and economic context.** *Kennedy Inst Ethics J.* 2013; **23**(4): 355–379.
PubMed Abstract | Publisher Full Text

17. Ravinetto RM, Afolabi MO, Okebe J, *et al.*: **Participation in medical research as a resource-seeking strategy in socio-economically vulnerable communities: call for research and action.** *Trop Med Int Health.* 2015; **20**(1): 63–66.
PubMed Abstract | Publisher Full Text

18. Nyirenda D, Sariola S, Kingori P, *et al.*: **Structural coercion in the context of community engagement in global health research conducted in a low resource setting in Africa.** *BMC Med Ethics.* 2020; **21**(1): 90.
PubMed Abstract | Publisher Full Text | Free Full Text

19. Lott JP: **Module three: vulnerable/special participant populations.** *Dev World Bioeth.* 2005; **5**(1): 30–54.
PubMed Abstract | Publisher Full Text

20. Emanuel EJ, Abdoler E, Stunkel L: **Research ethics: How to treat people who participate in research.** *Bethesda: National Institutes of Health.* 2010.

21. Dal-Ré R, Rid A, Emanuel E, *et al.*: **The potential exploitation of research participants in high income countries who lack access to health care.** *Br J Clin Pharmacol.* 2016; **81**(5): 857–864.
PubMed Abstract | Publisher Full Text | Free Full Text

22. Moher D, Liberati A, Tetzlaff J, *et al.*: **Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement.** *PLoS Med.* 2009; **6**(7): e1000097.
PubMed Abstract | Publisher Full Text | Free Full Text

23. Kapumba B: **PRISMA Checklist for "What do we know about ancillary care practices in East and Southern Africa? A systematic review and meta-synthesis".** *figshare.* Dataset. 2021.
http://www.doi.org/10.6084/m9.figshare.14703426.v1

24. Pearson A: **Balancing the evidence: incorporating the synthesis of qualitative data into systematic reviews.** *JBI Reports.* 2004; **2**(2): 45–64.
Publisher Full Text

25. Pearson A, Rittenmeyer L, Robertson-Malt S: **Synthesizing qualitative evidence**. Lippincott Williams & Wilkins Philadelphia, PA: 2011.
Reference Source

26. Dixon-Woods M, Sutton A, Shaw R, *et al.*: **Appraising qualitative research for inclusion in systematic reviews: a quantitative and qualitative comparison of three methods.** *J Health Serv Res Policy.* 2007; **12**(1): 42–47.
PubMed Abstract | Publisher Full Text

27. Lewin S, Glenton C, Munthe-Kaas H, *et al.*: **Using qualitative evidence in decision making for health and social interventions: an approach to assess confidence in findings from qualitative evidence syntheses (GRADE-CERQual).** *PLoS Med.* 2015; **12**(10): e1001895.
PubMed Abstract | Publisher Full Text | Free Full Text

28. Shea BJ, Reeves BC, Wells G, *et al.*: **AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both.** *BMJ.* 2017; **358**: j4008.
PubMed Abstract | Publisher Full Text | Free Full Text

29. Finfgeld DL: **Metasynthesis: the state of the art–so far.** *Qual Health Res.* 2003; **13**(7): 893–904.
PubMed Abstract | Publisher Full Text

30. Zimmer L: **Qualitative meta-synthesis: a question of dialoguing with texts.** *J Adv Nurs.* 2006; **53**(3): 311–318.
PubMed Abstract | Publisher Full Text

31. Thomas J, Harden A: **Methods for the thematic synthesis of qualitative research in systematic reviews.** *BMC Med Res Methodol.* 2008; **8**: 45.
PubMed Abstract | Publisher Full Text | Free Full Text

32. Lucas PJ, Baird J, Arai L, *et al.*: **Worked examples of alternative methods for the synthesis of qualitative and quantitative research in systematic reviews.** *BMC Med Res Methodol.* 2007; **7**: 4.
PubMed Abstract | Publisher Full Text | Free Full Text

33. Embleton L, Ott MA, Wachira J, *et al.*: **Adapting ethical guidelines for adolescent health research to street-connected children and youth in low- and middle-income countries: a case study from western Kenya.** *BMC Med Ethics.* 2015; **16**: 89.
PubMed Abstract | Publisher Full Text | Free Full Text

34. Kamuya DM, Theobald SJ, Munywoki PK, *et al.*: **Evolving friendships and shifting ethical dilemmas: fieldworkers' experiences in a short term community based study in Kenya.** *Dev World Bioeth.* 2013; **13**(1): 1–9.
PubMed Abstract | Publisher Full Text | Free Full Text

35. Lairumbi GM, Parker M, Fitzpatrick R, *et al.*: **Forms of benefit sharing in global health research undertaken in resource poor settings: a qualitative study of stakeholders' views in Kenya.** *Philos Ethics Humanit Med.* 2012; **7**: 7.
PubMed Abstract | Publisher Full Text | Free Full Text

36. Vreeman R, Kamaara E, Kamanda A, *et al.*: **A qualitative study using traditional community assemblies to investigate community perspectives on informed consent and research participation in western Kenya.** *BMC Med Ethics.* 2012; **13**: 23.
PubMed Abstract | Publisher Full Text | Free Full Text

37. Oduwo E, Edwards SJL: **A systematic review of factors affecting children's right to health in cluster randomized trials in Kenya.** *Trials.* 2014; **15**: 287.
PubMed Abstract | Publisher Full Text | Free Full Text

38. Kamuya DM, Marsh V, Njuguna P, *et al.*: ***"When they see us, it's like they have seen the benefits!": experiences of study benefits negotiations in community-based studies on the Kenyan Coast.*** *BMC Med Ethics.* 2014; **15**: 90.
PubMed Abstract | Publisher Full Text | Free Full Text

39. Chou VB, Omer SB, Hussain H, *et al.*: **The costs associated with adverse event procedures for an international HIV clinical trial determined by activity-based costing.** *J Acquir Immune Defic Syndr.* 2007; **46**(4): 426–432.
PubMed Abstract | Publisher Full Text

40. Devries KM, Child JC, Elbourne D, *et al.*: **"I never expected that it would happen, coming to ask me such questions":Ethical aspects of asking children about violence in resource poor settings.** *Trials.* 2015; **16**: 516.
PubMed Abstract | Publisher Full Text | Free Full Text

41. Mtunthama N, Malamba R, French N, *et al.*: **Malawians permit research bronchoscopy due to perceived need for healthcare.** *J Med Ethics.* 2008; **34**(4): 303–307.
PubMed Abstract | Publisher Full Text

42. Mfutso-Bengo J, Manda-Taylor L, Masiye F: **Motivational factors for participation in biomedical research: evidence from a qualitative study of biomedical research participation in Blantyre District, Malawi.** *J Empir Res Hum Res Ethics.* 2015; **10**(1): 59–64.
PubMed Abstract | Publisher Full Text

43. Gooding K, Phiri M, Peterson I, *et al.*: **Six dimensions of research trial acceptability: how much, what, when, in what circumstances, to whom and why?** *Soc Sci Med.* 2018; **213**: 190–198.
PubMed Abstract | Publisher Full Text

44. Mfutso-Bengo J, Ndebele P, Jumbe V, *et al.*: **Why do individuals agree to enrol in clinical trials? A qualitative study of health research participation in Blantyre, Malawi.** *Malawi Med J.* 2008; **20**(2): 37–41.
PubMed Abstract | Publisher Full Text | Free Full Text

45. Sullivan K, Mtande T, Jaffe E, *et al.*: **Views among Malawian women about joining HIV prevention clinical trials when pregnant.** *AIDS Res Ther.* 2020; **17**(1): 27.
PubMed Abstract | Publisher Full Text | Free Full Text

46. Barsdorf N, Maman S, Kass N, *et al.*: **Access to treatment in HIV prevention trials: perspectives from a South African community.** *Dev World Bioeth.* 2010; **10**(2): 78–87.
PubMed Abstract | Publisher Full Text | Free Full Text

47. Ramjee G, Coumi N, Dladla-Qwabe N, *et al.*: **Experiences in conducting multiple community-based HIV prevention trials among women in KwaZulu-Natal, South Africa.** *AIDS Res Ther.* 2010; **7**: 10.
PubMed Abstract | Publisher Full Text | Free Full Text

48. Nkosi B, Seeley J, Chimbindi N, *et al.*: **Managing ancillary care in resource-constrained settings: Dilemmas faced by frontline HIV prevention researchers in a rural area in South Africa.** *Int Health.* 2020; **12**(6): 543–550.
PubMed Abstract | Publisher Full Text | Free Full Text

49. Essack Z, Koen J, Barsdorf N, *et al.*: **Stakeholder perspectives on ethical challenges in HIV vaccine trials in South Africa.** *Dev World Bioeth.* 2010; **10**(1): 11–21.
PubMed Abstract | Publisher Full Text

50. Ward CL, Shaw D, Anane-Sarpong E, *et al.*: **The Ethics of Health Care Delivery in a Pediatric Malaria Vaccine Trial: The Perspectives of Stakeholders From Ghana and Tanzania.** *J Empir Res Hum Res Ethics.* 2018; **13**(1): 26–41.
PubMed Abstract | Publisher Full Text

51. Ngongo PB, Priddy F, Park H, *et al.*: **Developing standards of care for HIV prevention research in developing countries -- a case study of 10 research centers in Eastern and Southern Africa.** *AIDS Care.* 2012; **24**(10): 1277–1289.
PubMed Abstract | Publisher Full Text

52. Richards MR, Helmchen LA: **Adverse selection and moral hazard in the provision of clinical trial ancillary care.** *Health Econ Policy Law.* 2013; **8**(2): 225–234.
PubMed Abstract | Publisher Full Text

53. Pratt B, Hyder AA: **Designing research funding schemes to promote global health equity: An exploration of current practice in health systems research.** *Dev World Bioeth.* 2018; **18**(2): 76–90.
PubMed Abstract | Publisher Full Text

54. Chilengi R: **An ethics perspective on responsibilities of investigators, sponsors and research participants.** *Acta Trop.* 2009; **112 Suppl 1**: S53–62.
PubMed Abstract | Publisher Full Text

55. Stunkel L, Grady C: **More than the money: a review of the literature examining healthy volunteer motivations.** *Contemp Clin Trials.* 2011; **32**(3): 342–352.
PubMed Abstract | Publisher Full Text | Free Full Text

56. Cohen ERM, O'Neill JM, Joffres M, *et al.*: **Reporting of informed consent, standard of care and post-trial obligations in global randomized intervention trials: a systematic survey of registered trials.** *Dev World Bioeth.* 2009; **9**(2): 74–80.
PubMed Abstract | Publisher Full Text

57. Participants in 2006 Georgetown University Workshop on Ancillary-Care Obligations of Medical Researchers Working in Developing Countries: **The ancillary-care obligations of medical researchers working in developing countries.** *PLoS Med.* 2008; **5**(5): e90.
PubMed Abstract | Publisher Full Text | Free Full Text

58. Dickert N, Wendler D: **Ancillary care obligations of medical researchers.** *JAMA.* 2009; **302**(4): 424–428.
PubMed Abstract | Publisher Full Text

59. Tshikala T, Mupenda B, Dimany P, *et al.*: **Engaging with research ethics in central Francophone Africa: reflections on a workshop about ancillary care.** *Philos Ethics Humanit Med.* 2012; **7**: 10.
PubMed Abstract | Publisher Full Text | Free Full Text

60. Haire BG: **Ethics of medical care and clinical research: a qualitative study of principal investigators in biomedical HIV prevention research.** *J Med Ethics.* 2013; **39**(4): 231–235.
PubMed Abstract | Publisher Full Text

61. Taylor HA, Merritt MW, Mullany LC: **Ancillary care in public health intervention research in low-resource settings: researchers' practices and decision-making.** *J Empir Res Hum Res Ethics.* 2011; **6**(3): 73–81.
PubMed Abstract | Publisher Full Text

62. Hyder AA, Merritt MW: **Ancillary care for public health research in developing countries.** *JAMA.* 2009; **302**(4): 429–431.
PubMed Abstract | Publisher Full Text | Free Full Text

63. Mngadi KT, Singh JA, Mansoor LE, *et al.*: **Undue inducement: a case study in CAPRISA 008.** *J Med Ethics.* 2017; **43**(12): 824–828.
PubMed Abstract | Publisher Full Text

# Open Peer Review

## Current Peer Review Status: ✔

**Version 1**

Reviewer Report 08 October 2021

https://doi.org/10.21956/wellcomeopenres.18596.r46183



✔ **Dorcas Mwikali Kamuya**
Health Systems and Research Ethics, KEMRI-Wellcome Trust Research Programme, Kilifi, Kenya

The systematic review paper on ancillary care in medical research in resource-constrained settings (RSC) is a welcome review, given the ethical tensions that such care often raises in research conduct. There are no major issues. A few minor issues I noted which the authors are at the discretion on whether to include:

- Can add as a limitation of the review that the focus is on ancillary care to participants and possibly family members, but not to target populations of research. For example, some studies suggest that in RCS, narrowly focusing on participants and their immediate dependents can contribute to tensions in communities and rumours about ongoing research by those excluded from the research (see e.g. Gikonyo *et al.* 2013[1]; Angenywi *et al.* 2014[2]).

- Another element/concern is that providing ancillary care to populations rather than working within existing systems could undermine these systems and further raise issues of sustainability once the study and the ancillary care are withdrawn.

- Finally, a discussion about the role of the government agencies in providing such ancillary care would also be helpful, drawing attention to the mandate of government agencies to provide such care and that the researchers would be responding to situations that require humanitarian responses, and link to the previous point about sustainability.

### References

1. Gikonyo C, Kamuya D, Mbete B, Njuguna P, et al.: Feedback of research findings for vaccine trials: experiences from two malaria vaccine trials involving healthy children on the Kenyan Coast. *Dev World Bioeth*. 2013; **13** (1): 48-56 PubMed Abstract | Publisher Full Text
2. Angwenyi V, Kamuya D, Mwachiro D, Kalama B, et al.: Complex realities: community engagement for a paediatric randomized controlled malaria vaccine trial in Kilifi, Kenya. *Trials*. 2014; **15**: 65 PubMed Abstract | Publisher Full Text

**Are the rationale for, and objectives of, the Systematic Review clearly stated?**
Yes

**Are sufficient details of the methods and analysis provided to allow replication by others?**
Yes

**Is the statistical analysis and its interpretation appropriate?**
Not applicable

**Are the conclusions drawn adequately supported by the results presented in the review?**
Yes

***Competing Interests:*** We are members of the Global Health Bioethics Network – GHBN – which is a network that brings together researchers and practitioners in ethics and community engagement from across the Wellcome Trust core-funded Africa and Asia Programmes. JS is an adviser to one of the my WT fellowship.

**I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.**

**Chapter summary**

This paper has outlined the ancillary care reported that is currently provided in health-related research in East and Southern Africa. The findings highlight the need to explore further the current recognition of and guidance for ancillary care in ethics guidance documents. The subsequent chapters seek to offer an in-depth understanding of the language used to describe ancillary care in the ethics guidance documents and how that language has evolved. Chapter 6 focuses on research stakeholders' experiences of and perspectives on the provision of and ethical considerations regarding ancillary care in health-related research in the global south.

## Chapter 6. A chronological discourse analysis of ancillary care provision in guidance documents

### Introduction

This chapter addresses Objective 2, to examine the practical features that have underpinned the evolution of the concept of ancillary care in health-related research ethics guidance documents. As a result of what is perceived to be a lack of guidance regarding research ethics standards, there is considerable debate in the academic literature about the meaning and scope of ancillary care. This is the case even though its intended purpose is significant, and its application widespread. This paper presents findings from a discourse analysis of the concept of ancillary care as mentioned in research ethics guidance and policy documents, which examines how such documents provide guidance for research conducted in the global south. The paper was published in the peer-reviewed journal *BMC Medical Ethics* (Kapumba et al., 2022).

In conducting a chronological discourse analysis of ancillary care, I explored the practical features that have shaped the evolution of this concept within health-related research ethics guidance documents. Through a systematic examination of these documents over time, I traced the changes in language, terminology, and interpretations related to ancillary care. This approach allowed me to discern the shifts in emphasis, priorities, and ethical considerations associated with ancillary care within the context of health-related research. Furthermore, I adopted various approaches to discourse analysis in ethics guidance and policy documents, including examining the explicit definitions and guidelines pertaining to ancillary care, identifying key themes and concepts used to describe it, and analysing how the concept was situated in relation to other ethical principles. This comprehensive analysis shed light on the transformation of ancillary care within the ethical landscape of health-related research, providing valuable insights into its development and implications over time.

The findings were also presented at the Oxford Global Health and Bioethics International Conference organised by the Global Infectious Disease Ethics (GLIDE) Collaborative in June 2022. Numerous guidelines and policies for ethical research practice have evolved over time,

but how this translates to global health practice in RCS is unclear. The purpose of this paper is to describe how the concept of ancillary care has evolved over time and how it is included in the ethics guidelines and policy documents that guide the conduct of research in the global south, with both an international focus and a specific example (Malawi). The language used to describe ancillary care is used differently in different ethics guidance documents. However, the key terms that describe ancillary care are not explicit and do not provide guidance to researchers on the provision of ancillary care when research is conducted in RCS.

**Research paper**

The research paper cover sheet is presented below.

London School of Hygiene & Tropical Medicine
Keppel Street, London WC1E 7HT

T: +44 (0)20 7299 4646
F: +44 (0)20 7299 4656
www.lshtm.ac.uk

# RESEARCH PAPER COVER SHEET

**Please note that a cover sheet must be completed for each research paper included within a thesis.**

## SECTION A – Student Details

| | | | |
|---|---|---|---|
| **Student ID Number** | 418617 | **Title** | Mr |
| **First Name(s)** | Blessings Msango | | |
| **Surname/Family Name** | Kapumba | | |
| **Thesis Title** | Understanding Ancillary Care in the Global South: Examining Practice, current Ethical Guidance, and Stakeholder Perspectives in Malawi | | |
| **Primary Supervisor** | Prof. Janet Seeley | | |

**If the Research Paper has previously been published please complete Section B, if not please move to Section C.**

## SECTION B – Paper already published

| | | | |
|---|---|---|---|
| Where was the work published? | BMC Medical Ethics | | |
| When was the work published? | 14/05/2022 | | |
| If the work was published prior to registration for your research degree, give a brief rationale for its inclusion | Not applicable | | |
| Have you retained the copyright for the work?* | **Yes** | Was the work subject to academic peer review? | **Yes** |

*If yes, please attach evidence of retention. If no, or if the work is being included in its published format, please attach evidence of permission from the copyright holder (publisher or other author) to include this work.

## SECTION C – Prepared for publication, but not yet published

| | |
|---|---|
| Where is the work intended to be published? | |
| Please list the paper's authors in the intended authorship order: | |

| | |
|---|---|
| Stage of publication | Choose an item. |

**SECTION D – Multi-authored work**

| | |
|---|---|
| For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary) | |

**SECTION E**

| | |
|---|---|
| **Student Signature** | [redacted] |
| **Date** | 21/02/2023 |

| | |
|---|---|
| **Supervisor Signature** | [redacted] |
| **Date** | 23/02/2023 |

BMC Medical Ethics

RESEARCH Open Access

# A chronological discourse analysis of ancillary care provision in guidance documents for research conduct in the global south

Blessings M. Kapumba[1,2*], Nicola Desmond[3] and Janet Seeley[1]

## Abstract

**Introduction:** Numerous guidelines and policies for ethical research practice have evolved over time, how this translates to global health practice in resource-constrained settings is unclear. The purpose of this paper is to describe how the concept of ancillary care has evolved over time and how it is included in the ethics guidelines and policy documents that guide the conduct of research in the global south with both an international focus and providing a specific example of Malawi, where the first author lives and works, as a case study.

**Methods:** Discourse analysis was conducted on 34 international ethics guidelines and policy documents. Documents were purposively selected if they contained a set of key terms that reflect the concept of ancillary care. Following a process of inductive discourse analysis, five key interrelated text phrases relating to ancillary care were extracted from the documents. The evolution of these phrases over time was explored as they represented the development of the concept of ancillary care as a component of ethical health research guidance and practice.

**Results:** We found key interrelated phrases that represent discourses regarding the evolution of ancillary care including participant protection; provide care as appropriate; supererogation; patient needs prevail over science; and ancillary care as an obligation. Arguments for the provision of ancillary care were characterised by safeguarding the safety, health rights and well-being of study participants. However, despite the evolution of discourse around ethical obligations to provide ancillary care, this is rarely made explicit within guidance documents, leaving interpretive space for differential application in practice.

**Conclusion:** While there have been major changes to the ethics guidance that reflect significant evolution in the ethical conduct of research, the specific vocabulary or language used to explain the ethics of researchers' ancillary care obligations to the health needs of their research participants, lacks clarity and consistency. As a result, the concept of ancillary care continues to be under-represented in local ethical guidelines and regulations, with no clear directives for country-level research ethics committees to apply in regulating ancillary care responsibilities.

**Keywords:** Ancillary care, Discourse analysis, Ethics guidelines, Policy documents, Health-related research, Resource-constrained settings, Malawi

*Correspondence: Blessings.Kapumba1@lshtm.ac.uk

[1] London School of Hygiene and Tropical Medicine, London, UK
Full list of author information is available at the end of the article

## Introduction

Numerous guidelines and policies for ethical research practice have evolved over time. The abuse of study participants in early experiments, a violation of human

rights as spelt out in article 25 of the UN General Assembly [1], triggered the development of guidelines and regulatory policies for human research ethics. Many guidelines and regulatory policies have been developed in response to historical abuses of human participants in experiments, such as the Nazi research on prisoners which led to changes in research guidance and practice [2, 3]. The learning from lengthy international consultative processes which have taken place over recent decades resulted in the development of further guidance by the World Medical Association [4], the Belmont Report by the National Commission for the Protection of Human Subjects of Biomedical Behavioral Research [5], the International Conference on Harmonisation Guide- line for Good Clinical Practice (ICH GCP) [6] (not per se an ethics guideline but an international ethical and scientific quality standard commonly used as the basis for ethics and ethical decision making in health-related research that involve the participation of human subjects), and the Council for International Organisation of Medi- cal Sciences (CIOMS) [7]. In developing these research ethics guidelines, the primary focus was to ensure the safety and well-being of research participants to prevent the reoccurrence of historical abuse. Relatively limited attention has been paid to the genesis of these texts and how certain aspects of the guidance have evolved over time and how this evolution in language has influenced the emphasis on different aspects of ethical conduct of research in different contexts.

International research ethics guidelines and policies now espouse the commitment of researchers to serv- ing the participants who volunteer for research by being responsive to their health needs, both as a direct result of research participation and more broadly as an ethical obligation [8, 9]. Increasingly, these ethical guidelines emphasise optimal health benefits for research participants. The extent to which these guidelines are adhered to, especially when research is undertaken in resource-constrained settings, has increasingly formed a significant component of this discourse. According to these discussions, while the provision of care to study participants appears to be broadly recognised in international ethics guidelines such as the CIOMS [7], the World Med- ical Association Declaration of Helsinki [9], and the ICH GCP [10], its implementation has been slow, making the universality of these guidelines problematic.

Driven by a global discourse prioritising the rights of research participants in the ethics of health research practice, the concept of ancillary care has become increasingly common in medical research. Recent discussions (triggered by Belsky and Richardson [11]) highlight the body of literature available on the provision of care during medical research, but does not focus on how the central ethical concept of providing for the ancillary health needs of research participants became increasingly important [12]. Participants and communities in low resource settings where global health research takes place increasingly demand protection and care from researchers. The provision of ancillary care in low-resource settings may be advocated under a human rights approach that supports and strengthens medical research ethical standards of conduct and adds to the global scientific debate on ethics [13, 14]. Particularly, ancillary care concerns broaden appreciation of the critical nature of protecting the rights of study participants and the extent to which researchers demonstrate an ethical commitment to their subjects.

Richardson [12], Hyder, Merritt [15], Merritt [16], and Pratt et al. [17] have critically examined the basis for the need for ancillary care to be provided to study participants by researchers in medical research. The authors have emphasised three tenets for the provision of ancillary care related to: researchers special duty to care [18], partial-entrustment [11] and principles of justice [19]. Whilst these arguments are coherent as providing principles for ancillary care provision, there remains scant guidance on how this should practically be provided when medical research is undertaken in resource-constrained settings with no or limited availability of care in the communities where participants live, and typically without viable and functioning services for alternative treatment options.

Our earlier research on current practices of ancil- lary care in East and Southern Africa demonstrated that care and support for study participants during medical research remain lacking, with no standardized guidelines [20]. Furthermore, there are contextual fac- tors in resource-constrained communities in the global south that impact the decision regarding participation in health-related research, such as gaining access to bet- ter health care services. Given this, most research eth- ics committees (REC) in these settings lack the proper guidance to assess the issue of ancillary care in context. Specific guidelines should be available for those who are tasked with making these decisions.

Bringing together evidence of ancillary care from international and local ethics guidelines and policies, the anal- ysis presented in this paper provides a part of an evolving process that aims to develop specific ethics guidelines for ancillary care in medical research and its application in resource limited settings. The purpose of this paper is to describe how the concept of ancillary care has evolved over time and how it is included in the ethics guidelines and policy documents that guide the conduct of research in the global south with both an international focus and providing a specific example of Malawi, where the first

author lives and works, as a case study. This paper builds on the work done by Krubiner et al. [21] but focuses explicitly on how the language surrounding the provi- sion of ancillary care has changed over time. We trace the documents backwards to look at where the influences on ancillary care were and how that has influenced or impacted on the ethics of medical research in practice. Specifically, we describe what is defined in the research ethics guidelines and policies regarding researchers' responsibilities towards their participants, we document the chronology of how the concept of providing care to study participants has evolved over-time and through this, explore how the ethics of ancillary care has been jus- tified within guidance and policy documents for practice.

## Methods

### Design

To develop an understanding of how the concept of providing care to study participants has evolved over time, we used discourse analysis to interrogate a purposively selected sample of research ethics guidelines and institutional policy documents. We examined how unique discursive features of guideline documents contribute to the construction of ancillary care in medical research. Critical discourse analysis is a technique for exploring the links between discursive texts, events, and practices, as well as wider social and cultural structures, relationships, and processes [22]. In this study, it was used to determine how ancillary care is shaped by different research ethics guidelines and policies over time. According to Van Dijk [23] discourse analysis seeks to reveal implicit and hidden power dynamics enacted in discourse, as well as the various discursive strategies of dominance and resist- ance. Due to the lack of clarity on these relationships, it is probable that those responsible for developing these guideline documents may be unaware of the connections between ancillary care provision, power dynamics in research, and discourse.

### Document selection for analysis

This study involved the collection and analysis of research ethics guidance and policy documents relevant for the ethical practice of medical research globally. The use of ethics guidelines and policy documents as a frame- work to evaluate the idea of ancillary care was consid- ered because they directly dictate the ethical conduct of medical research involving human subjects. Additionally, these documents were chosen for this study because they provide ethical framework for scientifically and ethically sound medical research.

We conducted a search for and purposively selected the main international ethics guidance documents that are used as guidance for the conduct of medical research, including the Nuremberg code, the Declaration of Helsinki, the Belmont report, the ICH-GCP, and the CIOMS. We traced the emergence of guidance within the international ethics guidelines across time, based on the chronology of their publication made available on their official websites, for example, the World Medical Association, ICH-GCP, and CIOMS websites. Additional documents were included if they were mentioned or cited in already-included documents or secondary literature on the subject, and that they provide ethical guidance on the conduct of health research in resource-constrained settings (RCS) such as the Nuffield Council on Bioethics report. For the funding agencies, ethical guidelines and policy documents were obtained directly from organization or institution websites or, if the organisation did not make them available, from the regulatory authority that published the document. We sought to get access to documents from funding agencies that we consid- ered could have such guidelines and policies because they fund large-scale research projects in resource-constrained settings including in Malawi (Table 1). From the local regulatory institutions, BK requested for a collection of guidance documents by asking directly from local institutions to suggest ethics or policy documents that are used as guidelines, and which are not available online. When requesting for the documents, members of the institution or organisation were asked to suggest ethics or governance documents that could provide principles to guide the conduct of medical research. In total, we reviewed 88 ethics documents to determine their length, genre and primary objective or focus.

In the second phase, we applied discourse analysis to 34 documents that had key textual phrases related to ancillary care, these were then included in the final analy- sis (see Fig. 1). From the international ethics guidelines on the conduct of research involving human subjects we included 18 documents; 10 other documents included were for international financing organisations; and, in order to focus on our country case study, 6 guidelines and policy statements were from the Malawi research institu- tions and regulatory bodies such as the Malawi National Health Sciences Research Committee (NHSRC).

Selected supportive and supplemental resources were included if they related to provision of care or support to study participants. The selection was restricted to documents in English language. Documents that discussed general ethical principles of medical research, without explicit mention of the concepts related to provision of care to study participants, were excluded.

The first document we chose to review was the Nuremberg Code [2], an important guidance document with a global/universal ethics focus. A fundamental principle of the Nuremberg Code was the recognition of the dignity

**Table 1** Inclusion criteria for funding organisations, research institutions and documents

| Selection of research funding organisation | Selection of local (Malawi) research institutions and regulatory bodies | Inclusion criteria of document |
|---|---|---|
| Those directly provide funding for research studies in RCS (Malawi) | Involved in reviewing and approving study plans, and monitor study progress—Research Ethics Committees | The ethics guidelines and policy or regulatory documents were included if they contained statements with key phrases that represent various discourses that could imply the provision of ancillary care to research participants |
| | Conducts a wide range of research projects including clinical trials—Malawi-Liverpool Wellcome Trust Clinical Research programme | Protection of participants rights, safety, life, health, and well-being |
| | | Preparations or plans for participant's care |
| | | Respect for participants rights and integrity |
| | Responsible for regulation of all health research conducted in Malawi—Malawi Ministry of Health Research department | Care as an act of kindness |
| | | Beneficence |
| | | Participant interests considered first |
| | | Responsiveness of research towards participants health needs |
| | Responsible for the development of research ethics guidelines—National Commission for Science and Technology | Researchers' responsibility or duty to care |
| | | Morally praiseworthy |
| | | Provide care as appropriate, feasible, or necessary |
| | | Participants care obligation |

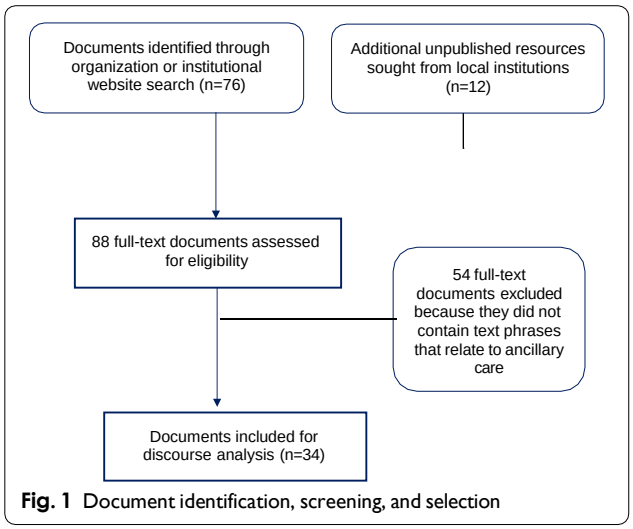



**Fig. 1** Document identification, screening, and selection

of the individual, which was also the cornerstone of the Universal Declaration on Human Rights [1]. Second, we included documents that were developed following the Nuremberg Code, including the Declaration of Helsinki [4, 9, 24, 25], the Belmont Report [5], CIOMS [7, 8, 26, 27], the ICH-GCP [6], and the Nuffield Council on Bio- ethics [28]. We traced these international research ethics guidance documents chronologically. The final selection of included documents was for those from funding agencies including Wellcome Trust, European & Developing Countries Clinical Trials Partnership (EDCTP), National Institute of Health (NIH), National Institute for Health Research (NIHR), Medical Research Council (MRC). We also included local (Malawi) research ethics guideline and policies including the research ethics committee guidelines, research institutions (Malawi-Liverpool Wellcome Trust) policies, ministry of health research policies, mainly to look at what documents they refer to and to see their wording for provision of care to study participants.

### Analysis

The selected documents were coded iteratively in NVivo (QSR, Melbourne) by BK. During the first coding process, the texts were reviewed several times starting with the Nuremberg code, paying attention to words, phrases, and concepts related to the provision of care and support to study participants during medical research and exploring how these changed over time. During the second step of the analysis of subsequent documents, we used the key phrases that had been identified for coding while also identifying new phrases that related to ancillary care. We also looked at the general structure, which included the formatting and their order, the use of quotes to introduce specific aspects, and the overall tone and verb tense of the text. We were particularly interested in tracing the use of such phrases in various research ethics guidelines and policies, as well as how the language has evolved over time. In the final stage of the analysis, the coded text phrases were read and key themes (described in the findings section) that best describes the discourses around

the provision of ancillary care to study participants and the related ethical justification were generated.

The analysis followed a framing used by Johnstone [29] for discourse analysis, which takes multiple fac- ets of a text into account simultaneously. Six factors are included in this framing: the medium (print or video), the language (particular word choices), the people or participants represented, the author's objectives or purpose, and the social and cultural context. As previously noted, representations of care provision are critical textual targets for this study, and as a result, we focused on ancillary care or guidance for the provision of care to study participants during medical research. We asked how documents explicitly or implicitly explain ancillary care and how does it appear to be referred to (for example, what ethical and other justifications apply?).

All authors discussed the interpretations during regular meetings and there was congruence among the findings that emerged. Therefore, the interpretation provided in this article is based on a critical discourse analysis of texts relevant to the ethics of ancillary care as described in international and local research ethics guidelines and policies.

#### Findings

Different constructions of the research ethics guidance documents were reflective of the discourses around the idea of ancillary care. The documents differed profoundly in how they characterised the evolution of provision of care to study participants. We illustrate these findings using relevant quotes describing each of the analysed texts separately and sequence from broad international ethics guidelines (the Declaration of Helsinki, Bel- mont Report, ICH-GCP, and CIOMS) to specific local research ethics guidance documents [30–33], and international funding agencies policies. We use key interrelated phrases extracted from guidance documents to illustrate the findings: participant protection; provide care as appropriate; supererogation; patient needs prevail over science; and ancillary care obligation. These phrases reflect defined views on ancillary care that have been included into ethical guidelines and policy statements for use in health-related research globally. We discuss how these extracts have been put into the context of research ethics over time and how they relate to ancillary care (Table 2).

#### Participant protection

The one thing that all the different guidelines and policies have in common is that of safeguarding the safety of study participants from undue risks of harm. The discussion around the protection of study participants is based on the established ethical principles that grew out of the ethical condemnation of Nazi experiments [2] and the philosophical underpinnings of ethical debates on justice and moral obligation [34, 35]. In the context of this paper, we found that, across all ethical guidance documents derived from the Nuremberg code, the protective obligation of researchers towards their participants is confined to study-related harm. Using the word "protectionism," Moreno [36] explains the ethical need to protect that is outlined in the ethics guidelines. In Moreno's description, protectionism is a concept that emphasises the need of protecting human subjects from the risks associated with involvement in research. This is founded on the concept that a special duty is owned to those who participate in research. This is the case for both international guidelines and their interpretation within funding requirements, regulatory bodies, and research ethics committees which refer exclusively to protection of human research participants and place a strong emphasis on study-related harm. In 1947, the Nuremberg code [2] established the first international guideline, stating that any study involv- ing human participants must guarantee that adequate safeguards against experiment-related harm are made available. The Nuremberg code's participant protec- tion provisions were wide, including even improbable risks of injury, impairment, or death. The Nuremberg code was the first guideline to put a high value on safe- guarding people from research-related harm. Follow- ing that, research ethics guidelines were developed to strengthen that protection, through the Declaration of Helsinki, for example, which emphasises the protection of the well-being of research participants as being more important than the research results. In 1964, the World Medical Association Declaration of Helsinki [4] widened the scope of the protective duty to include specifically, text on the life and health of participants.

> *It is the duty of the doctor to remain the protector of the life and health of that person on whom clinical research is being carried out [4].*

By adding a broader term such as "protection of the participant's life and health," attention may have been given to caring for any conditions that the participant may be suffering from while participating in the study, thus broadening the scope of responsibility assigned to those seeking to recruit participants in research. However, the focus remained on study-related issues, with little or no mention of care for additional health needs. Later, in the Belmont Report of 1978 [5], another broad idea of protection for study participants was emphasized, in which protection would be targeted at the overall well-being of a person who is involved in research. The Belmont Report went on to establish an additional idea of well-being, which corresponded to what is included in the

**Table 2** summary of specific phrases reflecting broader discourse

| Document Source and year of publication | Title | Discourses | | | | |
|---|---|---|---|---|---|---|
| | | Participant protection | Supererogation | Participant needs prevail over science | Provide care as appropriate | Ancillary care researcher's obligation |
| Nuremberg Code [2], 1947 | Permissible medical experiments | Protect participants against study related harm | | | | |
| World Medical Association [4], 1964 | Human Experimentation: Code of Ethics of the World Medical Association (Declaration of Helsinki) | Researchers protect life and health of the participant | | Respect the right of participants to safeguard their integrity | | |
| National Commission for the Protection of Human Subjects of Biomedical Behavioral Research [5], 1978 | The Belmont report: ethical principles and guidelines for the protection of human subjects of research | Secure participants well-being | | | | Beneficence (act of kindness) as an obligation |
| Council for International Organizations of Medical Sciences [51], 1991 | International ethical guidelines for review of epidemiological studies | Protect the rights and assure the welfare of subjects | | | Where participants need health care, arrangements should be made to have them treated or they should be referred to a local health service | |
| International Conference on Harmonisation—Guideline for Good Clinical Practice [6], 1996 | International Conference on Harmonisation of technical requirements for registration of pharmaceuticals for human use | Protect rights, safety, and well-being of participants | | Participants rights, safety, and well-being prevail over science | Provide adequate care for study related conditions | Provide care be considered for intercurrent conditions |
| World Medical Association [24], 2000 | Ethical principles for medical research involving human subjects (Declaration of Helsinki) | Protect the life, health, privacy, rights, and dignity of participants | | Participant well-being to take precedence over science | Providing care as combined with research | Responsibility for the human subject must always rest with a medically qualified person and never rest on the participant |
| World Health Organization [42], 2000 | Operational guidelines for ethics committees that review biomedical research | Safeguarding the dignity, rights, safety, and well-being of participants | | Research interests should not override the health, well-being, and care of research participants | Provide care to research participants during and after the course of the research | |
| Council for International Organisation of Medical Sciences [7], 2002 | International ethical guidelines for biomedical research involving human subjects | Protect the rights and welfare of vulnerable persons | Morally praiseworthy for researchers to provide ancillary care to participants | | For ancillary health needs researchers should, as appropriate, advise them to obtain, or refer them for, medical care | |
| Nuffield Council on Bioethics [28], 2002 | The ethics of research related to healthcare in developing countries | Protect participants from hard in RCS | | | Where it is feasible researchers have a duty to provide care for ancillary health needs | |

**Table 2** (continued)

| Document Source and year of publication | Title | Discourses | | | | |
|---|---|---|---|---|---|---|
| | | Participant protection | Supererogation | Participant needs prevail over science | Provide care as appropriate | Ancillary care researcher's obligation |
| Medical Research Council [41], 2004 | MRC Ethics guide: Medical research involving children | | | Participants' interests must prevail over those of science | | |
| World Medical Association [38], 2004 | Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects | Protect participants health, life, privacy, and dignity | | The well-being of the participants must take precedence over all other interests | | |
| Medical Research Council [40], 2007 | MRC Ethics guide: Medical research involving adults who cannot consent | | | Respect the interests of an individual participant is more important than any potential benefits of the research to others | | |
| Malawi National Health Sciences Research Committee [30], 2007 | General Guidelines on Health Research | | | | Provide care to research participants during and after the course of the research | |
| World Medical Association [25], 2008 | Ethical principles for medical research involving human subjects (Declaration of Helsinki) | Protect the life, health, dignity, integrity, right to self-determination, privacy, and confidentiality of personal information of research subjects | | The well-being of the individual research subject must take precedence over all other interests | | |
| Council for International Organisations of Medical Sciences [26], 2009 | International ethical guidelines for review of epidemiological studies | | Morally praiseworthy for researchers to provide ancillary care to participants | | | |
| College of Medicine Research Ethics Committee [31], 2010 | General guidelines on health research | Promote dignity, rights, safety, and well-being of research participants | | | | |
| Malawi Ministry of Health [32], 2012 | National Health Research Agenda 2012–2016 | Protect and promote the dignity and rights of all research participants | | | | |
| World Medical Association [9], 2013 | Ethical principles for medical research involving human subjects (Declaration of Helsinki) | Promote and safeguard the health, well-being, and rights of participants | | The goal of research should never take precedence over the rights and interests of individual research subjects | | |

**Table 2** (continued)

| Document Source and year of publication | Title | Discourses | | | | |
|---|---|---|---|---|---|---|
| | | Participant protection | Supererogation | Participant needs prevail over science | Provide care as appropriate | Ancillary care researcher's obligation |
| Council for International Organisations of Medical Sciences [8], 2016 | International ethical guidelines for health-related research involving humans | | | | Make adequate provisions for addressing participants' health needs during research and, if necessary | |
| Health Research Authority [43], 2017 | UK policy framework for health and social care research | Ensuring participants' safety and well-being in relation to their participation in the research | | Safety and well-being of the individual prevail over the interests of science | | |
| ICH E6(R1) Good Clinical Practice ICH E6(R2) ICH Consensus Guideline [10], 2016 | Integrated addendum to ICH E6 (R1): guideline for good clinical practice E6 (R2) | Protect rights, safety, and well-being of participants | | | | When the investigator becomes aware of an intercurrent condition, should notify the participant |
| Wellcome Trust [48], 2018 | Good research practice guidelines | protect the rights, interests and safety of research participants | | | | |
| H3Africa [47], 2018 | Guideline for the Return of Individual Genetic Research Findings | | | | Depending on clinical validity and relevance, advisable to provide referral as ancillary care | |
| Ministry of Health and Population [33], 2019 | National Health Research Policy: Strengthening health research to improve national health security | Protect the rights of research participants | | | | |
| Wellcome Trust [44], 2020 | Research involving human participants policy | Protect the rights, interests and safety of participants | | | Provision of care as collateral benefits of carrying out research, whether or not they are necessary for the research design | |
| Council for International Organisations of Medical Sciences [27], 2021 | Clinical research in resource-limited settings. A consensus by a CIOMS Working Group | | | | | Researchers have an ethical obligation to care for participants' health needs during research, if necessary |
| Guenter et al. [52], 2021 | Ethical considerations in HIV prevention trials: Joint United Nations Programme on HIV/AIDS and the World Health Organization | Researchers to take measures to protect the safety, dignity, human rights and welfare of participants | | | | |

**Table 2** (continued)

| Document Source and year of publication | Title | Discourses | | | | |
|---|---|---|---|---|---|---|
| | | Participant protection | Supererogation | Participant needs prevail over science | Provide care as appropriate | Ancillary care researcher's obligation |
| National Institutes of Health [49], 2021 | National Institute of Health Grants Policy Statement | Protect the rights and well-fare of these participants | | | | NIH-funding for research projects may include for costs towards participants hospitalisation, testing, or care services |

World Health Organization's 1948 definition of health, "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" [37].

> *Persons are treated in an ethical manner not only by respecting their decisions and protecting them from harm, but also by making efforts to secure their well-being [5].*

The above description of the range of protective duty of researchers towards their participants has evolved over time and used differently in guidance documents, however, the concept remains to refer to ensuring the safety of study participants. From the Nuremberg code which was concerned with the protection of experimental subjects (participants) from study related harm, the concept has evolved through different international ethics guidelines. Several other ethics guidelines have focused on the protection of the life and well-being of study participants for example, the Belmont Report, and the CIOMs (Fig. 2). The recently updated guidelines by the World Medical Association Declaration of Helsinki 2000, 2004, 2008 and 2013 include additional specific areas of protection such as for the life, health, privacy, and dignity of participants [9, 24, 25, 38]. These terms used are still very broad, for example, protection of health or life. In 2002, the CIOMs provided guidelines which refer to the World Medical Association Declaration of Helsinki and Belmont report. Accordingly, the guidelines uphold that the researchers must make special provision for the protection of the rights and welfare of participants. However, the focus in the CIOMs is toward that of vulnerable individuals. While the 2002 and 2016 CIOMs guidelines focus on protection of vulnerable participants in research, the 2021 CIOMs guidelines include RCS as the main target for the protective duty of researchers.

In the context of RCS protection of research participants has become more complex and requires a more multifaceted and interconnected system of protection. In the protective duty, guidance documents ensures that participants welfare is of central concern to the researchers by minimising the level of harm to which participants may be exposed and treat them with respect and dignity throughout the study.

The exact structure of protective duty for research participants varies among guidance documents. Despite this flexibility, however, there are some basic protection functions necessary to ensure safety of participants, for exam- ple, protection against foreseeable study related harm, it is essential that researchers meet these needs. The empirical literature and evidence from research ethics guidance documents that exist on protection of study participants tend to show that this may only be meant for protection against study related harm. However, the researchers may extend this protection duty to incidental conditions identified during the study among their participants and provide the needed ancillary care.

> *Subjects may be reimbursed for lost earnings, travel costs and other expenses incurred in taking part in a study; they may also receive free medical services. It might, for example, be agreed to treat cases of an infectious disease contracted during a trial of a vaccine designed to provide immunity to that disease, or to provide treatment of incidental conditions unrelated to the study [7].*

> *In addition to researchers' duty not to harm participants in research, there is a duty to benefit participants where possible. Thus, where it is feasible for researchers to diagnose and treat an illness which arises, or to ensure that effective treatment is available at a local level, they have a duty to do so [28].*

This call for the duty to provide ancillary care in essence can have protective benefits to study participants in RCS where they have several unmet health needs which may be more critical than the condition under study or as compared to the study related harm. Within the international ethics guidance documents from all years, explicit ancillary care obligation is not mentioned in the context of protecting study participants as one way of addressing their unmet health needs. Some participants may accept to participate in a study knowing that their needs will be taken care of and that they will be protected. It is sugges- tive of a strong belief that the moral grounds for such acts are dependent on the established relationship during the conduct of research. It is also suggestive of a strong belief that ancillary health care issues are a matter of personal responsibility, such that the researcher's obligation to protect the health of participants during research may be extended to include the provision of ancillary health care to their participants as a matter of personal responsibility. There was limited discourse on protection of study participants from funding agencies and local research regulatory bodies guidance and policy documents beyond study related conditions, however, it was noted that the majority refer to the international guidance documents [4–7].

#### Participant needs prevail over science

In this discourse, the key phrase is described in terms of researchers prioritising the responsiveness to the demands of participants in RCS. This discourse was first described in the 1989 World Medical Association Declaration of Helsinki [39] then later in CIOMS 1993, as cited in Nuffield Council on Bioethics [28], followed by the 1996 ICH-GCP [6] and is included in all the later

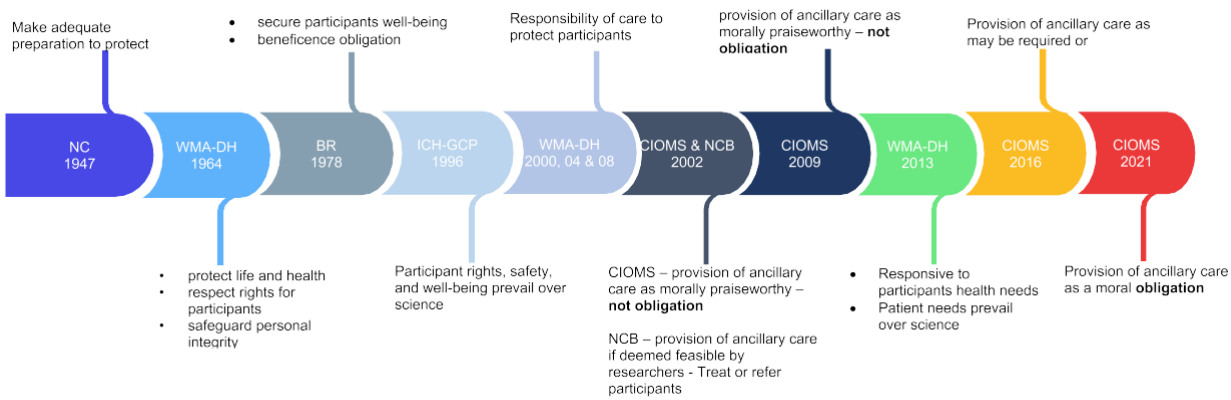



**Fig. 2** key phrases that reflect the evolution of providing care to participants

versions of the World Medical Association Declara- tion of Helsinki, CIOMS, ICH-GCP. This textual phrase is also used in some policies from funding and policy organisations such as the MRC [40, 41], and the World Health Organization [42].

> *In research on man, the interest of science and society should never take precedence over consid- erations related to the wellbeing of the subject. [39] Research in developing countries should be 'responsive to the health needs and the priorities of the community in which it is to be carried out' [CIOMS, 1993, as cited in [28]].*
> *The rights, safety, and well-being of the trial sub- jects are the most important considerations and should prevail over interests of science and society [6].*

> *In medical research on human subjects, considera- tions related to the well-being of the human subject should take precedence over the interests of science and society [24].*

We observed that both international research ethical standards and funding agencies guidelines emphasise the importance of medical research not taking prior- ity over participant demands. This discourse has been represented via the use of a variety of text phrases. The guidelines define the participants' interests as their well-being [6, 24, 42, 43], rights [6], safety [6, 43], health [42], and care [27, 42] (Table 1).

> *The goals of research, while important, should never be permitted to override the health, well- being, and care of research participants [42].*
> *The safety and well-being of the individual prevail over the interests of science and society [43].*

While some guidelines emphasise the importance of putting participants' interests above research and soci- ety, they do not specify whose participants' interests are being covered.

> *In all research involving people, an appropriate balance must be struck between the interests of participants (and, where relevant, the communi- ties to which they belong) and the interests of soci- ety or the advancement of knowledge [44].*

In a similar manner, this expression in the guidelines does not explicitly clarify whether it covers ancillary healthcare needs. While this may relate to the scientific information gained as a result of the study, it may also allude to the responsiveness of the research team to the participants' extra health requirements. Using more general phrases like well-being, health, and rights, does this suggest that researchers are responsible to provide care for the ancillary health needs of their participants? The most common and important expectation of par- ticipants for ancillary care that researchers must meet, is to ensure the effacement of self-interest in placing the interests of their participants first. In biomedical research, however, commercialization of research par- ticipant protection has contributed significantly to the conflict between self-interest and ethical responsibil- ity. This is particularly true in the situation of RCS in global south settings, where participants have a vari- ety of extra health requirements that are left unmet by the health system. Consequently, although researchers have some ethical duties toward their participants dur- ing medical research, such as the need to protect their safety, they also have scientific interests that compete with the services that their participants are expecting at the same time.

### Supererogation

A third discourse on the researcher's role in the ethi- cal conduct of research centred on behaviours that are morally praiseworthy but go above and beyond the call of duty in terms of research ethics. As defined by Jacobs [45], supererogation occurs when an agent performs activities that are morally right or morally praiseworthy, but which are not required by the actor's obligation. Even if particular acts fall short of what is objectively right, we should praise those who act from motives that are generally `utility maximising' because praising such well-motivated acts tend to promote the best results [46]. The CIOMS's earlier versions of 1993, as cited in Nuffield Council on Bioethics [28], 2002 [7] and 2009 [26] recognise ancillary care as an act that is commendable act to do for the participants but not required. Therefore, acts of ancillary care by researchers would be lacking in moral worth if they are not provided. This, on the other hand, does not serve as a guide for researchers, nor does it provide any legal framework under which researchers may be required to provide for the ancillary health care demands of their participants. The guidelines are explicit in stating that this is not a responsibility put on researchers, and that rather this is just an act of kindness. As such, the translation of this act into an obligation set out in guidance documents is not an imperative.

However, the CIOMS guidelines would appear to enshrine the research ethics guidance in the discussion of ancillary care responsibility:

> *Although sponsors are, in general, not obliged to provide health-care services beyond that which is necessary for the conduct of the research, it is morally praiseworthy to do so [7, 26].*

Additional to this commitment, the guideline moves on to say; "in some circumstances, it may be relatively easy for researchers to treat the condition or refer par- ticipants to local health centre where treatment can be provided [7]." The phrase "morally praiseworthy" speaks to the researchers as the most powerful partners in the research-participant relationship. However, while the provision of any ancillary care is considered morally praiseworthy in the 2002 and 2009 CIOMS guidelines, no other international or national body has praised or rec- ognized the provision of ancillary care or the researcher as being particularly "morally praiseworthy" for providing such services to their participants. According to a review of ethics guidance materials for both the local institu- tional review board [30, 31] and international funding agencies [40, 41, 44, 47, 48], there has been no evidence to suggest that such discourses of morally praisewor- thy conduct are translated into institutional policies and guidance documents. However, we found that in almost all the guidance documents reviewed from the local regulatory and international funding institutions they refer to the Nuremberg code [2], the Declaration of Helsinki [24], the Belmont report [5], the ICH-GCP [6], and the CIOMS [24].

### Provide care as appropriate

While morally praiseworthy was used in the 2002 and other earlier versions of CIOMS guidelines, this phrase has been removed in the 2016 guidelines. Instead, the 2016 guidelines encourage provision of ancillary care as it may seem 'appropriate or necessary' by the research- ers and other research stakeholders [8]. What is regarded suitable or required in this discourse seems to be depend- ent on the judgments that the researcher would make. So, similarly to the framing of ancillary care provision as 'morally praiseworthy' the statement "as it may seem appropriate or necessary" does not give any significant direction to researchers, particularly in RCS where every participant may have additional health-care requirements that qualify as being required or appropriate to provide care for. The Nuffield Council on Bioethics in their report which also serves as a guidance document on the ethical conduct of research particularly in developing countries and has been referenced by many other recent guidance documents including those for the international funding agencies such as the Wellcome Trust [44], also uses the phrase 'if necessary'. However, the report encourages that researchers provide care for incidental finding among their participants if deemed feasible [28].

> *In addition to researchers' duty not to harm participants in research, there is a duty to benefit participants where possible. Thus, where it is feasible for researchers to diagnose and treat an illness which arises, or to ensure that effective treatment is available at a local level, they have a duty to do so" [28].*

The inclusion of the words `have a duty' moves this provision from being an act of guidance, something that is 'morally praiseworthy' to being something that the researcher has an obligation to provide. However, like in the CIOMS 2016 guidelines, the Nuffield Council on Bioethics [28] report provides further guidance on what researchers can do when in that situation:

> *During research, participants may develop an entirely unrelated condition. In some circumstances, it may be relatively easy for researchers to treat the condition or refer participants to a local health cen- tre where treatment can be provided. In other cases, researchers may not have the expertise to treat the condition effectively and appropriate treatment may not be available locally as part of the public health*

*system [28].*

The use of the passive term "may" in these guidance documents including some from funding agencies [49] suggests that funding agencies wish to give researchers options and not to make it obligatory, but this remains problematic in the sense that it does not provide an explicit position. The researcher in this case may be required to make decisions on a case-by-case basis as described in the 2016 CIOMS guidelines [8]. This has translated into funding guidance. For example, the Wellcome guidance notes on research involving people in low- and middle-income countries only emphasises that any considerations for the provision of ancillary care should be that which is equal to the local standard-of-care:

> *Where it is proposed to offer healthcare unrelated to the specific research question, we recommend that this should usually be the standard treatment that is available locally [44].*

This is particularly problematic because there are disparities in standards of care between middle-income and low-income countries, as well as within those settings, and it contributes to further inequity, largely because there is a catch-all recommendation that is universalised without consideration for specific context.

#### Ancillary care researchers' obligation

The last and most recent discourse is about the ancil- lary care obligations researchers have towards their participants. The 2021 CIOMS guidance has been the first to clearly recognise ancillary care as an obligation of researchers toward their participants.

> *Researchers have an ethical obligation to care for participants' health needs during research and, if necessary, for the transition of participants to care when the research is concluded [27].*

These guidelines make some noticeable steps to demonstrate that researchers have a responsibility to care for their participants. This could be due to the fact that some researchers [50] have written on the conditions that the majority of RCS participants experience. These guidelines lay a strong focus on the fact that researchers have a commitment to provide ancillary care to their participants in order to assist them in addressing unmet health needs that remain unaddressed due to limited or unavailability of services in the local health care system, as stated in the guidelines. This discourse is suggestive of a social reality where the ethics of ancillary care during research places a greater value upon responding to participants needs. The guidelines provide further guidance that such care should not be considered as undue influence but rather that researchers should work to improve the health, quality, and access to health care services of their participants which are limited or not available.

While referral of participants requiring additional health care services from medical personnel with the necessary ability to continue the care (World Medical Association Declaration of Cordoba on patient-physician relationship), is supported in medical research guidance documents gives the same options to researchers. How- ever, issues of limited availability of the required services are not well addressed. Just as with issues of standard-of- care, what if such services are limited or not available at all? This has not been well addressed in guidance docu- ments particularly for the conduct of research in resource constrained settings.

#### The translation of international guidelines to local research ethics guidance

While international research ethical guidelines include clear guidance for the provision care to study participants, we found limited guidance on the same from local research ethics guidelines and policy documents, which provide a significant research oversight. On the other hand, we found that the majority of local research ethics guidelines and policy documents are established pursuant to the International Ethical Guidelines for the Conduct of Research Involving Human Subjects, which are mostly regarded as primary source of guidance on research ethics matters.

> *These Guidelines have been developed basing on a number of resource materials including the Republic of Malawi Constitution; National Science and Technology Policy; National Procedures and Guidelines for the Conduct of Research in Malawi; Policy Meas- ures for the Improvement of Health Research Coordination in Malawi; CIOMS; WHO Operational Guidelines for Ethics Committees That Review Biomedical Research; UNESCO Declaration on Bio- ethics and Human Rights, and other many relevant international ethical guidelines and regulations - Malawi National Health Sciences Research Committee [30]*

> *The rights, safety and standards for research design and conduct are governed by the: Declaration of Helsinki, Nuremberg Code, and CIOMS [44]*

These statements lay out a range of sources and options, demonstrating that the decision about which guidelines to follow is subjective. Lack of established local guidelines outlining the researchers' responsibilities towards their participants creates a gap when it comes to how researchers should respond to the additional health

needs of their participants while participating in research studies. For example, the general guidelines on health research state that "medical care should be provided to research participants while they are participating in the study" Malawi REC Guidelines p. 22 [30], but no description is given of what that means or to what extent researchers can provide that care or when do such obligations stop. Such broad generalizations can confound researchers when designing their studies, which is particularly true in global south settings, where participants may have a variety of additional unmet health needs.

Despite significant progress in encouraging research- ers doing studies in RCS to consider the provision of ancillary care by some funding agencies, there is limited attention on whether or not ancillary care should be con- sidered to be an obligation by researchers. And, even if it did, there are no clear guidelines over how it should or could be monitored.

## Conclusion

Through this discourse analysis, the Nuremberg Code's ethics guidance, first published in 1947 and subsequently the declaration by the World Medical Association in 1964, demonstrates commitments and values towards the ethical conduct of research. The primary focus of these two first ethics guidelines, as well as all subsequent guidelines, is on protecting study participants against risk associated with research participation. The 1993 CIOMS guidelines and subsequent revisions in 2002, 2009, and 2016 established the concept of providing care to study participants during research, including for non-study-related diseases, known as ancillary care [11]. However, ancillary care was not acknowledged as a researcher obligation until the recent guidelines by the Council for International Organisations of Medical Sciences [27], which appears to reflect a sensitivity to the ethical need of researchers to provide ancillary care to their participants. This demonstrates a shift in the language away from a sole focus on the protection of study participants to one that includes the provision of additional care. While there have been major changes to the ethics guidance that reflect significant evolution in the ethical conduct of research, the specific vocabulary or language used to explain the ethics of researchers' ancillary care obligations to the health needs of their research participants is often complex and lacks clarity and consistency. We acknowledge that this study has a limitation in that it is largely based on ethical guidance documents. We have not examined how such documents are implemented in practice, such as the actual procedure of ethics review by research ethics committees. Our analysis demonstrates how specific textual features guide researchers in both the global north and south to provide ancillary care to their study participants. Conducting additional qualitative methods research with research stakeholders in practice settings would provide insight into whether the shifts in language found within textual documents are reflected in current practices. That said, while this analysis is limited to ethics guidance documents, the research's broader message is applicable to guidance documents from funding agencies and local ethics bodies that do not provide explicit guidance on ancillary care.

Aspects of ancillary care are not currently standardised, as evidenced by several funding agencies' reluctances to express an opinion on the subject. Alternatively, it is possible that these funding agencies will defer to the researchers and the local research ethics guidelines in settings where the research is being conducted. However, these local research ethics guidelines also refer to international research ethics guidelines as described above, which leaves a gap on proper guidance on ancillary care provision. Additionally, this research found that, while discourses regarding the provision of care to study participants have evolved significantly over time, as demonstrated in the international ethics guidance documents, local ethics guidelines and policies of international funding agencies continue to refer to the Declaration of Helsinki of 2000, the Belmont report of 1978, the ICH-GCP of 1996, and the CIOMS of 2000. Due to a lack of explicit discourses on ancillary care in local research ethics guidelines and regulatory documents, research ethics committees have difficulty regulating or advising researchers regarding their ancillary care responsibilities. Additionally, we found that the current discourses used in international ethics guidelines, such as "morally praiseworthy," "if necessary or as appropriate," are too broad to serve as guidelines for researchers. Using such broad discourses fail to address general concern of ancillary care guidance on the extent to which this care can be provided and how does that apply to different contexts where medical research is conducted. These historical depictions have a significant impact on the solutions that are proposed for health challenges faced by study participants in the global south, and as a result, we argue for explicit consideration of the ways in which writing choices on ancillary care can address some ethical issues in research. Our findings suggest that newer versions of ethics guidance documents must illustrate that the idea of ancillary care is explicitly included to provide researchers with clear guidance, particularly in RCS.

**Abbreviations**

CIOMS: Council for International Organisations of Medical Sciences; COMREC: College of Medicine Research Ethics Committee; EDCTP: European & Developing Countries Clinical Trials Partnership; ICH-GCP: International Committee on Harmonization of Good Clinical Practice; MRC: Medical Research Council; NHSRC: National Health Sciences Research Committee; NIH: National Institute of Health; NIHR: National Institute for Health Research; RCS: Resource-constrained settings; REC: Research Ethics Committee.

**Acknowledgements**
We would like to express our gratitude to Dr. Deborah Nyirenda (Malawi-Liverpool Wellcome Trust Clinical Research Programme and GHBN fellow) for her guidance and assistance in document selection and manuscript review. We would like to convey our appreciation to those research institutes and funding agencies that provided us the necessary documents when requested. We would also like to express our gratitude to Markus Gmeiner for his assistance and direction in identifying the documents required from the national research ethics bodies. The authors would also like to acknowledge the contributions made by members of the Global Health Bioethics Network and the Malawi-Liverpool Wellcome Trust Clinical Research Programme.

**Author contributions**
BMK: Conceptualization, developed and conducted document searches, screened the documents identified using inclusion and exclusion criteria and extracted data from the included document, formal analysis, writing—original, drafts and final manuscript. ND: Supervision, Conceptualization, Validation, Methodology, Writing—critical review of all drafts. JS: Supervision, Conceptualization, Methodology, Validation, Resources, Writing—critical review of all drafts. All authors read and approved the final manuscript.

**Funding**
The Global Health Bioethics Network (GHBN) supported this research with a Wellcome Trust Strategic Award (096527) managed by the London School of Hygiene and Tropical Medicine. The funding agency had no part in the study's design, data collection, analysis, and interpretation, or manuscript preparation.

**Availability of data and materials**
Data sharing is not applicable to this article because all of the documents collected and analysed during the current study are already in the public domain. However, we are seeking to make available the documents we sourced via, CIOMS website (https://cioms.ch/), Wellcome Trust website (https://wellcome.org/grant-funding/guidance/research-involving-human-participants-policy), the H3Africa website (www.h3africa.org), NIH website (https://www.nih.gov/), MRC website (https://mrc.ukri.org/), ICH-GCP website (https://ichgcp.net/), World Medical Association website (https://www.wma.net/), and NCST website (https://www.ncst.mw/).

## Declarations

**Ethics approval and consent to participate**
Since this study involved analysis of only documents that are already in the public domain, this is not human subject research and does not require ethical approval. Though there was no formal research ethics review for the study, the researchers, on the other hand, were bound by all of the standard research ethics, research integrity and publication ethics guidelines, which ensured that study confidentiality would not be violated.

**Consent for publication**
Not applicable.

**Competing interests**
The authors declare that they have no competing interests.

**Author details**
[1]London School of Hygiene and Tropical Medicine, London, UK. [2]Malawi-Liverpool Wellcome Trust Clinical Research Programme, P.O. Box 30096, Chichiri, Blantyre 3, Malawi. [3]Liverpool School of Tropical Medicine, Liverpool, UK.

Received: 24 January 2022 Accepted: 25 April 2022
Published online: 14 May 2022

**References**

1. UN General Assembly. Universal declaration of human rights. UN General Assembly. 1948;302(2):14–25.
2. Nuremberg Code. Permissible medical experiments. Trials of War Criminals before the Nuremberg. 1947.
3. Pressel DM. Nuremberg and Tuskegee: lessons for contemporary American medicine. J Natl Med Assoc. 2003;95(12):1216–25.
4. World Medical Association. Declaration of Helsinki: recommendations guiding doctors in clinical research. Can Med Assoc J. 1964;91(11):619.
5. National Commission for the Protection of Human Subjects of Biomedical Behavioral Research. The Belmont report: ethical principles and guidelines for the protection of human subjects of research. United States: National Commission for the Protection of Human Subjects of Biomedical Behavioral Research; 1978.
6. International Conference on Harmonisation—Guideline for Good Clinical Practice. International Conference on Harmonisation of technical requirements for registration of pharmaceuticals for human use 1996.
7. Coucil for International Organisation of Medical Sciences. International ethical guidelines for biomedical research involving human subjects. Bull Med Ethics. 2002;182:17–23.
8. Council for International Organisations of Medical Sciences. International ethical guidelines for health-related research involving humans. International ethical guidelines for health-related research involving humans. 2017.
9. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA. 2013;310(20):2191–4.
10. ICH E6(R1) Good Clinical Practice ICH E6(R2) ICH Consensus Guideline. Integrated addendum to ICH E6 (R1): guideline for good clinical practice E6 (R2). Current Step. 2015;2:1–60.
11. Belsky L, Richardson HS. Medical researchers' ancillary clinical care responsibilities. BMJ. 2004;328(7454):1494–6.
12. Richardson HS. Moral entanglements: the ancillary-care obligations of medical researchers. Oxford: Oxford University Press; 2012.
13. Participants in the Georgetown University Workshop on the Ancillary-Care Obligations of Medical Researchers Working in Developing Countries. The ancillary-care obligations of medical researchers working in developing countries. PLoS Med. 2008;5(5):e90.
14. Tshikala T, Mupenda B, Dimany P, Malonga A, Ilunga V, Rennie S. Engaging with research ethics in central Francophone Africa: reflections on a workshop about ancillary care. Philos Ethics Humanit Med. 2012;7(1):1–7.
15. Hyder AA, Merritt MW. Ancillary care for public health research in developing countries. JAMA. 2009;302(4):429–31.
16. Merritt MW. Health researchers' ancillary care obligations in low-resource settings how can we tell what is morally required? Kennedy Inst Ethics J. 2011;21(4):311.
17. Pratt B, Zion D, Lwin KM, Cheah PY, Nosten F, Loff B. Ancillary care: from theory to practice in international clinical research. Public Health Ethics. 2013;6(2):154–69.
18. Dickert N, Wendler D. Ancillary care obligations of medical researchers. JAMA. 2009;302(4):424–8.
19. Hooper CR. Ancillary care duties: the demands of justice. J Med Ethics. 2010;36(11):708–11.
20. Kapumba BM, Desmond N, Seeley J. What do we know about ancillary care practices in East and Southern Africa? A systematic review and meta-synthesis. Wellcome Open Res. 2021;6:164.
21. Krubiner CB, Syed RH, Merritt MW. Health researcher's ancillary-care responsibilities in low-resource settings: the landscape of institutional guidance. IRB Ethics Hum Res. 2015;37(3):12–9.
22. Jørgensen M, Phillips LJ. Critical discourse analysis. Discourse analysis as theory and method. London: Sage; 2002. p. 60–95.
23. Van Dijk TA. Aims of critical discourse analysis. Jpn Discourse. 1995;1(1):17–28.
24. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. Bull World Health Organ. 2000;79(4):373.
25. World Medical Association. Declaration of Helsinki. Ethical principles for medical research involving human subjects. Jahrbuch Für Wissenschaft Und Ethik. 2008;14(1):233–8.
26. Council for International Organisations of Medical Sciences. International ethical guidelines for review of epidemiological studies. International ethical guidelines for epidemiological studies; 2009.
27. Council for International Organisations of Medical Sciences. Clinical research in resource-limited settings. A consensus by a CIOMS Working Group. Council for International Organizations of Medical Sciences; 2021.

28. Nuffield Council on Bioethics. The ethics of research related to healthcare in developing countries. London: Nuffield Council on Bioethics; 2002.
29. Johnstone B. Discourse analysis. 3rd ed. Oxford: Wiley; 2018.
30. Malawi National Health Sciences Research Committee. The national health Sciences research committee general guidelines on health research: "Valuing Collective Responsibility in Promoting Excellence in Scientific and Ethical Conduct of Health Related Research in Malawi" In: Health Mo, editor. Malawi: Malawi Governement; 2007.
31. College of Medicine Research Ethics Committee. General guidelines on health research—college of medicine research and ethics committee (COMREC). Malawi: Malawi College of Medicine; 2010.
32. Malawi Ministry of Health. National health research agenda 2012–2016. In: Health Mo, editor. Malawi: Ministry of Health; 2012.
33. Ministry of Health and Population. National Health Research Policy: Strengthening health research to improve national health security. In: Health Mo, editor. Malawi: Ministry of Health; 2019.
34. Levine RJ. International codes and guidelines for research ethics: a critical appraisal. In: Vandepool HY, editor. The ethics of research involving human subjects: facing the 21st century. Frederick: University Publishing Group; 1996. p. 235–59.
35. Freeman SJ, Engels DW, Altekruse MK. Foundations for ethical standards and codes: the role of moral philosophy and theory in ethics. Couns Values. 2004;48(3):163–73. https://doi.org/10.1002/j.2161-007X.2004.tb00243.x.
36. Moreno JD. Protectionism in research involving human subjects; 2001.
37. World Health Organization. WHO (2011). Presentation: "Designing the Road to Better Health and Well-Being in Europe" at the 14th European Health Forum Gastein; 2011.
38. World Medical Association. Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects; 2004.
39. World Medical Association. Declaration of Helsinki: Recommendations guiding physicians in biomedical research involving human subjects; 1989.
40. Medical Research Council. MRC ethics guide: Medical research involving adults who cannot consent. MRC London; 2007.
41. Medical Research Council. MRC Ethics Guide: Medical research involving children. Medical Research Council; 2004.
42. World Health Organization. Operational guidelines for ethics committees that review biomedical research: World Health Organization; 2000.
43. Health Research Authority. UK policy framework for health and social care research. Health Research Authority London; 2017.
44. Wellcome Trust. Research involving human participant policy. Wellcome. 2018. https://wellcome.org/grant-funding/guidance/research-involving-people-low-and-middle-income-countries Accessed 30 Apr 2021.
45. Jacobs RA. Obligation, supererogation and self-sacrifice. Philosophy. 1987;62(239):96–101.
46. Hill Jr TE, Cureton A. Supererogation. International Encyclopedia of Ethics; 2013.
47. H3Africa. Guideline for the Return of Individual Genetic Research Findings. 2018. https://h3africa.org/wp-content/uploads/2018/05/H3Africa%20Feedback%20of%20Individual%20Genetic%20Results%20Policy.pdf. 2021.
48. Wellcome Trust. Good Research Practice Guidelines—Grant Funding | Wellcome. Wellcome Trust. 2018. https://wellcome.org/grant-funding/guidance/good-research-practice-guidelines.
49. National Institutes of Health. National institutes of health grants policy statement. Bethesda, MD Retrieved June. 2021:IIB-142–IIB-6.
50. Laman M, Pomat W, Siba P, Betuela I. Ethical challenges in integrating patient-care with clinical research in a resource-limited setting: perspectives from Papua New Guinea. BMC Med Ethics. 2013;14(1):1–6.
51. Council for International Organizations of Medical Sciences. International guidelines for ethical review of epidemiological studies. Geneva: CIOMS; 1991.
52. Guenter D, Esparza J, Macklin R. Ethical considerations in international HIV vaccine trials: summary of a consultative process conducted by the Joint United Nations Programme on HIV/AIDS (UNAIDS). J Med Ethics. 2000;26(1):37–43.


## Publisher's Note

**Chapter summary**

The findings of this study have shown that although there have been some discernible shifts in the ethical guidelines for the conduct of medical research, the language that is used to describe ancillary care lacks clarity. The guidelines for research ethics do not provide clear direction for the actions that researchers are expected to take when they encounter participants who require ancillary care. This absence or lack of defined guidelines for ancillary care makes it difficult for research stakeholders in RCS, such as REC members, to determine what ancillary care researchers can provide. My results underscore a need for policymakers and research regulatory bodies to revisit the guidance for ancillary care in research ethics, and I propose that a process of stakeholder engagement would support this effort well.

## Chapter 7. Research stakeholders' perspectives on ancillary care in the Global South: A case study of Malawi

### Introduction

This chapter addresses Objectives 4 and 5 to investigate the experiences of research stakeholders and their perspectives on the process and practice of ancillary care, as well as the expectations of research participants; and to determine how the values and practices beyond perceived ancillary care obligations of medical researchers may need to be balanced in decisions about study demands and ethical requirements. It is composed of a paper which presents the analysis of data from qualitative in-depth interviews with research stakeholders in Malawi and those from research funding organisations. The manuscript for this work has been accepted for publication by the peer-reviewed journal *BMC Medical Ethics*. The findings were presented at the Research Dissemination Conference organised by Kamuzu University of Health Sciences, Malawi, in November 2022. This paper aims to highlight the perspectives of research stakeholders regarding the ancillary care obligations of medical researchers undertaking health-related research in Malawi, an RCS.

This paper demonstrates that the research stakeholders' perspectives on ancillary care in the global south, as highlighted in this case study of Malawi, underscore the urgent need for comprehensive and contextually relevant guidance on this crucial aspect of health-related research ethics. The study revealed that ancillary care was often overlooked or insufficiently addressed in research practices, leading to potential ethical and practical challenges. The absence of clear guidelines has been a longstanding issue, evident by the stakeholders' sentiments that such guidance should have been in place much earlier. To address these gaps, it is imperative for research institutions, policymakers, and ethicists to collaborate in developing robust and culturally sensitive guidance for ancillary care in the global south. This guidance should emphasize the importance of providing ancillary care to research participants and outline best practices for implementation. Additionally, it should consider the local socio-cultural contexts and healthcare infrastructure to ensure that the guidance is applicable and effective in safeguarding the well-being of research participants. By taking prompt action to establish

comprehensive guidance, we can enhance the ethical conduct of research in the global south and better protect the rights and welfare of research participants.

**Research paper**

The research cover sheet is presented below.

London School of Hygiene & Tropical Medicine
Keppel Street, London WC1E 7HT

T: +44 (0)20 7299 4646
F: +44 (0)20 7299 4656
www.lshtm.ac.uk

**RESEARCH PAPER COVER SHEET**

**Please note that a cover sheet must be completed for each research paper included within a thesis.**

**SECTION A – Student Details**

| | | | |
|---|---|---|---|
| **Student ID Number** | 418617 | **Title** | Mr |
| **First Name(s)** | Blessings Msango | | |
| **Surname/Family Name** | Kapumba | | |
| **Thesis Title** | Understanding Ancillary Care in the Global South: Examining Practice, current Ethical Guidance, and Stakeholder Perspectives in Malawi | | |
| **Primary Supervisor** | Prof. Janet Seeley | | |

**If the Research Paper has previously been published please complete Section B, if not please move to Section C.**

**SECTION B – Paper already published**

| | | | |
|---|---|---|---|
| Where was the work published? | BMC Medical Ethics | | |
| When was the work published? | 10/02/2023 | | |
| If the work was published prior to registration for your research degree, give a brief rationale for its inclusion | Not applicable | | |
| Have you retained the copyright for the work?* | **Yes** | Was the work subject to academic peer review? | **Yes** |

*If yes, please attach evidence of retention. If no, or if the work is being included in its published format, please attach evidence of permission from the copyright holder (publisher or other author) to include this work.

**SECTION C – Prepared for publication, but not yet published**

| | |
|---|---|
| Where is the work intended to be published? | |
| Please list the paper's authors in the intended authorship order: | |

| | |
|---|---|
| Stage of publication | Choose an item. |

**SECTION D – Multi-authored work**

| | |
|---|---|
| For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary) | |

**SECTION E**

| | |
|---|---|
| **Student Signature** | [redacted] |
| **Date** | 21/02/2023 |

| | |
|---|---|
| **Supervisor Signature** | [redacted] |
| **Date** | 23/02/2023 |

BMC Medical Ethics

RESEARCH Open Access

# 'Guidance should have been there 15 years ago' research stakeholders' perspectives on ancillary care in the global south: a case study of Malawi

Blessings M. Kapumba[1,2*], Deborah Nyirenda[2], Nicola Desmond[3] and Janet Seeley[1]

## Abstract

**Background** Medical researchers in resource-constrained settings must make difficult moral decisions about the provision of ancillary care to participants where additional healthcare needs fall outside the scope of the research and are not provided for by the local healthcare system. We examined research stakeholder perceptions and experiences of ancillary care in biomedical research projects in Malawi.

**Methods** We conducted 45 qualitative in-depth interviews with key research stakeholders: researchers, health officials, research ethics committee members, research participants and grants officers from international research funding organisations. Thematic analysis was used to analyse and interpret the findings.

**Findings** All stakeholders perceived the provision of ancillary care to have potential health benefits to study participants in biomedical research. However, they also had concerns, particularly related to the absence of guidance to support it. Some suggested that consideration for ancillary care provision could be possible on a case-by-case basis but that most of the support from research projects should be directed towards strengthening the public health system, emphasising public good above individual or personal benefits. Some researchers and ethics committee members raised concerns about potential tensions in terms of funding, for example balancing study demands with addressing participants' additional health needs.

**Conclusion** Our findings highlight the complexities and gaps in the guidance around the provision of ancillary care in Malawi and other resource-constrained settings more generally. To promote the provision of ancillary care, we recommend that national and international guidelines for research ethics include specific recommendations for resource-constrained settings and specific types of research.

**Keywords** Ancillary care, Ethics, Obligation, Consideration, Resource-constrained settings, Southern Africa

## Introduction

Conducting research in settings where participants have complex health, social and economic needs leaves researchers with difficult moral decisions about how to respond to the needs, which may be outside the scope of the research project [1]. The ancillary care (AC) provided to participants in medical research is defined as: 'care which is not required to make a study scientifically

*Correspondence:
Blessings M. Kapumba
Blessings.Kapumba1@lshtm.ac.uk
[1] London School of Hygiene and Tropical Medicine, London, UK
[2] Malawi-Liverpool Wellcome Trust Clinical Research Programme, P.O. Box 30096, Chichiri, Blantyre, Malawi
[3] Liverpool School of Tropical Medicine, Liverpool, UK

valid, to ensure a trial safety, or to redress research injuries.' [2] or 'care not required by sound science, safe trial conduct, morally optional promises, or redressing subject injury' [3]. In 2012, Richardson redefined ancillary care as 'medical care that the research subjects need, but that is not required to make a study scientifically valid, to ensure a study's safety, or to redress research injuries' [4 p.2–3]. According to Richardson [4], the definition of ancillary care clarifies that the purpose of providing this care, which is beyond the scope of the research or otherwise unrelated to the condition being studied, is to promote the health and well-being of study participants, as emphasised in research ethics guidelines [5–7]. This care could be in different forms, including direct care provision to the participants and support with diagnostic and/or other clinical services. While a growing literature on ancillary care has primarily focused on the ethics of researchers providing that care, little is known about the actual practice of AC in research settings in resource-constrained settings (RCS). Whether such care is available has implications for research participants, the health system, the conduct of the research and the regulatory and policy framework.

There are concerns that the local healthcare system in many RCS is unable to meet the healthcare needs of the population [8, 9]. Populations in these settings may be affected by poverty [10], lack of health insurance [11– 13], and a disproportionate share of health conditions such as HIV, tuberculosis, malaria and the recent rise in non-communicable diseases [14, 15]. Therefore, medical researchers conducting their research in these settings may encounter unmet health needs among their research participants that may require medical care unrelated to the study. Such situations pose difficult ethical questions about the ethical principles which underpin the provision of AC during medical research and the nature of the moral implications of researchers providing AC to study participants. Olson [8] has argued that if medi- cal researchers in RCS do not provide AC themselves or facilitate its provision by others, the health needs of their research participants may not be met, and their well-being may be compromised. The Council for International Organisations of Medical Sciences [7] includes in chapter 4 of their guidelines the statement that: "researchers have an ethical obligation to care for participants' health needs during research and, if necessary, for the transition of participants to care when the research is concluded" [7 p.44]. The challenge, however, is that while this recommendation is given, it is not always clear what it means in practice and the scale of such care.

In a review of the practices of AC and a discourse analysis of how the language of AC has changed over time in guidance documents [16, 17], we have shown that existing guidance for the provision of AC is unclear or unavailable in the majority of RCS. We also found that researchers who take the initiative to provide AC to their study participants do so on an individualised basis or on humanitarian grounds. In the absence of defined ethical guidelines, the complexity of the obligation of researchers to provide AC remains undervalued. A review of publicly available institutional guidance documents that are pertinent to AC showed that of the 23 institutions that explicitly took a position on AC, 21 advised researchers and partners to take some measures to consider AC, and 14 specifically recommended referral for AC to local health care services [18]. The provision of AC during medical research may give health benefits to study participants [19, 20], but the practical implications of providing that care in RCS will differ from place to place

Despite the call for AC considerations in medical research gaining prominence, it is evident that guidance on its practicality in RCS remains inexplicit [17]. In 2016, Merritt and colleagues [21] proposed a framework for AC referral planning. Their framework provides guidance on deliberations researchers could use when making decisions to refer their participants for AC during medical research in RCS. Merritt suggested two ethical questions that users (researchers) can ask regarding referral for AC: (1) what impact would AC have on the well-being of those (participants) that are being referred for care, and (2) what is the impact that AC may have on local people outside the research. Merritt and colleagues were concerned by the potential challenges that researchers and members of study ethics committees may have when trying to determine what criteria constitute an appropriate referral for AC.

In the current study, we look beyond referral plan- ning to the provision of direct or diagnostic care to study participants, as has been recognised in the theoretical literature on the topic [2, 4, 19]. In addition, we aimed to explore the perspectives of research stakeholders on the potential impact AC would have on the health of research participants, non-participants, the research and health system, and policy and regulatory frameworks. We have selected one RCS in Sub-Saharan Africa to explore differing perspectives on AC within a national setting. Malawi is a Lower- and Middle-Income Country ranked 174 out of 189 countries on the Human Development Index. Malawi's population is disproportionately affected by severe and persistent poverty, with 52.3% reporting inadequate access to health care, according to the 2020 Integrated Household Survey [22]. The country also faces significant health challenges due to the health system's limitations. Health care services are provided by the public and private sectors, with the government providing free services at the point of access in public health

facilities. However, the essential health package, which may appear to exist only on paper, does not correspond to actual practice. In general, access to basic health care services, including screening or diagnostics and treatment, is limited. The country is heavily reliant on development aid, which plays a significant role in the economy and accounts for more than 60% of overall support in the health sector, including in health research [23].

The findings we report here are drawn from research stakeholders involved in or funding biomedical research in Malawi who provided their perspectives on the provision of AC. This paper contributes to a small but growing literature on AC in RCS.

## Methods

### Study design

We used qualitative in-depth interviews with a purposively selected sample of research stakeholders to examine experiences of and perspectives on AC provision in medical research conducted in Malawi. We examine the perspectives of a wide range of key stakeholders with diverse research experiences on the practical implica- tions of AC. In this study, we considered all the different forms of AC offered to the individuals who participated in clinical and community-based studies. This would include the provision of treatment and/or support with other ancillary health care services such as diagnostic or referral services.

### The study setting and population

#### *Context*

This study was conducted at the Malawi-Liverpool Wellcome Trust Clinical Research Programme (MLW), Southern Region, Malawi. The MLW is affiliated with Kamuzu University of Health Sciences (KUHeS). Researchers from MLW conduct research and intervention studies in various rural and urban districts such as Blantyre (primarily urban), Chikwawa (primarily rural), Zomba (semi-urban), and Mangochi (primarily rural) in Malawi. The researchers are engaged in a wide range of interdisciplinary research, covering clinical, basic science, epidemiological, and public health aspects of Malawi's most prevalent paediatric and adult diseases.

#### *Ethics review and approval process in Malawi*

All studies conducted at MLW and other research institutions in Malawi are reviewed and approved by the independent local (College of Medicine Research Ethics Committee and/or the National Health Service Research Ethics Committee) and international scientific and ethical review committees, depending on affiliation or sponsoring institution. These ethics committees are tasked with protecting the rights and well-being of research participants by ensuring that ethical concerns in research are minimised and that researchers rigorously adhere to ethical principles and frameworks [24]. Both local research ethics committees (REC) derive their authority from the National Commission of Science and Technol- ogy, which oversees the development of local research ethics guidelines and regulates the conduct of research in Malawi [25]. Since the MLW research is embedded within the local health system across tertiary, district and primary health facilities and communities, permission is also sought from the District Health Office or the Queen Elizabeth Central Hospital (QECH) research committees.

#### *Sample*

The key stakeholders in this study included researchers, health officials (both at the ministry and district level), REC members, research funding organisation officials, and research participants from purposively selected research projects at MLW (see Table 1). The selection of participants who took part in this research was based on ensuring that the perspectives on ancillary care held by a diverse range of research stakeholder groups were sufficiently represented. We also ensured a gender balance among the stakeholders, as people's viewpoints and experiences can vary based on gender. However, gender was not found to influence the findings of our study.

Since international funding organisations fund many projects in Malawi and RCS in general, we also selected stakeholders from these organisations to gain an understanding of their perspectives on AC. Officials from these organisations were approached for an interview. Responses to the enquiry were not received from four organisations, while officials from two others indicated that they do not have any information on their approach to ancillary care, so declined the interview.

The sampling framework was designed to gain insights from diverse stakeholders with different functions. Principal investigators, frontline research staff, and study participants were selected from ongoing research studies at the time the interviews for this study were conducted. When selecting the research studies to use as case stud- ies, we carefully reviewed the protocols and selected only those with *ad-hoc* AC arrangements to provide such care or support to the study participants. The research eth- ics guidelines and regulatory policies in Malawi (a case in most of the RCS) do not provide researchers with any guidance on providing AC to study participants dur- ing medical research [17]. There are provisions for study compensation in research ethics guidelines [26], but these should not be regarded as AC as described by Richardson [4 p.115]. Accordingly, compensation for study participants was not part of our inclusion criteria for the selection of case studies. We also excluded studies that did not have

**Table 1** Number of study participants by role

| Participants | Function | Number of participants | |
|---|---|---|---|
| | | Male | Female |
| REC members | Provided experience with review and approval of research studies<br>Experience with monitoring the conduct of research | 5 | 0 |
| Research regulatory authority | Provided experience in the promotion and regulation of the ethical conduct of research | 1 | 0 |
| Principal investigators | Provided experience in the conduct of research | 2 | 3 |
| Frontline research staff | Provided experience in implementation research activities—working directly with research participants | 2 | 2 |
| Fieldworkers | | 1 | 4 |
| Nurses | | 2 | 1 |
| Clinicians | | | |
| Health officials | Provided insights into the management of health facilities at the district level and provision of permission for research implementation at the district level | 2 | 3 |
| District Health Office | | 1 | 0 |
| Ministry of Health | Provided overall research policy regulation | | |
| Study participants | Volunteers in medical research | 6 | 9 |
| Funding Partners | Provided experience on funding for research at MLW and other RCS | 1 | 0 |
| Total number of participants interviewed | | 45 (21 m & 24 f) | |

plans or *ad-hoc* arrangements to provide ancillary care. We used a selection criterion to purposively select studies that would help to learn from the experiences of the research stakeholders involved in those studies and to understand their opinions towards AC provision in medical research. In addition, we considered clinical/hospital-based or community-based research, adult or child participants, and the participant's health status (healthy versus unhealthy/sick). Using this criterion, we deter- mined the extent to which these various elements influ- enced the level of AC need among participants, as well as the extent to which this informed or influenced the diverse opinions of researchers. We included: (1) clini- cal trials, (2) cross-sectional studies, and (3) community- based cohort studies (see Table 2).

#### Data collection procedures

Interviews were conducted between September 2021—June 2022. Interviews used a semi-structured topic guide (see Additional file 1) with open-ended questions about the views and experiences of AC. Given the unique characteristics of each stakeholder group included in this study, the topic guide was used flexibly while ensur- ing that relevant information was gathered. We used an iterative approach [27] throughout the data collection and analysis process, in which initial interview sessions influenced the inputs for subsequent interviews. This open discussion format during the interviews allowed us to build on our understanding from previous interviews. Participants were first asked a broad question on their thoughts about AC in medical research, followed by specific questions on what they perceived to be key ethical issues and implications associated with AC provision. We used vignettes (see additional file 1) to present to participants scenarios as examples of situations where AC may be needed to elicit their views and experiences based on that understanding [28]. A clear description of AC and some examples were given at the start, and more specific examples were provided during the interview if further clarification on the topic was required. We used vignettes with study participants because we were cognizant of participants' potential misconceptions regarding the distinction between research and medical care [29].

All interviews were conducted by the first author (BK), a social scientist, and the interviews lasted from 25 to 60 min and were audio recorded. Written informed consent was obtained from all the participants. Where interviews were conducted virtually, either on zoom, WhatsApp call or telephone call, participants granted verbal consent for participation and digital recording of the interview. For the stakeholders who were participating in research studies (as indicated in Tables 1 and 2), we asked permission from the study principal investigators to request their participant's involvement and then approached the participant during their study visit days. However, we arranged to meet the participants for the interviews on different days from the routine follow-up visit to their main study to try and minimise the possible influence of the researchers involved in the study they were participating in. During this visit, we explained the aim of our study and gave those that were able to read a participant information sheet. For participants who were not able to read the participant information sheet, we explained to them the details of the study and encouraged them to ask questions that they did not understand. Consent was sought on the day of the interview. We did

**Table 2** Selected case studies at MLW

| Case study number & setting | Study type and the main aim | Study population | Study activities | Ad-hoc AC arrangements and provision |
|---|---|---|---|---|
| Case study 1<br>Blantyre—QECH MLW | Challenge study (clinical trial)<br>Feasibility of empirical pneumococcal carriage in Malawi and feasibility of all measures required to determine vaccine response | Healthy adult volunteers within Blantyre (all participants interviewed in our study were healthy volunteers working at QECH) | Inoculation with pneumococcal bacteria<br>Three days observation at an arranged accommodation<br>Follow-up on study participants | Referral for HIV if a participant is diagnosed at recruitment<br>Provision of care for any medical condition, even those unrelated to the study (participants are advised to report at Mwaiwathu—a private tertiary hospital).<br>Not specific to the extent to which the study can provide support for chronic Conditions |
| Case study 2<br>Blantyre—QECH | Randomised, factorial, open-label clinical trial<br>To compare the impact on 15-day and one-year mortality of combined systematic empirical treatment against TB and Cytomegalovirus plus standard of care versus standard of care in HIV-infected infants with severe pneumonia | Children less than 12 months old living with HIV (We interviewed mothers with children recruited in this study and were all coming from within Blantyre—participants were identified during follow-up visits) | Treatment and follow-up | Trial physician support with the review of participants when admitted to the ward [direct care]<br>Provide assisted referral<br>Provision of other social support such as food for the participant (infant milk) and clothes (diapers) [this was considered as AC by researchers, and they thought it is an important part of care]<br>Provide TB screening to mothers, and samples are tested at KUHeS/MLW laboratory |
| Case study 3<br>Blantyre—QECH | Cross-sectional study<br>To investigate the impact of HIV infection on the frequency and function of Mtb-specific Polycytotoxic T cells (P-CTLs) in the lung and peripheral blood in humans | Healthy, HIV-uninfected adults<br>Asymptomatic adults living with HIV<br>TB patients both living with and not living with HIV | Bronchoscopy sample collection and follow-up | Provision of direct care for other conditions unrelated to the study<br>Provide assisted referral for conditions that require a specialist opinion<br>For example, the study team had a participant with severe anaemia, and they facilitated her admission and transfusion |
| Case study 4<br>Chikwawa—community | A prospective serological community cohort study<br>To understand the acquisition of immunity to Non-typhoidal salmonella (NTS) and epidemiology of enteric NTS and how this immunity varies with risk factors (malaria, anaemia, malnutrition, and sickle cell disease) and geographical setting | Under-five children (we interviewed mothers who had their children recruited in the study, and they were all from Chikwawa district) | Sample collection and follow-up on participants | Support with the provision of diagnostic and treatment for non-study related conditions such as anaemia and malaria<br>Support with the referral of children diagnosed with sickle cell disease and malnutrition to QECH and Chikwawa district hospital, respectively |
| Case study 5<br>Blantyre—health centres | Phase 3 Clinical trial<br>To assess the efficacy in the prevention of severe rotavirus Gastroenteritis of the NRRV vaccine in comparison to Rotarix<br>To evaluate the safety of the Non-Replicating Rota Vaccine (NRRV) vaccine in healthy infants and compare it with that of Rotarix | Healthy infants, $\geq$ 6 weeks and < 8 weeks of age at the time of 1st study vaccination. (We interviewed mothers who had their children recruited in the study, they were all from Blantyre and identified during recruitment day at either Zingwangwa or Limbe health centre) | Vaccination at visits 1 - 4 and a blood draw at the 4$^{th}$ visit<br>Active surveillance of Gastroenteritis throughout the study through weekly contacts | Support participants with referrals for critical conditions<br>Provide assisted referral in cases where a participant requires to meet a specialist [when they are also sick from other diseases] after a study follow-up visit<br>Provide care (medical care and treatment) to participants, their mother, father, and other siblings when they are sick<br>Provide food to participants at their scheduled visits |

not provide any incentives to the study participants for their participation in the interview; however, participants were reimbursed for transportation.

When subsequent interviews with each research stakeholders group introduced did not yield new insights, we concluded that data saturation had been reached and ended data collection [30, 31]. In addition to that, due to the design of the study and the roles of some stakeholders, we were not required to recruit more than two participants. For instance, there was just one individ- ual working in the regulatory authority for research in Malawi, and we chose them based on their position and level of expertise regarding research ethics in Malawi.

### Data analysis

All audio-recorded interviews were transcribed ver- batim by the first author (BK), and those conducted in Chichewa were translated into English. The analysis was ongoing during fieldwork, using an iterative approach [32] to identify emerging themes that could be clarified or explored through later data collection. We conducted thematic coding, managed using NVivo [33], using broadly defined themes (such as consideration for AC or ethical concerns for AC) and inductively derived subthemes (such as AC levels of obligation).

BK conducted the initial open coding and later worked together with JS and ND at the time of writing. The study team met regularly to reflect on and discuss emerging themes throughout the analysis process. We used a framework analysis approach to compare the perspectives of different stakeholders by theme. In this paper, we use a descriptive narrative approach to explore relationships and patterns in the views expressed by research stakeholders and to synthesise ideas that contributed most significantly to the ethics of AC practices in Malawi.

### Ethical approval

The study was performed in accordance with the relevant guidelines and regulations. Ethical approval was obtained from the Malawi College of Medicine Research Ethics Committee—CoMREC Ethics (Ref: P.01/21/3242); and the London School of Hygiene and Tropical Medicine—LSHTM Ethics (Ref: 22890). Institutional permissions were sought from all participating institutions, and their letters of support were submitted to the CoMREC as part of the submission for study ethics review. We also sought permission from the principal investigators at MLW and the KUHeS, prior to the interviews, to speak to study participants in their respective selected studies. Additionally, the research governance approval was obtained from the MLW Clinical Research Support Unit. Informed consent was obtained from all participants who participated in this study.

## Results

The data are grouped into four broad themes, all related to the impact of providing AC: (1) on the well-being of study participants; (2) on research and the health system; (3) to study participants on the individuals outside the research; and (4) on policy and regulatory frameworks. We used these themes to order the presentation of our findings, moving from the impact on study participants to the impact on policy and the research ethics guidance framing for future AC consideration.

### The impact of providing ancillary care on the well-being of study participants

Stakeholders described three main ways in which the provision of AC would have an impact on individuals who are directly involved in medical research: the expected direct health care benefit to study participants, improvement in the referral of individuals with AC needs, increase in the risk for structural coercion [34] and undue inducement.

#### *Perceived direct health care benefit*

All stakeholders felt strongly that AC would offer a potential personal benefit to access health care which may not be available or limited in the public health system. A commonly raised expectation was that of participants thinking that they would get the best medical care once they joined the study. For the frontline research staff and the study participants, they thought this was also associated with the possibility of gaining quick access to medical care.

> *'But there are some who always say, I want my child to be helped, I do not want to come to the hospi- tal and stand on the line [queue] for a long time. Because on the long line [queue] there, my child can be getting sicker. But here, I just come straight, and the clinician checks on my child. So, I will prefer my child to be given health services by the researchers.' (Frontline research staff - fieldworker).*

In addition to medical care benefits that most of the participants perceived as better than that which they get from public/government hospitals or through standard routine care, some study participants asked if researchers could provide them with other support, such as food.

Most study participants interviewed were mothers whose children were the main participants. The mothers emphasised that for them, apart from the care their children receive in addition to research activities, they would like social support services such as receiving food and money rather than only medical support. In terms of medical care, they indicated that they were satisfied with

the care their children received as participants but while maintaining the emphasis that the provision of social support would have more impact than just medical care:

*'...when we join the research study, we have hope that the researchers will help us. So, they are still supposed to provide treatment for any disease which they have found in the child. Because whenever we join a research study, we believe it to be as our hos- pital; so even if our child suffers from any kind of disease, we are supposed to go there because the doc- tor who is doing research on the child is the one who knows the kind of disease which the child is suffering from.' (Study participant)*

Regarding the public health benefits associated with AC, the perspectives of participants in clinical studies and those in community-based studies were similar. However, there were variations over the expected health care and support needs. In comparison to mothers who enrolled their children in community-based studies, women who enrolled their children in clinical or hospital-based studies had higher expectations regarding the level of health care and social support the researchers would provide for their sick children. Adult participants had similar views on the ancillary care expectation from the researchers.

Despite these expressed expectations, the research- ers indicated that participants seldom ask directly for additional care or non-medical support during research. Frontline research staff mentioned that they encounter participants asking if their relatives or themselves would be accepted to be cared for by the researchers if they get sick from a condition not related to the study.

*'... we had some mothers who came to get recruited because they were told by their friends that we provide care to them. So, they asked us if we would be able to provide care to other children in the fam- ily when they are sick.' (Frontline research staff - research Nurse)*

None of the study participants we spoke to said that they had asked for AC; rather, they said that they were satisfied with the support/help they got from the researchers. When asked about the care that the researchers provide, some participants just said, `they (researchers) provide everything,' while others said that the researchers had told them that they could seek care at any time when they or their children were sick.

While recognising that AC has direct health care benefits for those participating in research, stakeholders from the district health office presented a different view on the impact of providing AC on the people who partici- pate in research. They stressed the role that they wanted researchers to play in supporting the health facilities where they were implementing their study.

*'From what I have noted with the majority of researchers, they are only there for the study; they do not want to be involved in other extra activities unless you tell them that if you do not want to help us, then we will chase (not allow their research to continue) you out of here. So, some do help because they have been told to do so and because they know that if not, then we will not give them an opportunity to do their study at our facilities.' (Health official).*

The health officials believed that AC could have a greater impact if it served the entire community and were therefore opposed to the notion that AC should only be provided to study participants.

#### *Improvement in the referral of individuals with ancillary care needs*

All stakeholders mentioned referral for AC as one benefit of participation in medical research as it is often considered a way of helping the participant to get care for incidental findings from the study [35] or when there is a positive screening ancillary health need. They emphasised that referrals might be considered if the researcher is unable to provide the participant with the necessary care or if the participant's condition cannot be managed at the study site.

*'So, let us say my patient in the study was enrolled and was eligible, but while in the study, has devel- oped a heart condition, right? I can't treat a heart condition because my focus is on pneumonia, but I can direct my patients to the right clinic and have the clinic follow up on the heart condition; still, they can still be eligible to be in the study with the heart condi- tion. And they have the people responsible for follow- ing that up while I continue following up on the care that we're providing, for example, in this case, pneu- monia'. (Frontline research staff–research clinician).*

Some frontline research staff mentioned that researchers support their participants with a referral for AC, which sometimes includes the provision of additional support, such as for transport. Usually, the researchers do that on their own initiative to show sympathy and solidarity.

*'Like most of the time, they come here when the baby is sick. So, whenever we are thinking of referring the child to [hospital xx], we call the office for the car, and we always escort them to the referral hospital so that there shouldn't be some delays.' (Frontline research staff–research nurse)*

Similarly, some REC members held the same view that AC referral directly benefits study participants to get help for their identified additional health needs that could not be addressed by the researchers. However, while the REC members supported referral for AC, they also raised concerns similar to those of health officials about the limited availability of services at the facilities where the participants are being referred to.

> *'I would think that referral [...] should be adequate, especially where such services are readily available. However, in the event that maybe this is something that is unique in a way that the facility would not provide, because sometimes those services may not be available even at the facility where the partici- pant is being told to go, then that's where I would probably advise that the guidelines should step in, and maybe emphasise that the study should do something about it.' (REC member).*

On the other hand, stakeholders from the district health office, while appreciative of the referral initia- tives for AC, were concerned that it could overburden the health system by increasing demand for the limited resources available at the facilities.

#### *Increase the risk of structural coercion and undue inducement*

The protection of the rights, safety, and well-being of participants is recognised in the international research ethics guidelines as the first obligation of researchers, above and beyond the advancement of science and the interests of society [5–7]. This provides researchers with a compel- ling argument for addressing the clinical needs of study participants who voluntarily contribute to the progress of medical knowledge. Concerns exist, however, that researchers may also encounter volunteers with ancillary healthcare needs and that the care provided for conditions related or unrelated to the study may be of a higher standard, which could be a form of structural coercion or undue inducement. The expectations of research participants that they may accrue benefits from taking part in research, as mentioned above, were felt to influence their decision to participate.

Stakeholders had mixed views on whether AC would be coercive to study participants. While many stakeholders, including researchers and some REC members, thought that since participants get fully informed about the study and willingly volunteered to participate, AC may not be regarded as coercion for study participation. On the other hand, some stakeholders emphasised that providing study participants with AC may, to some extent, constitute structural coercion, particularly in situations in which the participants believe that participating in research is the preferable alternative to gaining access to medical care. To avoid that, one principal investigator and some frontline research staff emphasised that they deliberately exclude such information from the participants' information sheet or when they explain the details of the study to the participants.

> *'Yes, ancillary care could be a bit coercive, and that's why, I think, we actually don't put it either in the informed consent, or we don't put it out there when even talking to our study participants that we will provide ABCD. But during the course of the study, that's when we just provide it.' (Principal investigator)*

In addition, some frontline research staff, REC members, and district health office stakeholders acknowl- edged that it is difficult to entirely rule out structural coercion while recognising that it is not possible to deter- mine with certainty what motivates a person to engage in a study.

> *'So, speaking of ancillary care, I'd say it's tricky because it doesn't matter how sugar-coated you may put it to make the participant not feel they are being coerced... yes, it might not sound as if they are coerced, but in one way or the other they may be influenced, because there are some like I said who just want to know what's going on with them and knowing that there is this advantage to come back later if they develop a problem, seriously it's some- thing that's tricky on their part really.' (Frontline research staff–research nurse).*

Undue inducement, which is usually used interchangeably with coercion, presents a concern that it compromises the voluntariness of participation in research, which is a requirement of informed consent. However, it should be noted that people in RCS have limited access to health care services, and every opportunity for having access to medical care that they see in medical research will encourage or motivate them to join the study. While the frontline research staff and principal investigators mentioned that in most cases, participants are influenced to join the study because of the associated benefits, in this case having access to medical care, they believed that this was not an issue because it is difficult to ascertain what motivates an individual to join a study. Some REC members had similar views that there are many other factors that could influence participants to take part in research, but there is not a particular issue with the provision of AC. For example, they mentioned that participants could be influenced by monetary compensation, access to medical care (assumed better care), and others

for altruistic motives. In addition, a principal investigator and a representative of the research regulatory authority stated that most of the participants might end up enrolling in the study without making an informed choice due to many participants' expectations regarding medical research [36].

All participants from the selected studies said that they thought that AC is part of the research and that by joining the research, it means getting better health care services in general. It is possible that participants' health- care expectations, rather than misconceptions [37], arise from previous knowledge of the benefits to themselves or others of participating in the research. However, while acknowledging the benefits of accessing better health care, the study participants said that they could not be forced or unduly influenced by AC to join the study.

### The impact of providing ancillary care on the research and the health system

Stakeholders considered two critical consequences that the provision of AC may have on the research being car- ried out in RCS as well as on the health system in general. Specifically, stakeholders were concerned about the planning for AC and the possible burden that AC may have on research as well as the health system.

#### *Planning for Ancillary care*

Partly linked to the consideration for the provision of AC, the inclusion of plans for AC in research protocols and grant applications was reported to be missing by all the researchers. A REC member, health officials and stakeholders from funding organisations mentioned that it is not common practice.

> *'So far, I haven't seen any protocol that I can recall seeing a protocol that had that kind of embedded as part of the study.' (REC member)*
> *'Researchers don't include ancillary care plans in their applications for funding; if they do, then it is those that are meant to provide care for the study- related condition.' (Research funding organisation official)*

Nonetheless, the PIs mentioned that they make plans to care for their study participants not only for study safety reasons but even for any other additional health needs. This substantiated what we found in the protocols of the selected studies, where ad hoc arrangements were made for the provision of some AC to study participants. In addition, stakeholders also mentioned that since there is no specific guidance on AC, studies do not have a specific budget to cover the ad-hoc AC plan that they include in the protocols. They make sure to provide everything with the limited research budget, which is meant for study activities.

Even though it was expected that the researchers (principal investigators and frontline research staff) would mention that they include plans for AC in their study protocols, since some claimed that they provide AC, they said that they exclude such plans to prevent suspicions of their influencing the participants to join the study. However, when discussing the inclusion of plans for AC, all stakeholders primarily referred to the research budget. Participants thought that including a budget to cover AC was necessary, knowing that the provision of AC would require resources.

> *'..., I think it's very essential that at the planning level, researchers should actually budget for ancillary care.' (Frontline research staff–study clinician).*
> *'But if the research team would like to include a budget line, to provide that care, either by supporting a nurse or ensuring that people who are referred are seen, [...] or if the team can support the health of the research participants. That, we would be happy to support that assuming that the team had made a justification.' (Research funding organisation official)*
> *'But for planning purposes, it should probably be included. Even in the budgeting aspects. Yes, [...] this ancillary care-related work I think should be budgeted.' (REC member).*

Some frontline research staff also suggested that identifying AC needs during study preparation can help with planning. They thought researchers could use the established networks in sites where the majority of research takes place to identify and advise on ancillary needs of people in that setting, for example.

> *'In terms of planning, I think it should be the researcher looking at the local situation. So, they should be versed with the local standards. At the same time, I also understand a little bit further in terms of while Malawi has got so many limitations, but still, there are other standards that stretch a lit- tle bit further in terms of care. So, they can use the health surveillance assistants and other people to tell them about the common health needs of people within their communities and use that for planning.' (Frontline research staff–study coordinator/clini- cian).*

Researchers and study participants were also asked about how the plans to provide AC may be communicated to those participating in the research. Most study participants said that researchers typically inform them of the care and support they would get as a result of their participation in research. However, while several

participants said that researchers tend to make this information very explicit during recruitment, they could not specify whether or not this information included conditions necessitating AC. Two study participants, one in a hospital-based and the other one in a community-based study, recalled what had happened in recent studies:

> *'When they came, before we joined, they first asked us do you agree to allow our child to join the study? And I agreed after seeing that my friends are join- ing and also because they told us that they will pro- vide treatment to our children if they find them with malaria.' (Study participant)*
>
> *'The researchers make it very clear about the care we will receive while participating in the study; for example, I remember one of the study nurses mentioning to me that I could come at any time I feel sick, and the study doctor will review me and give me medications.' (Study participant)*

However, the majority of participants could not differentiate between study-related care and AC or support but were very appreciative of all the care that they received while participating in the research.

Researchers had mixed views on whether to include AC statements in the participant's information and when to tell participants about AC. While most of the stakeholders thought that including AC statements would unduly influence participants to take part in the study, others suggested that everything must be explained to the participants. They thought the decision must be made by the participants to either take part in a study or not. One frontline research staff thought that if research- ers decide to include AC information in the consenting process, then that care should be equal to the standard of care provided in public health facilities.

#### *Burdens on research and healthcare system*

The view that AC would be a burden on local healthcare systems was emphasised by many researchers, REC members and health officials. They saw that this care would add extra responsibilities to the already constrained healthcare system. Health officials were concerned that there was already a lack of resources in most of the facili- ties; when researchers refer the participants for AC, it would, in the process, overburden the limited resources of the health system. Health officials who raised this issue believed that researchers could step in and assume some responsibility; they should not leave everything to the health system, lest the individuals they refer to the public health system be unable to get assistance.

However, one health official from the Ministry of Health thought AC would not create much of a burden to either the research or the healthcare system because each has a specific role to play in patient care.

> *'... I believe that this participant or patient has already spent much of his or her time with this researcher. Now this researcher has identified the problem and referred this patient to maybe another level of care. To me, I don't think it is a problem or burden on either the researchers or the health care system.' (Health official).*

On the part of the research, some researchers and REC members thought that giving the responsibility to researchers to provide direct AC would create an unnecessary burden on the research. Stakeholders were concerned that research resources are often restricted to study-related activities; therefore, using the same study resources for AC might deplete resources intended for study-related activities. Although the stakeholder from a funding organisation mentioned their flexibility to consider providing top-up funding for AC as it may be requested by researchers, this was not specific about what that would mean in practice or how much of the budget they would be willing to provide for AC.

### The impact of providing ancillary care to study participants on the general population

In this section, we focus on two critical viewpoints that came up in the interviews in relation to potential impacts of AC on the broader population. While most stakeholders emphasised that providing AC may be one strategy for strengthening the local public health system, some expressed concerns that it may promote health inequities regarding access to health care.

#### *Healthcare system capacity strengthening*

Many stakeholders emphasised that researchers could consider providing AC as a form of providing support to the public health system. They thought the way to address healthcare challenges that the majority of study participants in Malawi experienced could be through supporting health facilities in the districts where they conduct their research.

The district health officials emphasised that they want to benefit as much as possible from the research because they assume that researchers benefit in the process of conducting their research [38]. However, one frontline researcher was against the idea of researchers supporting the health care system as a whole, arguing that AC should be focused only on an individual who has voluntarily decided to participate in the study and perhaps knows his/her problems.

*'Targeting the whole system would deprive the needed care to the individual at the point they needed that scarce service which has been offered to someone else.' (Frontline research staff—research nurse).*

Some research stakeholders mentioned that, since some research procedures use resources which are already scarce within the government health care system, for example, laboratory testing supplies such as reagents, they need to come in to support the system.

*'These supplies are usually out of stock, and if researchers know that part of their study would require that, then they should be able to plan for that and help supply such commodities to the hospi- tal.' (REC member)*

Another aspect of social support emphasised by the district health officials was capacity building within the health care system. They said these are some of the important things they would like to see done by the researchers, which would also be considered AC. For example, teaching district health office personnel about research techniques and emerging medical technology undertaken by researchers throughout the implementa- tion of their research activities.

#### *Promote the potential for healthcare inequalities*

In this category, stakeholders brought up some concerns about the potential inequality that AC may cause between individuals involved in research and those who are not. The concern about inequality was predicated on the idea that limited health care impacts everyone in RCS, not only those who engage in research and have difficulties gaining access to vital health care services. Therefore, if the provision is limited to those who engage in medical research, there is a risk of exacerbating health- care access inequities [39]. The health officials and some REC members emphasised the need for researchers to focus on the public good versus the individual or per- sonal benefits to address such inequalities.

However, some stakeholders thought that including people not involved in the research would be a burden on the researchers. They mentioned that for the researchers to provide AC to their participants, there are several factors, including the trusting relationship that is established between the researchers and the participants.

*'First one is the researcher has identified a problem in the participant; they don't do that to people who are not participants in their study. Therefore, now there has been an established kind of relationship between the participant and the researcher. Therefore, the researcher should be sympathetic enough to address that challenge in the participant.' (REC member)*

The members of the REC, the researchers, and the health officials all shared the perspective that the general community could consistently profit from the results of the study.

### Ancillary care ethics, policy, and regulatory framing

#### *Ethics guidance for ancillary care*

The REC members, health officials and researchers all acknowledged that the current ethics guidance does not support or explicitly mention the provision of AC to study participants.

*'So, we don't have, as of now, we don't have any, you know, policy guidelines along those lines in terms of care. We only go by the fact that when people are doing research […] it should be beneficial to an individual directly or indirectly, or the community immediately or later on.' (REC member).*

Some REC members and one researcher mentioned that guidance for AC had been needed for some time.

*'Well, I think the guidance should have been there 15 years ago, but it wasn't. That is not written anywhere. But I think, you know, maybe they could request that. As I say, I've always put ancillary care in my budget, where I use the 10% contingency.' (Principal investigator).*

Both the REC members that we interviewed and stakeholders from research funding organisations accepted that AC had not been discussed in anything but an ad hoc way and had not been included as a priority issue in their deliberation on policies.

*'I would say, maybe the only time that we start to interrogate or talk about issues to do with or that could maybe feed into ancillary care is when we are looking at adverse events.' (REC member).*

*'We have had debate on compensation, but that issue has never come up and say if they are provid- ing care to the participants, then they will sway the participant to join that wouldn't otherwise join. So, to me, it's like if it is beneficial, it is difficult, rather just deal with the case on its merit.' (REC member).*

In response to our email, a representative from another research funding organisation that we did not interview stated that they do not have specific information on AC and instead refer researchers whose projects have been funded to the in-country regulations.

Some stakeholders, including the REC members and researchers, suggested that considerations to make some changes in the research ethics guidelines should happen now. One REC member mentioned that the landscape of international ethics guidelines has changed, and this must be reflected in the local research ethics guidelines to address issues of AC in medical research.

*'Okay, but putting my thoughts along those lines, I'm about to say that it should become pretty much like the guidelines; they should revisit that whole thing and maybe make it more kind of obligatory within certain kinds of boundaries. [...] they should be able to consider the type of maybe support they can provide, you know, and what that is doing, but that component should really be part of any study of this magnitude. So, yeah, I'll say that there's need for that to make sure that it reflects on the guidelines.' (REC member).*

When we asked the researchers about the guidance for AC, they mentioned Good Clinical Practice training on participant protection. To most researchers, this is the ethics guideline for the conduct of research, mainly to safeguard and protect participants from research harm.

When asked about the availability of specific guidance from the ministry of health for researchers when they conduct medical research in Malawi, health officials mentioned that there are no specific guidelines or policies on ancillary care or for the conduct of medical research in general. However, they contribute to developing the ethics guidelines the REC members use, which they believe all researchers are supposed to follow when conducting their research.

#### *Ancillary care obligations*

Research stakeholders had mixed views on the obligation of AC that may require that researchers take full or some responsibility towards providing care to their partici- pants during medical research.

While all research stakeholders expressed support for researchers to take responsibility for the provision of AC, some did not agree to make it an obligation.

An official from the Ministry of Health and other stakeholders, including the researchers, held the view that making the provision of AC an obligation for researchers would make the conduct of research in Malawi costly.

*'Making the provision of ancillary care obligatory will set up higher standards for research funding which will be difficult to sustain.' (Health official).*
*'Firstly, it shouldn't be the researcher's obligation. It shouldn't be because we have specific things to do in research, and there are already people who provide care for other conditions. But if something has been stated in your protocol, that this is how we'll do things, that should be implemented exactly the way you say it.' (Frontline research staff–research nurse).*

In addition to the concerns around the cost of making AC an obligation, some frontline research staff thought that this would put too much responsibility on research- ers as well as increase the demand for care services from participants when they learn that researchers provide AC as may be deemed necessary.

*'[...] at the same time, it might even make most studies not feel like a good ground for them to practice or to do research because of the demand from participants and knowing that it's an obligation.' (Frontline research staff–study Coordinator).*

Instead, stakeholders, including the REC members, researchers and the official from the research funding organisation, suggested that AC should be provided on a case-by-case basis because it is not all participants have additional health needs or incidental findings during medical research.

*'I think guidelines are clear around doing research and on uncovering or finding out that participants have sort of health needs, which I think are mostly kind of on an individual basis, so they should be supported as such.' (Research funding organisation official)*

For the stakeholders who held the view that AC should be an obligation, many thought that since it is not included in the guidelines, it was important to have a careful review of the guidelines and include AC obligations.

All the PIs and frontline research staff that we interviewed reported that they have an obligation to provide AC to their participants. Some of the reasons that they provided include the moral responsibility to help others.

*'Well, I think from the point of the [case study 2] trial, I feel like we find this a moral obligation, that you're not just a thing to be experimental in our study. There are some participants with additional needs that we should support if you want to sort of them participate in our study.' (Principal investiga- tor).*
*'It's certainly an obligation depending on the obligation kind of research that you are doing. So, to me, maybe the higher the risk, the more ancillary care could need to be provided.' (Principal investigator).*

The health officials, however, had different views on AC obligation. While indicating that researchers have an

obligation to provide care to their participants, they suggested that it would be better if the researchers focused on the health system and not an individual.

### Research funding constraints

Research funding was perceived as a limiting factor in AC provision plans. Some researchers thought it is now time for research funding organisations to start considering including or accepting some budgetary plans (as proposed by applicants) for AC.

> *'They need to really have an understanding of the challenges people face and plan to give researchers some additional funding for ancillary care needs which may be identified during the implementation of the study.' (Frontline research staff - research nurse).*

However, several stakeholders were concerned that it would be difficult to ask for extra money and that, given there is already usually a 10% contingency, that might be used for AC. One REC member commented that there really should be funding committed/allocated to supporting either AC or the health care system.

> *'One of the things that I have found almost immoral, I am going to use that term, is that you have a study with a huge budget, and a huge proportion of that money goes in the form of the fees or payments to the PIs. A huge component of the money would remain, for instance, if it's coming from outside this country, would be with those people that are from the other world or what is commonly known as the global north.' (REC member).*

A stakeholder from one of the funding organisations mentioned that while acknowledging that funding sup- port towards AC may not be supported by a policy within the organisation, the importance of AC in RCS cannot be overlooked. They suggested that funding for AC may be considered, provided that researchers include a clear justification and that it does not take the whole research budget.

> *'...we would expect that the team have comfortably budgeted for what they need and that they have provided some justification as to how they have arrived at the number for the cost of ancillary care.' (Research funding organisation official).*

The same respondent went on to suggest that funders might provide additional funding if it is meant to support the health system.

> *'If there's some other mechanism that basically, the team can support the health of the research participants. [...] we would be happy to support that, assuming that the team had made a justification. They just need to justify how they're going to use that money and what it's for and kind of the ethical considerations down to the participants.' (Research funding organisation official).*

However, some stakeholders were against the idea of directing funders to accept all the AC plans in the grant's application because they thought this might make the implementation of research very expensive and hence discourage research funders as well as researchers who fail to source funding for AC.

## Discussion

Our findings provide insights into the experiences and perspectives of research stakeholders regarding the provision of AC to study participants during medical research in Malawi. In this study, we found that, in theory, the stakeholders consider AC desirable, but when looked at more closely, questions arise about how applicable provision through referrals maybe if the health system is overwhelmed. There are also issues about costs when AC is not something provided for in research budgets. While funders may express the view that AC is something they could consider, the concern that this may make budgets prohibitively expensive, particularly in situations where research funding is scarce, does require careful consideration.

The historical rationale for research regulation was to protect study participants from study-related harm while also aiming to improve individual and public health through new discoveries [40]. Collectively, medical research has led to significant discoveries, the development of new therapies, and a remarkable improvement in health and public health [41]. However, often forgotten are the actual benefits that this has to the individuals who participate in medical research if they do not receive care for the additional health needs that they may have during the time they participate in research or beyond. Several studies have been undertaken to gauge public attitudes towards health research and the factors that influence individuals' willingness to participate in medical research [29]. However, less focus has been given to understanding the impact of research on individual participants. In relation to the AC expectations of study participants, our findings are consistent with previous studies [42–44]. Our results suggest that therapeutic misconception, or, indeed, the expectation [37, 45] that many partici- pants have regarding medical research, was the primary motivation for their engagement in research. In addition to expecting to be informed of the study's findings, participants may also have expectations regarding their

healthcare needs, especially at the time they enrol in the study or during the implementation of the study. Our findings suggest that the provision of AC in this regard may be associated with an expectation that study participants may have, such as the belief that they will have access to healthcare services that will address all their health needs, including services that are scarce or beyond the standard care. With such expectations, Sacristán et al. [46] argue that participation in research is often motivated by the possibility of personal benefits as well as the chance to assist others. In the context of RCS, despite the danger associated with exposure to experimental procedures and therapies, research participants continue to be driven by a choice to or a perceived belief that they will only get better care if they engage in research. This suggests that guidelines for AC provision might need to be different in these settings acknowledging the reality that, if given a chance, individuals would prefer to participate in research explicitly to receive access to better treatment. Similarly, our findings demonstrate that individual benefits of participating in medical research in RCS through AC would have a direct impact on the health of the participants, as suggested by Nass et al. [47].

In the context of AC referral, reported as the most common practice for AC in medical research [16], Mer- ritt et al. [21] pointed out that researchers ought to con- sider the prospect of AC (referral) as a benefit to studying participants in the light of the associated burden and risks. However, taking such responsibilities means that researchers have to make proper plans to ensure that the provision of any form of AC does not impinge on the primary obligations for research [48]. In our find- ings, we have demonstrated that AC plans are not usually included in research protocols or where researchers are applying for research grants. Those that do take the initiative to provide AC to their participants do so on a case-by-case basis. Taylor et al. [49] suggest that an essential part of AC planning is when researchers anticipate the possibility of giving some AC based on their knowledge of the health state of the community from whom eligible subjects will be recruited. We had similar findings in our study; however, for most of our research stakeholders, the term "planning" was interpreted as referring only to the inclusion of a budget or some other form of finan- cial allocation for activities that are considered to be AC. Because researchers do not have clear AC plans in their protocols, we assume that this was the reason why AC was not clearly explained to study participants [46].

Our findings also demonstrate that referral for AC may have been the most supported practice because it does not require unmanageable amounts of additional resources from researchers. However, a referral could be made on the premise that such health services are publicly supported by the facilities where participants are being referred, while this may not be the case. We found that additional support or non-medical support provided to study participants requiring referral for AC which was mentioned and also suggested by the stakeholders in this study, was similarly reported by Pratt et al. [39], where researchers in a trial took the responsibility of supporting referral for AC by providing transport.

In relation to the impact on the research and the health system, stakeholders' views reflected principles and potential tensions regarding the resources that are used for the successful implementation of research. While researchers were concerned about having limited funds or restrictions in their budget and that AC would consume resources meant for the study, health officials, on the other hand, saw AC as a burden on the health system. Although stakeholders were supportive of the provi- sion of AC during medical research, there were no clear reflections on the ethics of doing that. Many stakeholders' viewpoints were based on the social aspect of moral obligations, that it is in the nature of human beings to help one another in situations of need. Evans, Evans [50] describes the situation of need (vulnerability) of participants in medical research as evident, and this is particularly the case with participants in RCS. Despite the fact that stakeholders saw AC as complex and demanding on either the research or the health system, we argue that its influence on both study participants and the general population is highly beneficial.

In relation to the impact on the general population, enforcing the capacity of the local public healthcare system/facility was one consideration strongly suggested by research stakeholders in this study. This suggestion is strongly supported in the [CIOMS (1992): cited in 52 p. 141] (Guideline 15), which recommends that consideration should be made to strengthening the healthcare facilities and ensuring that it is sustainable in the local context once the research has been completed. In addi- tion to a range of activities for capacity building, such as specialised training for medical personnel working in health facilities, research stakeholders suggested that AC support may include helping with medical supplies, such as medical equipment and medications, as well as pro- viding direct care to individuals who seek medical treat- ment at the health facility. Stakeholders' viewpoints show that the AC responsibility of researchers and research funders should be directed toward strengthening the healthcare system so that it can benefit many. Taylor et al. [49] suggested that research sponsors should sup- port the researcher's commitment to contribute to the overall health and well-being of the community in RCS. Similarly, our findings demonstrate an emphasis by stakeholders for similar support, as they believed that if

researchers were supported with sufficient funding or resources, they would be able to assist the challenged health system, with the benefit being for the public good as opposed to individual benefit [51, 52]. However, in terms of the provision of AC, researchers cannot be fully responsible for providing everything that health officials in the health system may demand from institutions involved in research. For example, the research stakeholders' emphasis on good working relationships is to see that there is benefit sharing. Thus, the healthcare system will benefit from the resources brought by the research- ers, which may be used by individuals who are not participating in the study, in addition to those who are the study's primary beneficiaries (the study participants). In the healthcare system, there are many stakeholders who partner with the Ministry of Health, which impacts different healthcare systems/facility capacity strengthening. One example of such a stakeholder would be researchers or the research institutions to which the researchers are affiliated. As a tool to facilitate this relationship between patients (research participants or not), the researchers, and other players, with the goal of defending the patient's rights to health care, researchers are an important stake- holder [53]. Clearly, stakeholders emphasised/perceived value in healthcare system/facility strengthening activi- ties to support the fragile healthcare system. However, just as we described above on AC obligations, most of the stakeholders perceived this to be overburdening the research as well. They were also looking beyond the completion of the study to what would happen to the patients or participants who depended on the AC being provided by the researchers [54, 55].

In relation to the impact on policy and regulatory framing, our findings have demonstrated that ethics guidance for AC is lacking [18] and where it has been included is not explicit. As the debate on the ethics of AC provision during medical research continues, our findings suggest that the normative perspective of AC provision must be translated into practice, hence increasing the potential for the development of new guidelines. Advances in such areas of research ethics are facilitating a transformation in the ethics of research, which is generating new insights into the conduct of health research. Since the current ethics guidelines do not explicitly support the provision of AC, we contend that this increases the nonstandard method of providing AC to study participants, which further complicates an already complex issue. Lack of clear ethics guidance is also thought to make it difficult for researchers to decide on what to do when they iden- tify AC needs in their participants [17]. Even though our findings indicate that researchers assume some responsibility for providing AC (see Table 2), there is widespread controversy and a lack of ethical guidance regarding what researchers can provide as AC and the boundaries of AC provision. Our findings have also showed that discussions around AC have not been prioritised by the research ethics regulatory bodies. Commonly addressed concerns include remuneration or compensation of study participants, such as how the researcher might avoid pay- ing too much while determining an appropriate amount of compensation for study participants in order to avoid unduly influencing or coercing their participation. [6, 7].

Although our findings show some potential that research participants may be unduly influenced or coerced to participate in a study due to AC being pro- vided, we argue that this is a very minimal concern, similar to the views presented by the REC members. However, according to Nkosi et al. [56], participants in RCS frequently perceive study resources as a chance to improve their lives, which undermines their decision to deny involvement in the study, which might be viewed as structural coercion in a sense [34]. It is clear that the provision of AC is still a new concept to several of those interviewed for this project, and more discussion is needed, both within the country and internationally, to agree on what guidance can be given and what should appear in policy documents to guide this provision.

This study is not without limitations. Firstly, the representation from research funding organisation part- ners was insufficient to provide an adequate reflection of how different research funding partners regard AC support for researchers conducting medical research in RCS through grants. Similarly, it could have been ideal to interview research stakeholders from other research institutions that conduct medical research in Malawi and get funding from different partners. Since we were more interested in interviewing officials from funders that fund medical research in Malawi, and more spe- cifically at MLW, we believe that including funders from other research institutions in Malawi would have given other additional perspectives on AC provision. However, some officials from the funding organisations responded to our request for their involvement in the study through email by stating that they do not have any specific infor- mation on ancillary care. As the objectives of the study were related to experiences, opinions, and practices, it may be assumed that stakeholders who decided not to take part in the study or did not reply are likely to have perspectives that would support AC. From this viewpoint, stakeholders from other research funding organisations could have different opinions about what counts as AC. We may thus have missed important voices and perspectives. However, the responses we got from stakeholders (declined potential participating officials) from some funding organisations were considered as a finding for our study. Moreover, it is well established [17, 18] that

the majority of research institutions and funding organisations do not have explicit guidance for ancillary care.

Secondly, the findings of this paper provide an in-depth exploration of AC practices and the related ethical challenges experienced by researchers undertaking medical research in Malawi, where research ethics guidelines are not currently explicit on the provision of AC [17]. Conducting a similar qualitative in-depth interview study in other socio-economic, cultural, social, and geographical contexts on practices of AC provision in medical research should be considered to complement and contrast our findings. Given that we identified ethical challenges associated with the implementation of ancillary care in medical research conducted in Malawi and that it is difficult to determine how much AC can be provided to a participant, future studies should explore whether similar ethical challenges associated with AC exist in settings with some AC guidelines or in contexts where research is partially locally funded (do not largely depend on inter- national funding partners), as well as in settings where health services are not free to the public or with national health insurances. For instance, South Africa has projects financed by the South Africa Medical Research Council, whereas Kenya has projects funded by the Kenyan gov- ernment. Indeed, as much as our findings represent RCS, they should be interpreted cautiously.

## Conclusion

This paper highlights the broader questions that researchers need to ask when considering the provision of AC to their study participants in medical research. Despite the best intentions of some researchers to provide AC, our findings demonstrate that the concept of AC is still new among many research stakeholders. Most of the responses from the stakeholders are that AC should be encouraged as a moral practice in research. However, the planning and provision of AC should not be mandatory. When considering the provision of AC in medical research, researchers should not limit themselves to protecting study participants from study-related harm or illness. Instead, they should adopt a broader care perspective that includes caring for their study participants' additional health needs. In addition, standard criteria must be specified for RECs and researchers to use as guidelines when reviewing research proposals and determining the type and extent of AC that researchers can provide to study participants. Therefore, we recommend the development of a more explicit internationally agreed-upon ethical framework to guide decisions regarding AC that would be applicable to all stakeholders, including sponsors or research fund- ing organisations from the global north. In the absence of internationally binding regulations on AC, this would also guide researchers in protecting the well-being and health of their participants in RCS.

**Abbreviations**

| | |
|---|---|
| AC | Ancillary care |
| CIOMS | Council for international organisations on medical sciences |
| KUHeS | Kamuzu university of health sciences |
| MLW | Malawi-Liverpool Wellcome Trust Clinical Research Programme |
| RCS | Resource-constrained settings |
| REC | Research Ethics Committee |
| NRRV | Non-replicating rota vaccine |
| NTS | Non-typhoidal salmonella |
| QECH | Queen Elizabeth Central Hospital |

## Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12910-023-00889-x.

**Additional file 1.** Topic guide for KIIs with research stakeholders in Malawi.

**Acknowledgements**

We are grateful to the principal investigators of the selected studies at MLW, frontline research staff, and all other research stakeholders who participated in the study. We also thank Professor Moffatt Nyirenda for supporting us with approaching potential key research stakeholders. The author also wishes to thank members of the Global Health Bioethics Network, supported by a Wellcome Trust Strategic Award (096527), for their input.

**Author contributions**

BMK: designed the study, developed data collection tools, collected data, conducted analysis, writing—original, drafts and final manuscript. DN: input on study design and supported data collection. ND: Supervision, Conceptualization, Validation, Methodology, Writing- critical review of all drafts. JS: Supervision, Conceptualization, Methodology, Validation, Resources, Writing—a critical review of all drafts. The authors read and approved the final manuscript.

**Funding**

The Global Health Bioethics Network (GHBN) supported this research with a Wellcome Trust Strategic Award (096527) managed by the London School of Hygiene and Tropical Medicine. The funding agency had no part in the study's design, data collection, analysis, interpretation, or manuscript preparation.

**Availability of data and materials**

The datasets generated and analysed during the current study are not publicly available owing to privacy concerns; however, they are available from the corresponding author upon reasonable request.

## Declarations

**Ethical approval and consent to participate**

The study was performed in accordance with the relevant guidelines and regulations. Ethical approval was obtained from the Malawi College of Medicine Research Ethics Committee—CoMREC Ethics (Ref: P.01/21/3242); and the London School of Hygiene and Tropical Medicine—LSHTM Ethics (Ref: 22890). Institutional permissions were sought from all participating institutions, and their letters of support were submitted to the CoMREC as part of submissions for study ethics review. We also sought permission from the principal investigators at MLW and the KUHeS, prior to the interviews, to speak to study participants in their respective selected studies. Additionally, the research governance approval was obtained from the MLW Clinical Research Support Unit. Informed consent was obtained from all participants who participated in this study.

**Consent for publication**

Not applicable.

**Competing interests**
The authors declare that they have no competing interests.

Received: 5 November 2022 Accepted: 31 January 2023
Published online: 10 February 2023

**References**

1. Nkosi B, Seeley J, Chimbindi N, Zuma T, Kelley M, Shahmanesh M. Managing ancillary care in resource-constrained settings: dilemmas faced by frontline HIV prevention researchers in a rural area in South Africa. Int Health. 2020;12(6):543–50. https://doi.org/10.1093/inthealth/ihaa045.
2. Belsky L, Richardson H. Medical researchers' ancillary clinical care responsibilities. BMJ. 2004;328(7454):1494–6.
3. Richardson HS, Belsky L. The ancillary-care responsibilities of medical researchers: an ethical framework for thinking about the clinical care that researchers owe their subjects. Hastings Cent Rep. 2004;34(1):25–33.
4. Richardson HS. Moral entanglements: the ancillary-care obligations of medical researchers. Oxford University Press; 2012.
5. International Conference on Harmonisation-Guideline for Good Clinical Practice. In: International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use. 1996.
6. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. Jama. 2013;310(20):2191-4.
7. Council for International Organisations of Medical Sciences. International ethical guidelines for health-related research involving humans. In: International Ethical Guidelines for Health-Related Research Involving Humans. 2017.
8. Olson NW. Medical researchers' ancillary care obligations: the relationship-based approach. Bioethics. 2016;30(5):317–24. https://doi.org/10.1111/bioe.12212.
9. World Bank and WHO. Half the world lacks access to essential health services–UN-backed report: @UN_News_Centre2017 2017–12–13.
10. The World Bank. Poverty and Health. The World Bank, Washington D.C. 2014. https://www.worldbank.org/en/topic/health/brief/poverty-health. Accessed 07/09/2022 2022.
11. Averill C, Marriott A. Universal health coverage: why health insurance schemes are leaving the poor behind. Oxfam International; 2013.
12. Abiiro GA, Mbera GB, De Allegri M. Gaps in universal health coverage in Malawi: a qualitative study in rural communities. BMC Health Serv Res. 2014;14(1):1–10.
13. Hooley B, Afriyie DO, Fink G, Tediosi F. Health insurance coverage in low-income and middle-income countries: progress made to date and related changes in private and public health expenditure. BMJ Glob Health. 2022. https://doi.org/10.1136/bmjgh-2022-008722.
14. Boutayeb A. The burden of communicable and non-communicable diseases in developing countries. In: Handbook of disease burdens and quality of life measures. 2010;531.
15. Boutayeb A, Boutayeb S. The burden of non communicable diseases in developing countries. Int J Equity Health. 2005;4(1):1–8.
16. Kapumba BM, Desmond N, Seeley J. What do we know about ancillary care practices in East and Southern Africa? A systematic review and meta-synthesis. Wellcome Open Res. 2021;6:164.
17. Kapumba BM, Desmond N, Seeley J. A chronological discourse analysis of ancillary care provision in guidance documents for research conduct in the global south. BMC Med Ethics. 2022;23(1):51. https://doi.org/10.1186/s12910-022-00789-6.
18. Krubiner CB, Syed RH, Merritt MW. Health researcher's ancillary-care responsibilities in low-resource settings: the landscape of institutional guidance. IRB Ethics Hum Res. 2015;37(3):12–9.
19. Participants in 2006 Georgetown University Workshop on Ancillary-Care Obligations of Medical Researchers Working in Developing Countries. The ancillary-care obligations of medical researchers working in developing countries. PLoS Med. 2008;5(5):e90. doi:https://doi.org/10.1371/journal.pmed.0050090.
20. Tshikala T, Mupenda B, Dimany P, Malonga A, Ilunga V, Rennie S. Engaging with research ethics in central Francophone Africa: reflections on a workshop about ancillary care. Philos Ethics Hum Med. 2012;7:10. https://doi.org/10.1186/1747-5341-7-10.
21. Merritt M, Katz J, Mojtabai R, West KP Jr. Referral of research participants for ancillary care in community-based public health intervention research: a guiding framework. Public Health Ethics. 2016;9(1):104–20.
22. Malawi Government. The Malawi Integrated Household Survey. Malawi: National Statistical Office2020 November, 2020.
23. Government of Malawi Ministry of Health. Malawi Health Sector Strategic Plan II 2017–2022: Towards Universal Health Coverage. Government of Malawi Ministry of Health Lilongwe, Malawi; 2017.
24. ten Have H, Gordijn B. Handbook of global bioethics. Netherlands: Springer; 2014.
25. National policy measures and requirements for the imrpovement of health research coordination in Malawi. 2012.
26. National Commission for Science and Technology. Circular on Human Biology samples and participants recompense in research involving human subject. In: Ministry of Health and Population, editor; 2019.
27. Srivastava P, Hopwood N. A practical iterative framework for qualitative data analysis. Int J Qual Methods. 2009;8(1):76–84.
28. Evans SC, Roberts MC, Keeley JW, Blossom JB, Amaro CM, Garcia AM, et al. Vignette methodologies for studying clinicians' decision-making: Validity, utility, and application in ICD-11 field studies. Int J Clin Health Psychol. 2015;15(2):160–70. https://doi.org/10.1016/j.ijchp.2014.12.001.
29. Mfutso-Bengo J, Ndebele P, Jumbe V, Mkunthi M, Masiye F, Molyneux S, et al. Why do individuals agree to enrol in clinical trials? A qualitative study of health research participation in Blantyre. Malawi Malawi Med J. 2008;20(2):37–41. https://doi.org/10.4314/mmj.v20i2.10898.
30. Guest G, Bunce A, Johnson L. How many interviews are enough? An experiment with data saturation and variability. Field Methods. 2006;18(1):59–82.
31. Roller M. Designing a quality in-depth interview study: how many interviews are enough. Recuperado el. 2012;10.
32. Northcutt N, McCoy D. Interactive qualitative analysis: a systems method for qualitative research. Sage; 2004.
33. Q.S.R. International Pty Ltd. NVivo: Qualitative Data Analysis Software for Researchers | released in March 2020. 2022. https://www.qsrinternational.com/nvivo-qualitative-data-analysis-software/home?_ga=2.211552405.1443535480.1662730467-1193225661.1662730467. Accessed 07/09/2022 2011.
34. Nyirenda D, Sariola S, Kingori P, Squire B, Bandawe C, Parker M, et al. Structural coercion in the context of community engagement in global health research conducted in a low resource setting in Africa. BMC Med Ethics. 2020;21(1):1–10.
35. Richardson HS. Incidental findings and ancillary-care obligations. J Law Med Ethics. 2008;36(2):256–70. https://doi.org/10.1111/j.1748-720X.2008.00268.x.
36. Lidz CW, Appelbaum PS. The therapeutic misconception: problems and solutions. Medical care. 2002:V55-V63.
37. Lawrence DS, Ssali A, Moshashane N, Nabaggala G, Maphane L, Harrison TS, et al. Decision making in a clinical trial for a life-threatening illness: therapeutic expectation, not misconception. Soc Sci Med. 2022;305:115082. https://doi.org/10.1016/j.socscimed.2022.115082.
38. Ulrich MR, editor. Researchers Without Borders?: Limiting Obligations of Ancillary Care Through the Rescue Model. Limiting Obligations of Ancillary Care Through the Rescue Model (January 31, 2011). Vanderbilt Law School Health Law and Public Policy Forum; 2011.
39. Pratt B, Zion D, Lwin KM, Cheah PY, Nosten F, Loff B. Ancillary care: from theory to practice in international clinical research. Public Health Ethics. 2013;6(2):154–69. https://doi.org/10.1093/phe/pht015.
40. Bhatt A. Evolution of clinical research: a history before and beyond james lind. Perspect Clin Res. 2010;1(1):6–10.
41. Gostin LO, Levit LA, Nass SJ. Beyond the HIPAA privacy rule: enhancing privacy, improving health through research. 2009.
42. Hyder AA, Merritt MW. Ancillary care for public health research in developing countries. JAMA. 2009;302(4):429–31. https://doi.org/10.1001/jama.2009.1072.
43. Slack CM. Ancillary care in South African HIV vaccine trials: addressing needs, drafting protocols, and engaging community. J Empir Res Hum Res Ethics. 2014;9(1):83–95. https://doi.org/10.1525/jer.2014.9.1.83.
44. Metz T. Ancillary care obligations in light of an African bioethic: From entrustment to communion. Theor Med Bioeth. 2017;38(2):111–26.

45. Appelbaum PS, Anatchkova M, Albert K, Dunn LB, Lidz CW. Therapeutic misconception in research subjects: development and validation of a measure. Clin Trials. 2012;9(6):748–61. https://doi.org/10.1177/1740774512456455.
46. Sacristán JA, Aguarón A, Avendaño-Solá C, Garrido P, Carrión J, Gutiérrez A, et al. Patient involvement in clinical research: why, when, and how. Patient Prefer Adherence. 2016;10:631–40. https://doi.org/10.2147/ppa.S104259.
47. Nass SJ, Levit LA, Gostin LO. The value, importance, and oversight of health research. Beyond the HIPAA privacy rule: enhancing privacy, improving health through research. National Academies Press (US); 2009.
48. Jacobson N, Krupp A, Bowers BJ. Planning for ancillary care provision: lessons from the developing world. J Empir Res Hum Res Ethics. 2016;11(2):129–34. https://doi.org/10.1177/1556264616637961.
49. Taylor HA, Merritt MW, Mullany LC. Ancillary care in public health intervention research in low-resource settings: researchers' practices and decision-making. J Empir Res Hum Res Ethics. 2011;6(3):73–81. https://doi.org/10.1525/jer.2011.6.3.73.
50. Evans D, Evans M. A decent proposal. Chichester: Wiley; 1996.
51. Sherratt TN, Roberts G, Kassen R. Evolutionary stable investment in products that confer both an individual benefit and a public good. Front Biosci. 2009;14(12):4557–64. https://doi.org/10.2741/3548.
52. O'Keefe CM, Rubin DB. Individual privacy versus public good: protecting confidentiality in health research. Stat Med. 2015;34(23):3081–103.
53. Russo F. What is the CSR's focus in healthcare? J Bus Ethics. 2016;134(2):323–34. https://doi.org/10.1007/s10551-014-2430-2.
54. Merritt M, Grady C. Reciprocity and post-trial access for participants in antiretroviral therapy trials. AIDS. 2006;20(14):1791–4.
55. Doval DC, Shirali R, Sinha R. Post-trial access to treatment for patients participating in clinical trials. Perspect Clin Res. 2015;6(2):82.
56. Nkosi B, Van Nuil JI, Nyirenda D, Chi PC, Schneiders ML. 'Labouring' on the frontlines of global health research: mapping challenges experienced by frontline workers in Africa and Asia. Glob Public Health. 2022. https://doi.org/10.1080/17441692.2022.2124300.


## Publisher's Note

**Chapter summary**

This paper has demonstrated that in the context of inadequate healthcare services or limited access to medical care, ancillary care has the potential to provide research participants with access to care that addresses their unmet health needs. When speaking with various research stakeholders about the hypothetical willingness of individuals to participate in health-related research, I found that it was extremely common for them to mention access to healthcare as the primary motivation. Many such individuals need care which is otherwise unavailable in the public health system or, if it is available at a private health institution, the services are unaffordable for the average Malawian. Multiple implications of ancillary care for health-related research have been outlined in the paper. However, there are also concerns that must be addressed properly, such as undue inducement and structural coercion.

Reflecting on the analysis of the different ethical positions that the participants adopted in this study, it became evident that the diverse ethical stances significantly influenced the specific comments provided by the participants. The range of perspectives expressed by the research stakeholders highlighted their varying beliefs, values, and priorities concerning ancillary care in the context of health-related research in the global south. Some participants expressed the need for clear and comprehensive ethical guidance to address the challenges posed by ancillary care in research settings, while others emphasized the importance of cultural sensitivity and local contexts in shaping ethical considerations. The analysis brought attention to the complexity of ethical decision-making surrounding ancillary care and underscored the necessity of context-specific and inclusive approaches to address the diverse concerns and needs of research stakeholders in the global south, particularly in countries like Malawi. The insights gained from this analysis contribute to a more comprehensive understanding of the ethical landscape surrounding ancillary care in the region and serve as a foundation for developing ethical frameworks that prioritize both research integrity and the well-being of participants.

From a wider perspective, the findings show that ancillary care should address the public good in addition to benefiting the individual participant. Chapter 7 draws on the insights from Chapters 4 to

6 to highlight the implications of this thesis for health-related research ethics and ancillary care policy and practice.

## Chapter 8. Discussion

### Introduction

In this thesis, my aim was to thoroughly examine and analyze various ethical dimensions related to the practice of ancillary care in RCS. The literature review brought to light a significant research gap, as there is a lack of comprehensive information and understanding regarding the ethical considerations that underlie the provision of ancillary care, particularly within RCS contexts. Although some studies have touched on certain aspects of ancillary care ethics, a comprehensive exploration of the ethical dimensions shaping its practice in RCS remains limited. Additionally, the perspectives of research stakeholders, including healthcare providers, researchers, and research participants, have not been extensively investigated in the existing literature, leaving an important gap in our understanding of their experiences and viewpoints on ancillary care. This study aims to address this research gap by conducting a detailed analysis of the ethical aspects guiding ancillary care provision, offering valuable insights into the complexities and challenges of ethical practices within RCS contexts. By filling this gap, the thesis seeks to contribute to the advancement of ethical standards and the enhancement of ancillary care practices in research settings, particularly in resource-constrained regions of the global south like Malawi. This study, therefore, was conducted to start documenting ethical principles for ancillary care considerations during health-related research conducted in RCS. Qualitative approaches were used, and the design permitted the development of an integrated set of concepts that provided a thorough theoretical explanation of the ethical practices and approaches that can be used for ancillary care consideration. Additionally, the study's exploration of ancillary care practices in a post-colonial context raises critical questions about power dynamics, cultural considerations, and the influence of historical legacies on research practices. By engaging with decolonisation, the thesis encourages researchers to critically examine their roles and responsibilities in promoting ethical research conduct that respects the autonomy and dignity of participants. The findings contribute to the ongoing debates within bioethics and research ethics, advocating for more inclusive and

culturally sensitive approaches to ancillary care, while also underscoring the importance of addressing historical injustices and power imbalances in research settings.

This chapter summarises the key findings from this thesis, discusses how they add to the current understanding of ancillary care during health-related research conducted in RCS, highlights the study's strengths and limitations, and provides an overall conclusion with recommendations for future research, development of specific ancillary care guidelines, and change in ancillary care practice. The chapter begins by setting out the key findings on the current practice of ancillary care and the implications for health-related research conducted in RCS. Then, reflections are presented on how the conceptual framework presented in Chapter 2 enabled the development of my theoretical and empirical understanding of how ancillary care impacts research volunteers and how that relates to the ethics surrounding the provision of ancillary care in health-related research in RCS. I conclude by discussing how this research contributes to the knowledge base regarding the inclusion of ancillary care in ethics guidelines for research in RCS and make recommendations for further research and practice.

**Summary of study findings**

I described the complexities of ancillary care in Chapter 2, as well as the many factors that contribute to those complexities when ancillary care is provided in RCS, such as Malawi. Some of these factors include the limited availability of healthcare services, a lack of standard guidance on how researchers may provide ancillary care and what they may provide, and the ethical concerns surrounding the potential for undue inducement and structural coercion associated with ancillary care. In addition, other factors, as highlighted in the conceptual framework, directly affect the research participant in RCS; for example, their level of vulnerability, which links to their dependency on the researcher, and the depth of the established relationship between the researcher and the participant. These factors place pressure on health-related researchers in RCS and make decisions around the provision of ancillary care more ethically challenging. However, medical researchers also face additional

challenges that limit their capacity to consider decisions on ancillary-care provision solely from a moral perspective, such as a limited research budget to cover ancillary care.

The systematic review and meta-synthesis in Chapter 5, which sought to determine the extent to which ancillary care is provided in East and Southern Africa and examine the ethical justifications researchers provide for their views on ancillary care obligations, highlighted the evidence on the provision of ancillary care during health-related research in East and Southern Africa. The majority of studies included in the systematic review and meta-synthesis were qualitative studies, and they reported that researchers provide some care to their study participants during health-related research. However, studies generally reported on care provided to study participants during clinical trials or health-related research but did not explicitly refer to the distinction between study-related and ancillary care – it was difficult to differentiate. Papers from clinical trials were excluded from this systematic review and meta-synthesis because they lacked information on the care provided to study participants during the research. In Chapter 6, I presented the findings from a review of the language on ancillary care in 34 ethics guidance documents, which aimed at gaining an overview of what was given in terms of guidance for ancillary care. I found that the language used in the guidance documents did not explicitly describe ancillary care. To further understand the practices of ancillary care in RCS, I also used data collected from 45 key research stakeholders involved in health-related research in Malawi, to explore their views on and experiences of ancillary care in health-related research. The findings from this research are presented in Chapter 7. In the in-depth qualitative study with key research stakeholders, I found that there was limited ethics guidance, and researchers provided ancillary care to their study participants on an ad hoc basis.

The results of this thesis can be summarised in four key findings, as presented in Table 4: 1) The practices of ancillary care were difficult to determine because there is a general misconception of what ancillary care is and should be; it was challenging to distinguish between what was considered ancillary care and what was not. However, ancillary care in the

form of referral, provision of direct care, and provision of non-medical support was reported in some of the studies included in the systematic review and meta-synthesis study. 2) The language that describes ancillary care in ethics guidance documents has changed over time; for example, information on ancillary care has become clear in recent guidelines and policy documents. However, actual guidance for ancillary care is not yet explicit enough to guide research stakeholders' practice in RCS. 3) Ancillary care has potential healthcare benefits for research participants and the potential to benefit the general public if it extends to supporting the public health system in settings where healthcare services are limited or unavailable. 4) There are concerns that ancillary care could unduly induce people to participate in research without them making a fully informed decision about their participation, as well as there being a risk of exploitation of vulnerable populations in RCS. Below, I discuss my findings in more detail, set out according to the objectives of this study.

Table 4 Summary of thesis objectives and key findings

| Thesis objective | Key finding |
|---|---|
| **1.** To describe the provision and explore the practices relating to ancillary care in health-related research in east and southern Africa over the last decade. | • Some researchers take the initiative to consider providing ancillary care to their study participants.<br>• For many scholars, the obligation to provide ancillary care is justified by the duty of justice and entrustment. However, to others, the ancillary care obligation is one means of helping participants with limited access to healthcare in RCS to access the needed care. |
| **2.** To examine the practical features that have underpinned the evolution of the topic of ancillary care in health-related research ethics guidance documents. | • There is an absence of explicit ethics guidance for ancillary care in research guidance documents, making it difficult for researchers to decide how to plan for and provide ancillary care, and what care to provide.<br>• This also leave an interpretive gap of what to be considered as ethical ancillary care, particularly in the global south. |
| **3.** To investigate the experiences and perspectives of research stakeholders on the process, practice, and expectations of research participants regarding the provision of ancillary care.<br>**4.** To determine how the values and practices beyond perceived ancillary care obligations of medical researchers may need to be balanced in decisions about study demands and ethical requirements. | • Ancillary care has the potential to improve the health and well-being of study participants if they are given the opportunity to access the healthcare services that are not provided by the local public health system.<br>• Tension exists between what researchers can offer as ancillary care for participants' healthcare needs and their obligations linked to the ethics of conducting health-related research, which include providing care for study-related injury.<br>• There is a need to consider extending ancillary care to include activities or approaches that aim at strengthening the health system so that the care can benefit many. |

**Objective 1: To describe the provision and explore the practices relating to ancillary care in health-related research in east and southern Africa over the last decade.**

The systematic review and meta-synthesis presented in Chapter 5 highlighted that evidence on the practices of ancillary care during health-related research conducted in RCS is lacking and that the approaches used by international researchers in considering the provision of ancillary care are not standardised and are not supported by consistent guidelines for ethical practice. Although there has been no direct implementation of, or ethical guidance for, ancillary care, the obligation of the researchers to ensure the safety of their participants could be taken to imply that ancillary-care benefits should be considered in RCS because participants may have multiple additional healthcare needs as presented in chapter 2 and 3. Or, it could be argued that when participants decide to take part in a research study knowing that they have nothing to gain from the study itself (mostly based on what participants are told at the time of recruitment: that there are no direct benefits to individuals), the researchers owe some measure of ancillary care to the participants as a return for their act of altruism (Brownsword, 2010).

The findings of this study highlight that the provision of ancillary care should be considered in some circumstances. The key research stakeholders in this study strongly emphasised that a case-by-case approach would help the researchers avoid being the sole healthcare providers in settings where such services are unavailable. The provision of ancillary care on a case-by-case basis, as outlined in the commentary to Guideline 6 of the International Ethical Guidelines set out by the CIOMS (2016 pg. 20) indicates that in the conduct of health-related research, a researcher can plan for the provision of ancillary care in partnership with the local public healthcare system and following a recommendation from the REC:

> *"How to provide ancillary care in this situation is a complex issue, and decisions will need to be made on a case-by-case basis following discussion with research ethics committees, clinicians, researchers and representatives of government and health authorities in the host country. Accordingly, before research begins, an agreement*

> *must be reached on how to provide care to participants who already have, or who develop, diseases or conditions other than those being studied (for example, whether care will be provided for health conditions that are readily treated in the local health-care system)"* (CIOMS, 2016 pg. 22).

However, such wording does not provide researchers with precise ethical guidance on how to approach ancillary care, particularly in RCS, where ancillary care needs may be identified among many study participants. Although the 2016 CIOMS recommendations stipulate that researchers should take ancillary care decisions on a case-by-case basis, such referrals would need to be made to institutions operating in the public healthcare system. This type of guidance does not account for all of the obstacles encountered by individual study participants (or potential participants) in RCS or for the limitations of many public healthcare systems. I suggest that further guidance should be added to direct researchers on how to address such challenges, as opposed to leaving decisions to be made on a case-by-case basis. I contend that guidelines should be developed to move beyond individual, and somewhat inconsistent, responses to the provision of ancillary care and that we should instead move towards developing guidance for systematic ethical practice in relation to ancillary care. Such guidance could include how sponsors and researchers can support the participant when the ancillary care needed is not available in the public health system. Based on the arguments that are presented in this thesis, I believe that none of the research rights of study participants that are presented in current international ethics guidelines (World Medical Association, 2013, CIOMS, 2016, CIOMS, 2021) would run counter to the basic concept of background needs for the provision of ancillary care when health-related research is being conducted in RCS. In this case, the real question concerns the conditions that the international and local research regulatory bodies would set for the recognition of background-positive obligations of medical researchers to address the ancillary care needs of their participants. I suggest that the conditions set would reflect the research stakeholders' (researcher, sponsors, funder, and RECs) understanding and application of three considerations.

- First, consideration should be given to developing international ethics guidelines for ancillary care while making sure that they apply to context-specific (based on the setting where the study takes place, funding source, and study type) needs. The guidelines should move beyond a case-by-case approach and consider, on a more comprehensive level, any and all kinds of positive ancillary care needs participants might have. This is particularly important in contexts where researchers are likely to encounter participants with several unmet health needs, owing to factors such as limited availability of healthcare services provided by the public healthcare system and high disease burden.
- Second, consideration should be given to what constitutes "*reasonable ancillary care*". How much ancillary care could the researchers provide to their study participants without introducing further ethical concerns about undue inducement? Is this based on the standard of care provided by the public health system? Can the researcher provide care that goes beyond that standard of care? If the participant invited to join the project volunteers to participate in research that is likely to benefit people globally, and if the researcher has the capacity to provide care that exceeds the standard of care available in the local context (perhaps that which is equivalent to the standard of care in the global north), I argue that this should not be considered to be unethical. Regarding this care as undue inducement would go against the ethical principles of beneficence and non-maleficence (World Medical Association, 2013), potentially leaving research participants in RCS with inadequate care or exacerbating existing health disparities and vulnerabilities (Khirikoekkong et al., 2020). Additionally, providing ancillary care at either the local or global north's standard may align with international ethical guidelines that prioritize promoting the well-being of research participants. Thus, delivering ancillary care equivalent to that standard should be seen as an ethical obligation rather than undue inducement, as it protects the dignity, rights, and welfare of research participants, fostering fair and ethical research practices. Perceiving ancillary care as

undue inducement could also undermine the equitable provision of healthcare and researchers' ethical obligations to safeguard their participants' health. Instead of dismissing it as undue inducement, ancillary care should be recognized as a critical aspect of ethical research practices in developing countries, ensuring participant well-being, and conducting research responsibly and ethically (Emanuel et al., 2005). The emphasis should be on aligning ancillary care with local healthcare standards and ensuring its responsible provision. I consider these questions by briefly drawing on decolonisation (Kwete et al., 2022, Barcham, 2022) as a current topic of debate. I consider ancillary care to be one of the key issues that should be raised and highlighted on the agenda driven by low-income communities who define the parameters for conducting health-related research, which may include public good or individual benefits. If we are moving towards a decolonialised approach to global health (Kwete et al., 2022, Ong'era et al., 2021), then ancillary care is a key concept for changing the dynamics of global health research practice.

- Third, the consideration for fairness and reciprocity, which demands that researchers should be responsible for assisting their study participants in the same manner that they assist researchers in achieving their study goals. This is because researchers rely on the assistance of participants to accomplish their research goals. In this respect, the provision of ancillary care is a way of addressing apparent imbalances in the benefit sharing resulting from health-related research (Sofaer, 2014).

Despite the lack of explicit ethical guidance for ancillary care, some researchers take the initiative to provide that care to their study participants. I found evidence of this through the studies included in the systematic review and meta-synthesis (Kapumba et al., 2021) as well as in the selected case studies at MLW (see Table 2 in Chapter 7). My findings highlight that medical researchers conducting their research in settings like Malawi, which has limited resources in the public health system to provide for the health needs of the population, acknowledge some ancillary care obligations, similar to those reported by the Participants in

the 2006 Georgetown University Workshop (2008). Some of the examples that research stakeholders mentioned in my study were having a study doctor to meet any additional health needs that participants may have or providing a psychosocial counsellor during HIV and tuberculosis studies to give counselling to study participants. This type of planning is part of the "*practical provisions*" one of the guidance points on ancillary care obligations which the Georgetown workshop participants advocated (Participants in the 2006 Georgetown University Workshop, 2008). However, in most of the studies conducted in Malawi and other RCS, ancillary care arrangements have tended to be ad hoc because there are no guidelines.

**Objective 2: To examine the practical features that have underpinned the evolution of the topic of ancillary care in health-related research ethics guidance documents.**

International and local guidelines and current best practices all indicate that the protection of research participants should be a primary focus for all researchers. In line with the framework presented in Chapter 2, it is well established that research ethics guidelines underpin and govern the ethical conduct of health-related research, with a particular focus on fostering the protection of research participants from harm and ensuring that they have given valid consent (World Medical Association, 2013, CIOMS, 2016). In addition, it is also meant to be critical of the welfare of the study participants (Slowther et al., 2006). However, the problem is finding ways to include the ancillary care obligations of researchers to their participants in the regulatory framework. When applying the concept of ancillary care, researchers must not only always consider what will be best for their research or focus only on achieving the study objectives but also consider what is best for the participants who make the research possible. These are often framed as the researchers' commitment to participants and society more broadly, invoking notions such as the public good or public interest. The concept of promoting public good is discussed by Hyder and Merritt (2009), who argue that a community or society has collective unmet health needs, which are best addressed by services offered at the group level. In this case, that would mean improving ancillary care through, among other things, strengthening the public healthcare system in RCS.

In this study, I have traced the emergence of language or text in ethics guidance documents that describes the provision of care to study participants, and how that has changed over time. The main purpose of doing a discourse analysis, presented in Chapter 6, was to track the availability of wording providing guidance for ancillary care, if any, from research ethics guidance documents. All policy and ethics documents that provide guidance for the conduct of health-related research were included in this study. I started by looking at ethics guidance from the Nuremburg Code (Nuremberg Code, 1947) and continued up to the most recent CIOMS guidelines (CIOMS, 2021).

I found that attention to ancillary care was scant in the documentation overall. The broad language utilised in existing ethics guidance documents was limited, as had been reported by the Participants in the 2006 Georgetown University Workshop (2008) and Krubiner et al. (2015). The Declaration of Helsinki, for example, contains broad guidance in general Principle 9: "*It is the duty of physicians who are involved in medical research to protect the life, health, dignity, integrity, right to self- determination, privacy, and confidentiality of personal information of research subjects*" (World Medical Association, 2013). The possibility that the duty to "protect life" might extend to ancillary care provision is not explored. Therefore, while these statements are meant to guide researchers on how they can protect the life of their participants, they do not explicitly describe how the researcher can or should address ancillary care demands.

I found that the language used to describe ancillary care interventions, both before and after the conceptualisation of ancillary care in 2004 (Belsky and Richardson, 2004), to be very broad, and it does not explicitly provide any guidance to medical researchers. For example, guidance documents use phrases such as "protection of study participant's well-being, rights, and health". The key phrases with some clear description of ancillary care started emerging in the CIOMS guidelines in 2002, where terms such as "morally praiseworthy" appear:

> *Although sponsors are, in general, not obliged to provide healthcare services beyond that which is necessary for the conduct of the research, it is* morally praiseworthy [my

emphasis] *to do so. Such services typically include treatment for diseases contracted in the course of the study. It might, for example, be agreed to treat cases of an infectious disease contracted during a trial of a vaccine designed to provide immunity to that disease, or to provide treatment of incidental conditions unrelated to the study* (CIOMS, 2002).

The context in which the phrase "morally praiseworthy" is used describes the grounds for ancillary care since it demonstrates that researchers are not morally required to provide ancillary care, but that if they do, it is especially commendable. One could argue that progress has been made towards this objective with the introduction of these terms, which is a result of the recognition that researchers must begin to view their participants holistically and consider meeting their ancillary care needs, even if they are not required to do so in order to make the study scientific valid or as a means of minimising study harm.

**Objective 3: To investigate the experiences and perspectives of research stakeholders on the process, practice, and expectations of research participants regarding the provision of ancillary care.**

***Ancillary care as an ethical issue***

The primary obligation of researchers, regardless of whether they conduct their research in higher-income settings or LMICs, is to ensure that the individuals who participate in their studies or trials are not harmed in any way. Within this general movement in ethical focus, there is consensus that researchers take full responsibility for protecting their study participants from study-related harm – as a moral wrong – and that such harm should be minimised at all costs (Emanuel et al., 2000). This is the case regardless of where the researchers are based. Ensuring that participants are not harmed may extend to addressing healthcare needs identified in the course of the research, which, if left unattended to, may cause harm. Such care may extend beyond study or trial focus, to encompass the ancillary-care requirements of the participants in their studies. However, there is a lack of consensus as to who has the responsibility to support (for example, with referral) or provide care to

participants who have a medical condition that is beyond the scope of the research if such support or care does not contribute in any way to the research itself. In other words, this condition is not relevant or related to the research in any way (Belsky and Richardson, 2004). Nevertheless, translating normative ethics arguments into practical ethics guidance and practice raises significant ethical dilemmas in health-related research globally, and these challenges might often be heightened where the background context for health-related research is RCS.

The CIOMS (2021) recognises that many of the decisions about the conduct of health-related research and the consideration of ancillary care can be determined by the independent oversight of the local RECs. However, the findings from this study have revealed that in Malawi (the case study country), there are no explicit guidelines on the provision of ancillary care. The lack of detailed and explicit criteria on how researchers might respond to the ancillary care needs of their participants was identified as a stumbling block for RECs and researchers when making decisions regarding ancillary care considerations. Based on the findings from this study, I support the argument that it is challenging for REC members to make any meaningful decision on the need for ancillary care when reviewing research protocols. I therefore suggest, as highlighted in Chapter 7, that regionally informed, precise, and applicable ancillary care guidelines in Malawi that might also be generally useful for researchers, RECs and other stakeholders in RCS should be developed. This would enable RECs to make ancillary care decisions and provide further appropriate guidance to researchers.

The power given to the local RECs because of their independent oversight means that, with guidance, they are well placed to advise on ancillary care needs. The members of a local REC with their knowledge of the local context, should be able to determine the level or extent of ancillary care that can be provided, keeping in mind issues of structural coercion, undue inducement, and the susceptibility to exploitation of vulnerable populations. This argument is supported by Henrikson et al. (2019), who claim that REC members should be familiar with institutional culture and sensitive to the needs of the local study population. In every setting,

RECs serve as the bedrock for ethical and regulatory oversight of all domestic/local research involving human participants. They are primarily responsible for ensuring that human participant research is conducted in accordance with local and international standards and guidelines. However, it is apparent from my findings that the absence of explicit guidance for ancillary care has meant that it is seldom addressed in research protocols or in the REC members' scrutiny of the research plans. Some members of the REC and lead investigators also highlighted that the provision of ancillary care might have been widely incorporated into ethical research practice if guidelines had been explicit following Belsky and Richardson's (2004) conceptualisation of the topic.

***Protecting study participants from exploitation***

The potential to exploit study participants has been widely discussed with respect to research in RCS (Dal-Ré et al., 2016, Emanuel et al., 2004, Singh et al., 2017). In particular, it is recognised that individuals and host communities in RCS may face the risks and burdens of health-related research or clinical trials while the benefits go to those living in higher-income nations (Hawkins and Emanuel, 2008, Benatar, 2000). According to Wertheimer (2008), exploitation is when the research sponsor or researcher takes *unfair advantage* of the research participant, a situation which could be exacerbated by their vulnerability. When used in this context, the word "exploitation" refers to behaviour that is transaction-specific and is concerned with the results of individual transactions. This means that an individual may be exploited even though she or he consents to participate in research. In RCS, there is an increased chance that the majority of people who volunteer to participate in health-related research will face the risks and burdens of research participation while the benefits accrue to others if the learnings from the study are implemented within better resourced settings, even within the same country or region. The provision of ancillary care calls attention to this concern and is regarded as a possible way of addressing exploitation in health-related research.

As I detail in Chapter 3, healthcare provision is challenging in Malawi, largely because the population is predominantly rural (80%), and availability of and access to medical care

services are usually limited in rural areas, making at least 15% of Malawians unable to meet their medical-healthcare needs (Msokwa, 2021). This indicates that the number of individuals with unmet healthcare needs is large, and as a result researchers are likely to be confronted with the need to provide for ancillary care if an individual decides to participate in a study.

**Objective 4: To determine how the values and practices beyond perceived ancillary care obligations of medical researchers may need to be balanced in decisions about study demands and ethical requirements.**

Through exploring practical ethical issues with research stakeholders in this study, I provide a case study of critical ethical reflexivity in health-related research about what it takes for the researcher to make decisions about ancillary care while ensuring study objectives are met. While this thesis highlights the limitations of what RECs and researchers can do to resolve ethical issues that may arise in health-related research as a result of limited guidance on ancillary care, I contend that RECs play an essential role in determining whether what some researchers or research institutions propose to provide as ancillary care is appropriate within particular contexts. Specifically, RECs must ensure that context is thoroughly addressed during their deliberations regarding the approval of studies that may require researchers to provide ancillary care to study participants, as well as determining the levels of ancillary care to be provided without raising ethical concerns. The level or proportionality of ancillary care may refer to the principle of providing care that is commensurate with the needs and risks faced by research participants in a study. In practice, this means tailoring the level of ancillary care to the specific context and requirements of each research project. For instance, in low-risk studies with minimal health-related interventions, ancillary care may involve providing basic medical monitoring and support to address any unforeseen health issues that arise during the study. On the other hand, in high-risk trials or studies involving vulnerable populations, proportionality would entail ensuring more comprehensive ancillary care provisions, such as access to specialised medical facilities, timely treatment, and ongoing healthcare support. Striking a balance between the intensity of ancillary care and the nature

of the research helps protect participant well-being without creating undue inducements or unwarranted burdens or exploitation as reflected in the conceptual framework presented in chapter 2. RECs responsibility of determining the proportionality of ancillary care ensures that participants receive appropriate care without diverting excessive resources from the primary research objectives. In addition to planned ancillary care, RECs must also be attentive to a proposal's ability to demonstrate that the researcher has thought through the strategies they will employ and the local support structures they will draw on when having to deal with inevitable unforeseen ethical challenges in the field.

The findings from this study have revealed that the majority of researchers have limited capacity to provide ancillary care to their participants because of restrictions in their budget. Researchers usually have to make sure that priority is given to implementing the study activities in order to fulfil the requirements and regulations for research funding. This explains the possible reason why most of the researchers do not include explicit plans for ancillary care. Concerning the absence of ancillary care plans in study protocols, stakeholders stressed that, despite these restrictions, they still provide some ancillary care where necessary. They based their argument on the fact that there are some ancillary care needs identified among participants that do not require a huge budget. Therefore, ad hoc measures are taken to support their participants with ancillary care. However, such ad hoc arrangements could lead to inconsistencies in the provision of ancillary care, potentially affecting the quality and equity of care received by participants. The findings emphasize the urgent need for formal guidance and ethical frameworks to address the ad hoc nature of ancillary care provision and ensure that researchers follow established ethical standards to protect participant well-being and uphold research integrity in the global south. Hyder and Merritt (2009) propose a ten-step process for consideration of ancillary care. Two of these steps relate to the issues under discussion here: 1) that researchers must understand the range of options that might be considered as ancillary care; and 2) that researchers must clearly define the package of

ancillary care that will be offered, with their rationale resulting from deliberative processes carried out with stakeholders at the local level (the context where the study will be conducted).

Relating these ideas to the conceptual framework presented in Chapter 2, I argue that all factors must be considered in order to balance the study demands with the ancillary care needs of study participants. For example, even if the research funding is limited to activities directly relevant to the study objective or the provision of care related to the study, researchers must demonstrate fairness to their participants by meeting their ancillary care needs. The most significant factors to consider here are achieving health justice (Hooper, 2010, Pratt and Loff, 2014) and avoiding exploiting vulnerable participants (Nordentoft and Kappel, 2011).

**Controversy around the provision of ancillary care and potential responses**

The values associated with the provision of ancillary care identified in this thesis offer the opportunity to understand better common ethical tensions arising from the provision of ancillary care to study participants during health-related research. In particular these values shed light on problematic issues with research ethics guidelines and policies governing health-related research. Some, including research stakeholders who participated in this study, argue that providing ancillary care benefits to those in RCS who lack access to healthcare services may inadvertently encourage them to participate in research, thus acting as a form of undue inducement. As outlined in Chapter 2, undue inducement arises when the benefits offered to potential study participants are sufficiently large that they convince people to enrol in a study that is manifestly against their best interests (Emanuel et al., 2005, Largent et al., 2013). Recognising that this concern was also raised by the research stakeholders who participated in the case study research in Malawi for this thesis, the most effective response to concerns regarding potential undue inducement is to ensure that the level of ancillary care to be provided should be commensurate with risks and burdens posed by the study as well as recognising the fact that the majority of study participants in RCS are vulnerable as a result of poverty and have limited access to medical care. In addition, to address concerns about undue inducement without raising the potential for exploitation, RECs should ensure that the ancillary

care provided to study participants is equal to the standard of care provided in the local context and is not excessive. Importantly, REC guidance given to researchers should not attempt to address concerns regarding undue inducement by eliminating any potential benefits from planned ancillary care.

Still, others are concerned that providing ancillary care to study participants during health-related research will impose high costs on research sponsors. First, I believe it is important to address the potential for exploitation of the study participants, even if this may raise costs. The issue of ancillary care imposing heavy costs on health-related research was emphasised by the Participants in the 2006 Georgetown University Workshop (2008), who suggested that the level of ancillary care should be minimal in order to avoid an inhibitory effect and ethically unsound for the conduct of health-related research in RCS. However, Ulrich (2011) provides a justification for the cost of providing ancillary care with the duty-to-rescue model, which demands that a researcher can take action to help their participants regardless of the cost and if they have the capacity to do so. Second, I support the notion that sponsors of health-related research are obligated to provide benefits to participants proportional to the benefit that the sponsor derives from the participant's involvement in the study. This is well supported by the fair benefit framework, which argues that host communities and research participants should receive a fair level of benefits, given the extent to which they contribute to the study (El Setouhy et al., 2002). Hence, sponsors are never obligated to provide more benefits to participants than the sponsor derives from the participants' involvement. Third, as suggested in my findings, it can be feasible for sponsors to provide additional support or benefit to participants, especially as the expenses will likely be small compared to the cost of conducting clinical trials (Adams and Brantner, 2010, Jambo, 2022).

Finally, some may object that providing ancillary care only to those who participate in health-related research is unfair and will reduce pressure to provide all individuals with access to healthcare services. To address this concern, it is important that medical researchers ensure that participant selection is rigorously designed to avoid excluding individuals who may

potentially have additional health needs. However, this would still be challenging because of the incidental findings or positive ancillary care needs only identified during the study.

In addition, it is suggested that the provision of ancillary care should also focus on strengthening the healthcare system. Researchers would provide structural support to public healthcare facilities to promote public good rather than just focusing on care directed at an individual. Consequently, this idea maintains fairness for current participants while maintaining the essential objective of ensuring access for all individuals in the future.

**Implications of the study**

This thesis makes some significant contributions to our understanding of the practices regarding ancillary care in RCS, some of which can be linked to clear policy implications and recommendations. My original contribution to the understanding of ancillary care was the revelation that ancillary care practices in RCS are based on ad hoc arrangements, and this provided evidence that ancillary-care plans are not included in health-related research protocols. This was also related to the fact that ethics guidance for ancillary care is not explicitly included or defined in current international and local research ethics guidelines. The implications of these findings for policy and development of research ethics guidance lie in the need to recognise the heightened challenges to accessing healthcare that people face in RCS. One of the most notable aspects of the health situation in Malawi, which is similar to many other RCS, is the huge burden of health problems (malaria, tuberculosis, HIV/AIDS and non-communicable diseases, etc.), poor quality of life, and often, lack of access to even limited essential basic medical care services.

Globally, research funding from partner organisations is directed towards generating new knowledge through research and mainly comprises funding for research-related activities. However, there are increasing calls for research sponsors and funders to make research funding adaptable enough to include ancillary-care plans. For researchers who are sceptical or indifferent about ancillary care, perhaps because of the cost and the perceived burden on

the research team, if the provision of such care became a requirement of research funders or sponsors, and if because of this they were likely to secure adequate funding for ancillary care considerations, then such explicit funding guidance might override individual researcher decisions.

One of the findings from the stakeholder interviews was that funding for research has consistently been restricted to research-related activities, while the additional costs that may be incurred when researchers consider providing ancillary care to their study participants have been underestimated. Clearly, the research practice will benefit from specific guidance that calls for a focus on the research-specific context, such as that recently developed by CIOMS, which states that *"researchers have an ethical obligation to care for participants' health needs during research"* (CIOMS, 2021), even though this guidance does not specify whether the health needs include those of ancillary care to the study. An additional gap in the guidelines is the issue of when ancillary care may stop – Is it to be provided only during the study or also after the study is completed? When and for how long should ancillary care be considered?

The methodological implications of my recommendations on ancillary care are significant and vary depending on the type of study being conducted. For a clinical trial, ancillary care may involve offering additional medical support and interventions to research participants to ensure their safety and well-being throughout the study. This can have implications on the trial's design, as researchers need to carefully consider how ancillary care provisions might impact the study outcomes and participant recruitment. In an observational study, ancillary care may focus more on providing health assessments and monitoring participants' health status without directly intervening in their treatment. This can affect data collection and analysis, as researchers must consider how ancillary care might influence the study variables and potential confounding factors. For a social science study, ancillary care may not involve direct medical interventions but could entail providing support services or resources to participants to address social or psychological needs. The methodological implications here lie in understanding the participants' broader well-being and how ancillary care might influence the study's outcomes

and interpretation of the results. Overall, the methodological implications of recommendations on ancillary care underscore the need for careful planning and consideration of how ancillary care aligns with the specific research objectives and the ethical principles guiding the study design.

**Research limitations and challenges**

This study had some limitations and challenges, so the findings should be interpreted carefully. In this section, I summarise these limitations and challenges, some of which have already been presented in Chapters 5, 6, and 7, and mainly centred around the methodology.

First, when recruiting research stakeholders, I learned that it was generally more challenging to recruit some potential participants, such as REC members, Ministry of Health officials, and officials from research-funding partner organisations, than it was to recruit frontline research staff and study participants. In retrospect, this is hardly surprising. Some key research stakeholders are generally motivated to participate in research relevant to their lived experience of a health condition or situation. In contrast, my research was, to some extent, detached from their lived experience but sought their views on the provision of and practices regarding ancillary care. Additionally, people had time constraints, so getting involved in my research while also attending to their significant day-to-day responsibilities was likely too much for some. Researchers clearly also face significant time pressures, but they had a more direct interest in my research, as they are obliged to improve the health of their participants to satisfy research funders such as the National Institute for Health and Care Research and Wellcome Trust. Regardless of the reasons, there was a representation of all the groups of research stakeholders interviewed. Regarding the officials from research-funding partner organisations, as indicated in Chapter 7, most of those who were approached for interviews and declined indicated that it was because they did not have information regarding ancillary care. However, in their response, two officials shared some documents they used as a guide on issues of ancillary care.

Second, the focus of the review is on ancillary-care provision to study participants and possibly family members, but it does not target populations of research or people from within the community where the study is being conducted. For example, some studies suggest that in RCS, narrowly focusing on participants and their immediate dependants can contribute to tensions in communities and rumours about ongoing research by those excluded from the research (Gikonyo et al., 2013, Angwenyi et al., 2014). On the other hand, it could also create some inequalities to healthcare access if care is only provided to study participants. Another element/concern is that providing ancillary care to participants rather than working within existing systems raises issues of sustainability once the study and ancillary care are withdrawn.

Third, the qualitative data collection within Malawi had an important limitation. The results mostly represent the perspectives of research stakeholders in Malawi, which may not reflect the full picture of the practice of ancillary care in settings with better healthcare delivery systems. However, I interviewed a diverse group of research stakeholders, which gives some confidence that I accessed the views of a range of different people, some of which reflect experience and knowledge from outside Malawi. In addition, the focus was to talk to stakeholders who could give views about LMICs with a constrained healthcare system.

## Conclusions and recommendations

### *Conclusions*

Considering all my findings and given the current discourses on decolonisation, ancillary care appears to be a key concept to reconsider if we are going to amend the way global health research is conducted. It is time to recognise and address the ancillary care needs of study participants during health-related research conducted in RCS, because of exposure to poverty and lack of access to healthcare services. However, providing ancillary care (fair benefits) to participants may be challenging precisely because most potential participants often lack access to healthcare services and have several additional health needs, and researchers cannot address them all. These findings have addressed some of the questions about the

extent to which ancillary care can and should, be made to serve healthcare purposes, and they suggest the need for further deliberation regarding any ethical obligation to provide ancillary care that focuses on promoting the public good over individual research participant benefit. It is increasingly suggested that the obligation to provide ancillary care should extend to helping people who are not participating in the research, such as relatives of the participants, and to supporting the health facilities where the research is conducted. I propose that research ethics regulators and interested stakeholders, including research funders and sponsors, should revise current research ethics guidelines and regulatory policies to recognise and address issues of ancillary care. One possibility would be for the research funders or sponsors to provide targeted additional support to researchers conducting health-related research in RCS that could be used to address the ancillary care needs of their study participants when identified, even if it would be aiming at strengthening the healthcare system.

***Suggested principles of ancillary care consideration***

When conducting health-related research in RCS, ancillary care refers to the provision of additional medical services that are not directly related to the research study but are necessary for the well-being and safety of the research participants. This care is essential to ensure that participants receive appropriate medical attention and support beyond what is specifically required by the research protocol. Beyond ancillary care, the emphasis is placed on the need for standardised approaches and ethical guidelines in research practice in the global south to ensure the well-being of research participants and protect them from exploitation.

| **Principle** | **Description** |
|---|---|
| Solidarity | Solidarity, as a principle of ancillary care in health-related research conducted in resource-limited settings, emphasizes the importance of collective responsibility and support for research participants (Ba et al., 2021, Atuire and Hassoun, 2023). It involves recognising the disparities and challenges faced by individuals in resource-limited settings and taking |

| | |
|---|---|
| | actions to address them. Here are some examples of how solidarity can be practiced in ancillary care:<br><br>1. **Access to essential medications**: In RCS, participants may have limited access to essential medications or may not be able to afford them. As an expression of solidarity, researchers can ensure that participants have access to necessary medications beyond what is directly provided by the research study. This may involve collaborating with local healthcare providers or organizations to secure medication supplies or establishing a mechanism to provide subsidized or free medications.<br>2. **Diagnostic and treatment services**: Research participants may require diagnostic tests or specialized treatment for conditions unrelated to the research study but vital for their health. Solidarity entails arranging access to such services, which may not be available or affordable in resource-limited settings. For example, researchers can collaborate with local healthcare facilities or specialists to provide diagnostic services, such as imaging or laboratory tests, or refer participants to appropriate healthcare providers for treatment. |
| Justice | Justice, as a principle of ancillary care in health-related research conducted in RCS, focuses on ensuring fairness, equity, and the equitable distribution of benefits and burdens (Benatar, 2001). It emphasizes that all participants should have equal access to healthcare services, regardless of their socio-economic status or other factors. By upholding justice as a principle of ancillary care, researchers can ensure that access to healthcare is fair, |

| | |
|---|---|
| | equitable, and responsive to the needs of participants, promoting social justice and avoiding further exacerbation of health disparities in RCS. |
| Informed consent | Informed consent is a fundamental principle of ethical research. It ensures that research participants are fully informed about their rights, the nature of the research, and any associated risks and benefits (Beauchamp, 2011, World Medical Association, 2013). As a principle for ancillary care, informed consent requires researchers to go beyond routine information giving about the study. Researchers must clearly communicate the availability and types of care that will be provided, any associated costs, and how to access these services.<br><br>For example, researchers should include detailed information about ancillary care services in the informed consent document, including a clear description of the services, their purpose, and any financial implications for the participants. |
| Respect for human dignity | Respect for human dignity is a core principle of ancillary care in health-related research, regardless of the setting (World Medical Association, 2013, Council for International Organisations of Medical Sciences, 2017). It emphasizes treating research participants with dignity, autonomy, and respect for their inherent worth as human beings. In resource-limited settings, where there may be additional vulnerabilities and challenges, upholding this principle becomes even more critical. This principle recognizes that participants are not just subjects of research but individuals with health needs, emotions, and vulnerabilities. Researchers should foster a collaborative relationship with participants, engaging them in discussions about their health, involving them in care planning, and seeking their input in decisions regarding ancillary care services. |

| | |
|---|---|
| Clear ethics guidelines and policies | Clear ethics guidelines and policies are crucial in promoting ethical conduct and ensuring the appropriate provision of ancillary care in health-related research conducted in resource-limited settings. These guidelines and policies establish a framework that governs the ethical responsibilities of researchers and outlines the principles that guide the provision of ancillary care.<br>Ethics guidelines and policies should clearly state the following:<br>The definition of ancillary care: ethics guidelines and policies should provide a precise definition of ancillary care to ensure a shared understanding among researchers, participants, and relevant stakeholders. This definition helps distinguish between the primary research interventions and the additional care provided, guiding researchers in determining the scope and nature of ancillary care services. The definition suggested here is simplified version from Richardson (2012): as “healthcare services that are beyond the scope of the research study but are necessary for the well-being of research participants.”<br><br>Outlining the responsibilities and obligations: ethics guidelines and policies should outline the responsibilities and obligations of researchers regarding ancillary care provision. The guidelines should specify the duties of researchers in ensuring participants' health and well-being, as well as their obligations in providing appropriate access, quality, and coordination of ancillary care services. The guidelines should clearly suggest the extent of the researcher’s obligation to provide ancillary care.<br>Ethical review of ancillary care in protocols: Ethical review and oversight mechanisms should include specific considerations for the provision of ancillary care services. Researchers should include in their protocols |

| | |
|---|---|
| | detailed information for ancillary care, outlining the purpose, scope, qualifications of providers, resources needed, and any potential risks or benefits associated with the care. For example, researchers should describe the ethical justifications, mechanisms for quality assurance, and any safeguards in place to protect participants' well-being. |

By following these principles, researchers can strive to provide ethical and comprehensive ancillary care to participants in health-related research conducted in RCS, thus promoting the well-being and safety of the individuals involved.

The development of ethical frameworks and guidelines for ancillary care based on the above proposed principles should involve a collaborative and multidisciplinary approach. Various stakeholders play crucial roles in ensuring comprehensive and contextually relevant guidance. First and foremost, research ethics committees and institutional review boards are essential contributors, as they oversee the ethical conduct of research and can provide insights into the specific challenges and needs of RCS. Researchers and healthcare professionals with expertise in both health-related research and local healthcare practices should also be involved to ensure practicality and feasibility. Additionally, representatives from the communities and populations who will be impacted by ancillary care provisions should have a voice in the process to address concerns, preferences, and cultural considerations. Policymakers and government representatives can contribute to the alignment of guidelines with national healthcare policies and regulations. The international organizations and experts in research ethics can offer a broader perspective and global best practices. Lastly, the funders of research, a key part of the conceptual framework I used to guide this research, presented in Chapter 2, have a pivotal role and can significantly influence the ethical and practical considerations surrounding the provision of ancillary care. Funders play a crucial role in determining the scope and resources available for research studies, including provisions for ancillary care. Their decisions on funding allocations can impact the extent to which

researchers can provide ancillary care to study participants. In the majority of the RCS, where healthcare infrastructure and resources may be limited, funders can prioritise and support research projects that include ancillary care provisions to enhance participant well-being. By actively encouraging the inclusion of ancillary care in research proposals and funding applications, funders can foster a culture of ethical responsibility and commitment to participant welfare in the research community. Engaging this diverse group of stakeholders will help ensure that the developed ethical frameworks and guidelines are inclusive, contextually relevant, and responsive to the unique challenges and considerations of RCS but applicable globally as well.

***Recommendations for further research***

This research has been foundational in its examination of the practices regarding ancillary care in Malawi and other RCS in the global south. It builds on previous work from the ethics research community in using multiple data sources to assess the implementation of ancillary care in health-related research conducted in developing countries. However, there is a growing need to use data-prompted ancillary care to inform ethics guidelines and policy development for the consideration of ancillary care.

I concur with Merritt (2011), who states that "*developing sound guidance for ancillary care requires a normative model that includes a principled basis for determining that researchers have ancillary care obligations, specification of the content of these obligations, and the definition of the upper and lower limits of these obligations*". While many scholars as well as the findings presented in this thesis have highlighted the ethics of ancillary care obligation in health-related research conducted in RCS, determining the level of obligation remains an area of discussion especially in consideration with the context (funding, study setting) of research.

Although methodologically challenging, it would be very useful to conduct some longer-term studies which sought to monitor the implementation and use of ancillary care over the life of a research study to quantify the impact of ancillary care on key parameters such as on the

budget, to ascertain the cost incurred by ancillary care which would be used to justify inclusion in the budget within the grant application.

A final relatively narrow but important question that I identified after data collection was: how ready is the Malawi Ministry of Health or its partners to continue providing care supported through data-led ancillary care when research comes to an end? Some stakeholders were particularly concerned about the sustainability of ancillary care if there were no other partners to take up the responsibility. This came from the background that the public healthcare system is already overburdened. This could be addressed by conducting a participatory workshop with research stakeholders, including policymakers, in order to define the package of ancillary care that will be offered, with the rationale resulting from a deliberative process.

## References


ADAMS, C. P. & BRANTNER, V. V. 2010. Spending on new drug development 1. *Health Economics,* 19**,** 130-141.

AFRICAN INSTITUTE FOR DEVELOPEMENT POLICY 2016. Mid-term Review of the Performance of the National Health Research Agenda. Lilongwe: African Institute for Developement Policy.

ALBERTS, B. & SHINE, K. 1994. Scientists and the integrity of research. *Science,* 266**,** 1660.

ALI, N., HILL, C., KENNEDY, A. & IJSSELMUIDEN, C. 2006. What factors influence national health research agendas in low and middle income countries. *COHRED Record Paper.* New York: Council on Health Research for Development (COHRED), the Capstone Programme of New York University.

ANGWENYI, V., KAMUYA, D., MWACHIRO, D., KALAMA, B., MARSH, V., NJUGUNA, P. & MOLYNEUX, S. 2014. Complex realities: community engagement for a paediatric randomized controlled malaria vaccine trial in Kilifi, Kenya. *Trials,* 15**,** 65.

APPELBAUM, P. S., LIDZ, C. W. & GRISSO, T. 2004. Therapeutic misconception in clinical research: frequency and risk factors. *IRB: Ethics & Human Research,* 26**,** 1-8.

ARRIBAS-AYLLON, M. & WALKERDINE, V. 2008. Foucauldian discourse analysis. *In:* WILLIG, C. & W, S.-R. (eds.) *The Sage Handbook of Qualitative Research in Psychology.* London: Sage.

ARTHUR, S. & NAZROO, J. 2003. Designing fieldwork strategies and materials. *In:* RITCHIE, J., LEWIS, J., MCANUGHTON-NICHOLLS, C. & ORMSTON, R. (eds.) *Qualitative research practice: A guide for social science students and researchers.* London: Sage.

ASSOCIATION FOR SOCIAL ANTHROPOLOGISTS OF THE UK THE COMMONWEALTH. 2011. *Ethical guidelines for Good Research Practice* [Online]. Available: https://www.theasa.org/downloads/ASA%20ethics%20guidelines%202011.pdf [Accessed 17 November 2022].

ATUIRE, C. A. & HASSOUN, N. 2023. Rethinking solidarity towards equity in global health: African views. *International Journal for Equity in Health,* 22**,** 52.

AZEVEDO, M. J. & AZEVEDO, M. J. 2017. The Colonial Medical System (s) and the Health of Africans. *Historical Perspectives on the State of Health and Health Systems in Africa, Volume I: The Pre-Colonial and Colonial Eras***,** 183-214.

BA, M., GEBREMEDHIN, L. T., MASAKO, P., MSIGALLAH, F., KONE, K. E. & BAIRD, T. L. 2021. Diversity and solidarity in global health. *The Lancet Global Health,* 9**,** e391-e392.

BARCHAM, M. 2022. Decolonizing Public Healthcare Systems: Designing with Indigenous Peoples. *She Ji: The Journal of Design, Economics, and Innovation,* 8**,** 454-472.

BARSDORF, N., MAMAN, S., KASS, N. & SLACK, C. 2010. Access to treatment in HIV prevention trials: perspectives from a South African community. *Developing World Bioethics,* 10**,** 78-87.

BEAUCHAMP, T. L. 2011. Informed consent: its history, meaning, and present challenges. *Cambridge Quarterly of Healthcare Ethics,* 20**,** 515-523.

BEAUCHAMP, T. L. & CHILDRESS, J. F. 2001. *Principles of biomedical ethics*, Oxford University Press, USA.

BELSKY, L. & RICHARDSON, H. 2004. Medical researchers' ancillary clinical care responsibilities. *British Medical Journal,* 328**,** 1494-6.

BENATAR, S. R. 2000. Avoiding exploitation in clinical research. *Cambridge Quarterly of Healthcare Ethics,* 9**,** 562-565.

BENATAR, S. R. 2001. Justice and medical research: a global perspective. *Bioethics,* 15**,** 333-340.

BLACKMER, J. 2010. The ethical obligations of researchers in protecting the rights of human research subjects. *World Medical & Health Policy,* 2**,** 91-96.

BOWIE, C. & MWASE, T. 2011. Assessing the use of an essential health package in a sector wide approach in Malawi. *Health Research Policy and Systems,* 9**,** 1-10.

BRAUN, V. & CLARKE, V. 2006. Using thematic analysis in psychology. *Qualitative research in psychology,* 3**,** 77-101.

BRIDGET, P., DEBORAH, Z., MAUNG, L. K., YEONG, C. P., FRANCOIS, N., BEATRICE, L., PRATT, B., ZION, D., LWIN, K. M., CHEAH, P. Y., NOSTEN, F. & LOFF, B. 2013. Ancillary care: from theory to practice in international clinical research. *Public Health Ethics,* 6**,** 154-169.

BRIGHT, P. L. & NELSON, R. M. 2012. A capacity-based approach for addressing ancillary care needs: implications for research in resource limited settings. *Journal of Medical Ethics,* 38**,** 672-676.

BROWNSWORD, R. 2010. The ancillary-care responsibilities of researchers: Reasonable but not great expectations. *In:* HARRINGTON, J. & STUTTAFORD, M. (eds.) *Global Health and Human Rights.* London: Routledge.

CASH, R. A. 2006. What is owed to the community before, during and following research: an ethical dialogue. *EMHJ-Eastern Mediterranean Health Journal,* 12**,** S37-41.

CIOMS 2002. International ethical guidelines for biomedical research involving human subjects. *Bulletin of Medical Ethics***,** 17-23.

CIOMS 2016. International ethical guidelines for health-related research involving humans. *International ethical guidelines for health-related research involving humans.* Geneva: WHO.

CIOMS. 2017. *Clinical Research in Resource-Limited Settings* [Online]. Geneva: CIOMS. Available: https://cioms.ch/working_groups/clinical-research-rls/ [Accessed 09 January 2020].

CIOMS. 2021. *Clinical research in resource-limited settings. A consensus by a CIOMS Working Group* [Online]. Geneva. Available: https://cioms.ch/wp-content/uploads/2021/06/CIOMS_ClinicalResearch_RLS.pdf [Accessed].

CLARKE, V. & BRAUN, V. 2021. Thematic analysis: a practical guide. *Thematic Analysis***,** 1-100.

COUNCIL FOR INTERNATIONAL ORGANISATIONS OF MEDICAL SCIENCES 2017. International ethical guidelines for health-related research involving humans. *International ethical guidelines for health-related research involving humans.*

CRESWELL, J. W. & POTH, C. N. 2016. *Qualitative inquiry and research design: Choosing among five approaches*, Sage publications.

DAL-RÉ, R., RID, A., EMANUEL, E. & WENDLER, D. 2016. The potential exploitation of research participants in high income countries who lack access to health care. *British Journal of Clinical Pharmacology,* 81**,** 857-864.

DE MELO-MARTÍN, I. & HO, A. 2008. Beyond informed consent: the therapeutic misconception and trust. *Journal of Medical Ethics,* 34**,** 202-205.

DENZIN, N. K. & LINCOLN, Y. S. 2018. *The SAGE handbook of qualitative research,* Los Angeles, SAGE.

DICKERT, N. & WENDLER, D. 2009. Ancillary care obligations of medical researchers. *JAMA,* 302**,** 424-428.

DIXON-WOODS, M., AGARWAL, S., JONES, D., YOUNG, B. & SUTTON, A. 2005. Synthesising qualitative and quantitative evidence: a review of possible methods. *Journal of health services research & policy,* 10**,** 45-53.

DUNN, L. B., PALMER, B. W., KEEHAN, M., JESTE, D. V. & APPELBAUM, P. S. 2006. Assessment of therapeutic misconception in older schizophrenia patients with a brief instrument. *American Journal of Psychiatry,* 163**,** 500-506.

EL SETOUHY, M., AGBENYEGA, T., ANTO, F., CLERK, C., KORAM, K., ENGLISH, M., MOLYNEUX, C., PESHU, N., JUMA, R. & KUMWEND, N. 2002. Ethics: Fair benefits for research in developing countries: Participants in the 2001 conference on ethical aspects of research in developing countries. *Science,* 298**,** 2133-2134.

EL SETOUHY, M., AGBENYEGA, T., ANTO, F., CLERK, C. A., KORAM, K. A., ENGLISH, M., JUMA, R., MOLYNEUX, C., PESHU, N. & KUMWENDA, N. 2004. Moral Standards for Research in Developing Countries from" Reasonable Availability" to" Fair Benefits". *The Hastings Center Report,* 34**,** 17-27.

EMANUEL, E., ABDOLER, E. & STUNKEL, L. 2014. Research ethics: How to treat people who participate in research. Washinton D.C.: National Institutes of Health: National Institutes of Health Clinical Center Department of Bioethics.

EMANUEL, E. J. 2005. Undue inducement: nonsense on stilts? *The American Journal of Bioethics,* 5**,** 9-13.

EMANUEL, E. J., CURRIE, X. E. & HERMAN, A. 2005. Undue inducement in clinical research in developing countries: is it a worry? *The Lancet,* 366**,** 336-340.

EMANUEL, E. J., WENDLER, D. & GRADY, C. 2000. What makes clinical research ethical? *JAMA,* 283**,** 2701-2711.

EMANUEL, E. J., WENDLER, D., KILLEN, J. & GRADY, C. 2004. What Makes Clinical Research in Developing Countries Ethical? The Benchmarks of Ethical Research. *The Journal of Infectious Diseases,* 189**,** 930-937.

ERWIN, E. J., BROTHERSON, M. J. & SUMMERS, J. A. 2011. Understanding Qualitative Metasynthesis: Issues and Opportunities in Early Childhood Intervention Research. *Journal of Early Intervention,* 33**,** 186-200.

FAIRCLOUGH, N. 2013. Critical discourse analysis. *The Routledge handbook of discourse analysis.* Routledge.

FAIRCLOUGH, N., WODAK, R. & VAN DIJK, T. A. 1997. Discourse as social interaction. *In:* VAN DIJK, T. A. (ed.) *Discourse studies: A multidisciplinary introduction.*

FORD, J. M. 2004. Content analysis: An introduction to its methodology. *Personnel Psychology,* 57**,** 1110.

GIKONYO, C., KAMUYA, D., MBETE, B., NJUGUNA, P., OLOTU, A., BEJON, P., MARSH, V. & MOLYNEUX, S. 2013. Feedback of Research Findings for Vaccine Trials: Experiences from Two Malaria Vaccine Trials Involving Healthy Children on the Kenyan Coast. *Developing World Bioethics,* 13**,** 48-56.

GILSON, L. 2006. Trust in health care: theoretical perspectives and research needs. *Journal of Health Organisation and Management,* 53**,** 194-200.

GOVERNMENT OF MALAWI MINISTRY OF HEALTH 2017. Malawi Health Sector Strategic Plan II 2017–2022: Towards Universal Health Coverage. Government of Malawi Ministry of Health Lilongwe, Malawi.

GRADY, C. 2006. Ethics of international research: what does responsiveness mean? *AMA Journal of Ethics,* 8**,** 235-240.

GRANT, R. W. & SUGARMAN, J. 2004. Ethics in human subjects research: do incentives matter? *Journal of Medicine and Philosophy,* 29**,** 717-738.

GULLIFORD, M., FIGUEROA-MUNOZ, J., MORGAN, M., HUGHES, D., GIBSON, B., BEECH, R. & HUDSON, M. 2002. What does' access to health care'mean? *Journal of health services research & policy,* 7**,** 186-188.

GYEKYE, K. 2011. *African ethics* [Online]. Available: https://plato.stanford.edu/entries/african-ethics/ [Accessed].

HADORN, D. C. 1991. Setting health care priorities in Oregon. Cost-effectiveness meets the rule of rescue. *JAMA,* 265**,** 2218-2225.

HAIRE, B. G. & OGUNDOKUN, O. 2014. Ethics of ancillary care in clinical trials in low income countries: a Nigerian case study. *African Journal of Reproductive Health,* 18**,** 135-42.

HARDEN, A. & THOMAS, J. 2010. Mixed methods and systematic reviews: Examples and emerging issues. *In:* TASHAKKORIE, A. & TEDDLIE, C. (eds.) *SAGE Handbook of Mixed Methods in Social & Behavioral Research.*

HAWKINS, J. S. & EMANUEL, E. J. 2008. *Exploitation and developing countries: The ethics of clinical research,* Princeton, Princeton University Press.

HEALTH POLICY PROJECT 2016. Health Financing Profile.

HENDERSON, G. E., CORNELI, A. L., MAHONEY, D. B., NELSON, D. K. & MWANSAMBO, C. 2007. Applying research ethics guidelines: the view from a sub-saharan research ethics committee. *Journal of Empirical Research on Human Research Ethics,* 2**,** 41-48.

HENRIKSON, N. B., BLASI, P. R., CORSMO, J. J., SHEFFER SERDOZ, E., SCROL, A., GREENE, S. M., MATTHEWS, T. L. & RALSTON, J. D. 2019. “You really do have to know the local context”: IRB administrators and researchers on the implications of the NIH single IRB mandate for multisite genomic studies. *Journal of Empirical Research on Human Research Ethics,* 14**,** 286-295.

HOOPER, C. R. 2010. Ancillary care duties: the demands of justice. *Journal of Medical Ethics,* 36**,** 708-711.

HORNG, S. & GRADY, C. 2003. Misunderstanding in clinical research: distinguishing therapeutic misconception, therapeutic misestimation, & therapeutic optimism. *IRB: Ethics & Human Research,* 25**,** 11-16.

HYDER, A. A. & MERRITT, M. W. 2009. Ancillary care for public health research in developing countries. *Jama,* 302**,** 429-431.

ICH - GCP GUIDELINES. 1996. *International Conference on Harmonisation of technical requirements for registration of pharmaceuticals for human use* [Online]. Available: https://www.ich.org/#:~:text=The%20International%20Council%20for%20Harmonisation,pharmaceuticals%20and%20develop%20ICH%20guidelines. [Accessed].

JACOBSON, N., KRUPP, A. & BOWERS, B. J. 2016. Planning for ancillary care provision: lessons from the developing world. *Journal of Empirical Research on Human Research Ethics,* 11**,** 129-134.

JAMBO, K. 2022. I have funds to buy reagents, but not remedies. *Nature,* 606**,** 625-625.

JANSEN, L. A. 2011. Two concepts of therapeutic optimism. *Journal of Medical Ethics,* 37**,** 563-566.

KAPUMBA, B. M., DESMOND, N. & SEELEY, J. 2021. What do we know about ancillary care practices in East and Southern Africa? A systematic review and meta-synthesis. *Wellcome Open Research,* 6**,** 164.

KAPUMBA, B. M., DESMOND, N. & SEELEY, J. 2022. A chronological discourse analysis of ancillary care provision in guidance documents for research conduct in the global south. *BMC Medical Ethics,* 23**,** 51.

KAPUMBA, B. M., JAMBO, K., RYLANCE, J., GMEINER, M., SAMBAKUNSI, R., PARKER, M., GORDON, S. B. & GOODING, K. 2020. Stakeholder views on the acceptability of human infection studies in Malawi. *BMC Medical Ethics,* 21**,** 1-15.

KERASIDOU, A. 2017. Trust me, I'ma researcher!: the role of trust in biomedical research. *Medicine, Health Care and Philosophy,* 20**,** 43-50.

KHIRIKOEKKONG, N., JATUPORNPIMOL, N., NOSTEN, S., ASARATH, S.-A., HANBOONKUNUPAKARN, B., MCGREADY, R., NOSTEN, F., ROEST, J., PARKER, M., KELLEY, M. & CHEAH, P. Y. 2020. Research ethics in context: understanding the vulnerabilities, agency and resourcefulness of research participants living along the Thai–Myanmar border. *International Health,* 12**,** 551-559.

KIM, J. U., OLERIBE, O., NJIE, R. & TAYLOR-ROBINSON, S. D. 2017. A time for new north-south relationships in global health. *International Journal of General Medicine,* 10**,** 401-408.

KRUBINER, C. B., SYED, R. H. & MERRITT, M. W. 2015. Health researchers' ancillary-care responsibilities in low-resource settings: the landscape of institutional guidance. *IRB: Ethics & Human Research,* 37**,** 12-19.

KRUK, M. E., GAGE, A. D., ARSENAULT, C., JORDAN, K., LESLIE, H. H., RODER-DEWAN, S., ADEYI, O., BARKER, P., DAELMANS, B. & DOUBOVA, S. V. 2018. High-quality health systems in the Sustainable Development Goals era: time for a revolution. *The Lancet global health,* 6**,** e1196-e1252.

KWETE, X., TANG, K., CHEN, L., REN, R., CHEN, Q., WU, Z., CAI, Y. & LI, H. 2022. Decolonizing global health: what should be the target of this movement and where does it lead us? *Global Health Research and Policy,* 7**,** 3.

LACHAL, J., REVAH-LEVY, A., ORRI, M. & MORO, M. R. 2017. Metasynthesis: An Original Method to Synthesize Qualitative Literature in Psychiatry. *Frontiers in Psychiatry,* 8**,** 269.

LARGENT, E., GRADY, C., MILLER, F. G. & WERTHEIMER, A. 2013. Misconceptions about coercion and undue influence: reflections on the views of IRB members. *Bioethics,* 27**,** 500-507.

LIGNOU, S. 2011. The 'standard of care'debate and global justice in research. *Research Ethics,* 7**,** 5-12.

LOTT, J. P. 2005. Module three: vulnerable/special participant populations. *Developing World Bioethics,* 5**,** 30-54.

LUBBE, W. 2017. [The Rule of Rescue - Irrational and Discriminating?]. *Gesundheitswesen,* 79**,** 877-882.

LUBBE, W. 2019. Appeal to the Rule of Rescue in health care: discriminating and not benevolent? *Medicine, Health Care and Philosophy,* 22**,** 53-58.

MACKLIN, R. 2004. *Double standards in medical research in developing countries,* Cambridge, Cambridge University Press.

MALAWI MINISTRY OF HEALTH 2017. National Community Health Strategy: Integrating health services and engaging communities for the next generation. Malawi: Malawi Government.

MALAWI MINISTRY OF HEALTH AND ICF INTERNATIONAL 2014. Malawi Service Provision Assessment Survey 2013-14: Key Findings. Rockville, Maryland, USA: MMOH and ICF International. .

MASIYE, J., WROE, E., AMBERSIR, A., BANDA, G., BERMAN, J., CHILUMPHE, S., CHIPOLOBWE, J., CHUNDA, L., CRAMPIN, A., DULLIE, L., DUNBAR, B., GOPAL, S., KASOMEKERA, N., LUPAFYA, C., MANJOMO, R., MASAMBA, L., MWAGOMBA, B., MUULA, A., NAMARIKA, D. & COMMISSION, M. 2018. *Malawi NCDI Poverty Commission: Commission Report,* Malawi, Ministry of Health.

MAYS, N., POPE, C. & POPAY, J. 2005. Systematically reviewing qualitative and quantitative evidence to inform management and policy-making in the health field. *Journal of health services research & policy,* 10**,** 6-20.

MCINTYRE, D., THIEDE, M., DAHLGREN, G. & WHITEHEAD, M. 2006. What are the economic consequences for households of illness and of paying for health care in low-and middle-income country contexts? *Social science & medicine,* 62**,** 858-865.

MCKIE, J. & RICHARDSON, J. 2003. The rule of rescue. *Social Science and Medicine,* 56**,** 2407-19.

MCKINSTRY, B., ASHCROFT, R. E., CAR, J., FREEMAN, G. K. & SHEIKH, A. 2006. Interventions for improving patients' trust in doctors and groups of doctors. *Cochrane Database Systematic Review***,** Cd004134.

MEACHAM, M. C., STARKS, H., BURKE, W. & EDWARDS, K. 2010. Researcher perspectives on disclosure of incidental findings in genetic research. *Journal of Empirical Research on Human Research Ethics,* 5**,** 31-41.

MERRITT, M. W. 2011. Health researchers' ancillary care obligations in low-resource settings how can we tell what is morally required? *Kennedy Institute of Ethics Journal,* 21**,** 311-347.

MERRITT, M. W., KATZ, J., MOJTABAI, R. & WEST JR, K. P. 2015. Referral of research participants for ancillary care in community-based public health intervention research: A guiding framework. *Public Health Ethics,* 9**,** 104-120.

MERRITT, M. W., TAYLOR, H. A. & MULLANY, L. C. 2010. Ancillary care in community-based public health intervention research. *American Journal of Public Health,* 100**,** 211-216.

MFUTSO-BENGO, J., NDEBELE, P., JUMBE, V., MKUNTHI, M., MASIYE, F., MOLYNEUX, S. & MOLYNEUX, M. 2008. Why do individuals agree to enrol in clinical trials? A qualitative study of health research participation in Blantyre, Malawi. *Malawi Medical Journal,* 20**,** 37-41.

MILLER, F. G., MELLO, M. M. & JOFFE, S. 2008. Incidental findings in human subjects research: what do investigators owe research participants? *The Journal of Law, Medicine & Ethics,* 36**,** 271-279.

MILLER, F. G. & ROSENSTEIN, D. L. 2003. The therapeutic orientation to clinical trials. Mass Medical Soc.

MILLER, P. B. & WEIJER, C. 2006. Trust based obligations of the state and physician-researchers to patient-subjects. *Journal of Medical Ethics,* 32**,** 542-547.

MINISTRY OF JUSTICE 2006. Constitution of the Republic of Malawi. *In:* JUSTICE, M. O. (ed.). Malawi: Malawi Government.

MSOKWA, R. 2021. Improving access to health services in Malawi. *South Eastern European Journal of Public Health (SEEJPH),* 2.

MTUNTHAMA, N., MALAMBA, R., FRENCH, N., MOLYNEUX, M. E., ZIJLSTRA, E. & GORDON, S. 2008. Malawians permit research bronchoscopy due to perceived need for healthcare. *Journal of Medical Ethics,* 34**,** 303-307.

MUELLER, D. H., LUNGU, D., ACHARYA, A. & PALMER, N. 2011. Constraints to implementing the essential health package in Malawi. *PloS One,* 6**,** e20741.

MUNTHALI, A., MANNAN, H., MACLACHLAN, M., SWARTZ, L., MAKUPE, C. & CHILIMAMPUNGA, C. 2014. Non-use of formal health Services in Malawi: perceptions from non-users. *Malawi Medical Journal,* 26**,** 126-132.

NATIONAL BIOETHICS ADVISORY COMMISSION 2001. Ethical and Policy Issues in International Research : Clinical Trials in Developing Countries - Volume II Commissioned Papers and Staff Analysis. Washington D.C.: United States of America.

NATIONAL STATISTICAL OFFICE 2017. Malawi Integrated Household Survey: Household socio-economic characteristics. Malawi: National Statistical Office.

NATIONAL STATISTICAL OFFICE 2019. 2018 Malawi Population and Housing Census: Main Report. Malawi: National Statistical Office.

NEUENDORF, K. A. 2017. *The content analysis guidebook*, sage.

NOBLIT, G. W. & HARE, R. D. 1988. *Meta-ethnography: Synthesizing qualitative studies,* Newbury Park, SAGE.

NORDENTOFT, H. M. & KAPPEL, N. 2011. Vulnerable participants in health research: Methodological and ethical challenges. *Journal of Social Work Practice,* 25**,** 365-376.

NORTHCUTT, N. & MCCOY, D. 2004. *Interactive qualitative analysis: A systems method for qualitative research,* London, SAGE.

NUFFIELD COUNCIL ON BIOETHICS 2002. *The ethics of research related to healthcare in developing countries,* London, Nuffield Council on Bioethics.

NUREMBERG CODE 1947. Permissible medical experiments. *Trials of War Criminals before the Nuremberg Trials.* Washington D.C.: US Government Printing Office.

O'NEILL, O. 2002. *Autonomy and trust in bioethics*, Cambridge University Press.

OCHALEK, J., REVILL, P., MANTHALU, G., MCGUIRE, F., NKHOMA, D., ROLLINGER, A., SCULPHER, M. & CLAXTON, K. 2018. Supporting the development of a health benefits package in Malawi. *BMJ Global Health,* 3**,** e000607.

ONG'ERA, F. M., STEWART, J. & BUKUSI, E. 2021. Why and for whom are we decolonising global health? *The Lancet Global Health,* 9**,** e1359-e1360.

PARTICIPANTS IN THE 2006 GEORGETOWN UNIVERSITY WORKSHOP 2008. The ancillary-care obligations of medical researchers working in developing countries. *PLoS Medicine,* 5**,** e90.

PATTON, M. Q. 2002. *Qualitative research & evaluation methods. Intergrating theory and practice,* London, SAGE Publications.

PHILPOTT, S., WEST SLEVIN, K., SHAPIRO, K. & HEISE, L. 2010. Impact of Donor-imposed Requirements and Restrictions on Standards of Prevention and Access to Care and Treatment in HIV Prevention Trials. *Public Health Ethics,* 3**,** 220-228.

PRATT, B. & LOFF, B. 2011. Justice in international clinical research. *Developing World Bioeth,* 11**,** 75-81.

PRATT, B. & LOFF, B. 2014. A Framework to Link International Clinical Research to the Promotion of Justice in Global Health. *Bioethics,* 28**,** 387-396.

PRATT, B. & LOFF, B. 2015. A comparison of justice frameworks for international research. *Journal of Medical Ethics,* 41**,** 539-544.

PRICE, A. J., CRAMPIN, A. C., AMBERBIR, A., KAYUNI-CHIHANA, N., MUSICHA, C., TAFATATHA, T., BRANSON, K., LAWLOR, D. A., MWAIYEGHELE, E. & NKHWAZI, L. 2018. Prevalence of obesity, hypertension, and diabetes, and cascade of care in sub-Saharan Africa: a cross-sectional, population-based study in rural and urban Malawi. *The lancet Diabetes & endocrinology,* 6**,** 208-222.

Q.S.R. INTERNATIONAL PTY LTD. 2022. *NVivo: Qualitative Data Analysis Software for Researchers* | [Online]. released in March 2020. Available: https://www.qsrinternational.com/nvivo-qualitative-data-analysis-software/home?_ga=2.211552405.1443535480.1662730467-1193225661.1662730467 [Accessed 07/09/2022 2011].

RESNIK, D. B. 2003. Exploitation in biomedical research. *Theoretical Medicine and Bioethics,* 24**,** 233-259.

RICHARDSON, H. S. 2007. Gradations of researchers' obligation to provide ancillary care for HIV/AIDS in developing countries. *American Journal of Public Health,* 97**,** 1956-1961.

RICHARDSON, H. S. 2012. *Moral Entanglements: The Ancillary-Care Obligations of Medical Researchers,* Oxford, Oxford University Press.

RUGER, J. P. 2010. *Health And Social Justice,* Oxford, Oxford University Press.

RULLI, T. & MILLUM, J. 2016. Rescuing the duty to rescue. *Journal of Medical Ethics,* 42**,** 260-4.

RUSSELL, S. 2004. The economic burden of illness for households in developing countries: a review of studies focusing on malaria, tuberculosis, and human immunodeficiency virus/acquired immunodeficiency syndrome. *The Intolerable Burden of Malaria II: What's New, What's Needed: Supplement to Volume 71 (2) of the American Journal of Tropical Medicine and Hygiene*.

SACRISTÁN, J. A. 2015. Clinical research and medical care: towards effective and complete integration. *BMC Medical Research Methodology,* 15**,** 4.

SANDELOWSKI, M., VOILS, C. I. & BARROSO, J. 2006. Defining and designing mixed research synthesis studies. *Research in the Schools,* 13**,** 29.

SEERS, K. 2015. Qualitative systematic reviews: their importance for our understanding of research relevant to pain. *British Journal of Pain,* 9**,** 36-40.

SINGH, M., SCHROEDER, D., FENET, S., KIMANI, J., LAAS, K., LEISINGER, K., LUC, G., MUTHUSWAMY, V., VAN NIEKERK, J. & SCHMITT, K. 2017. *Exploitation Risks and Research Ethics Guidelines* [Online]. EU: Trust Project. Available: https://trust-project.eu/wp-content/uploads/2016/03/TRUST-Deliverable-Risks-Principles-Final-for-submission.pdf [Accessed].

SLOWTHER, A., BOYNTON, P. & SHAW, S. 2006. Research governance: ethical issues. *Journal of Royal in Society of Medicine,* 99**,** 65-72.

SMIRNOFF, M., WILETS, I., RAGIN, D., ADAMS, R., HOLOHAN, J., RHODES, R., WINKEL, G., RICCI, E. M., CLESCA, C. & RICHARDSON, L. D. 2018. A paradigm for understanding trust and mistrust in medical research: the Community VOICES study. *AJOB empirical bioethics,* 9**,** 39-47.

SMITH, P. 1990. The Duty to Rescue and the Slippery Slope Problem. *Social Theory and Practice,* 16**,** 19-41.

SOFAER, N. 2014. Reciprocity-based reasons for benefiting research participants: most fail, the most plausible is problematic. *Bioethics,* 28**,** 456-71.

SOFAER, S. 1999. Qualitative methods: what are they and why use them? *Health Services Research,* 34**,** 1101-18.

SPENCER, S. A., RYLANCE, J., QUINT, J. K., GORDON, S. B., DARKD, P. & MORTON, B. 2023. Prevalence of multimorbidity and chronic health conditions among adult patients in sub-Saharan Africa – a new review. *Bulletin of the World Health Organization*.

STILSON, B. 2019. A Failure to Care: Colonial Power and Healthcare in Africa, 1850-1939. *The Undergraduate Historical Journal at UC Merced,* 6.

STUNKEL, L. & GRADY, C. 2011. More than the money: a review of the literature examining healthy volunteer motivations. *Contemporary Clinical Trials,* 32**,** 342-352.

THOROGOOD, N. & GREEN, J. 2018. Qualitative methods for health research. *Qualitative methods for health research***,** 1-440.

TILLEY, H. 2016. Medicine, empires, and ethics in colonial Africa. *AMA Journal of Ethics,* 18**,** 743-753.

TINDANA, P. O., ROZMOVITS, L., BOULANGER, R. F., BANDEWAR, S. V., ABORIGO, R. A., HODGSON, A. V., KOLOPACK, P. & LAVERY, J. V. 2011. Aligning community engagement with traditional authority structures in global health research: a case study from northern Ghana. *American journal of public health,* 101**,** 1857-1867.

TSHIKALA, T., MUPENDA, B., DIMANY, P., MALONGA, A., ILUNGA, V. & RENNIE, S. 2012. Engaging with research ethics in central Francophone Africa: reflections on a workshop about ancillary care. *Philosophy, Ethics, and Humanities in Medicine,* 7.

ULRICH, M. R. Researchers Without Borders?: Limiting Obligations of Ancillary Care Through the Rescue Model. Limiting Obligations of Ancillary Care Through the Rescue Model (January 31, 2011). Vanderbilt Law School Health Law and Public Policy Forum, 2011 Nashville, TN. 28-34.

UNICEF & WHO 2013. Health in the post-2015 development agenda: need for a social determinants of health approach: joint statement of the UN Platform on Social Determinants of Health. *Health in the post-2015 development agenda: need for a social determinants of health approach: joint statement of the UN Platform on Social Determinants of Health.*

UNITED NATIONS 1948. Universal Declaration of Human Rights. New York: United Nations.

UNITED STATES - NCPHS OF BIOMEDICAL AND BEHAVIORAL RESEARCH 1978. *The Belmont report: ethical principles and guidelines for the protection of human subjects of research,* United States of America, Department of Health, Education, and Welfare, National Commission for the Protection of Human Subjects of Biomedical and Social Research.

WELLCOME TRUST. 2010. *Research involving people living in low and middle income countries: Guidance notes on research involving human participants living in low- and middle-income countries.* [Online]. Available: https://wellcome.ac.uk/grant-funding/guidance/research-involving-people-low-and-middle-income-countries [Accessed 26 May 2020].

WERTHEIMER, A. 2008. Exploitation in clinical research. *In:* EMMANUEL, E. J., GRADY, C. C., CROUCH, R. A., LIE, R. K. & MILLER, F. G. (eds.) *The Oxford textbook of clinical research ethics.* Oxford.

WHO. 2021. *Universal Health Coverage* [Online]. Geneva: World Health Organisation. Available: https://www.who.int/news-room/fact-sheets/detail/universal-health-coverage-(uhc) [Accessed 30 November 2022].

WOLF, S. M., CROCK, B. N., VAN NESS, B., LAWRENZ, F., KAHN, J. P., BESKOW, L. M., CHO, M. K., CHRISTMAN, M. F., GREEN, R. C. & HALL, R. 2012. Managing incidental findings and research results in genomic research involving biobanks and archived data sets. *Genetics in Medicine,* 14**,** 361-384.

WORLD BANK. 2022a. *Life expectancy at birth, total (years) - Malawi* | *Data* [Online]. Washington D.C.: World Bank. Available: https://data.worldbank.org/indicator/SP.DYN.LE00.IN?locations=MW [Accessed 28 November 2022].

WORLD BANK. 2022b. *Malawi Overview: Development news, research, data* | *World Bank* [Online]. Washington D.C.: World Bank. Available: https://www.worldbank.org/en/country/malawi/overview [Accessed 28 November 2022].

WORLD MEDICAL ASSOCIATION 2013. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA,* 310**,** 2191-2194.

WRIGHT, S. 2010. Trust and trustworthiness. *Philosophia,* 38**,** 615-627.

## Appendices

### Appendix 1: Topic guide for stakeholder interviews

#### A. Research principal investigators and frontline research staff (MLW fieldworkers, nurses, clinicians)

Interview questions focused on interviewee's familiarity with the concept of ancillary care and the description of the current practice as well as what ought to happen.

**Introduction**

1. To start, could you tell me about what you do, the study that you are working on or that you have done before.
2. How long have you been working/involved in research or in your current position?

**Research ethics guidance**

So, just like with any other research project, I believe there are specific research ethics guidelines that you use or follow when conducting your medical research.

3. What specific research guidance do you use or follow for the conduct of your study? Or what specific ethics guidelines do you and your study team follow when implementing study activities?
    a. International
    b. Local
4. What guidance do the local research ethics committees provide on supporting the provision of ancillary care during medical research, particularly on research conducted in our resource-constrained settings?

In some ethics guideline e.g., the CIOMS guidelines, they describe some consideration for the provision of care to study participants during research using terms such as morally praiseworthy, as necessary – but not calling it as an obligation.

5. What do you think of such guidance statements to researchers conducting research in RCS?
    a. What do you think about the current local research ethics guidance?
6. How does that apply to the studies that you conduct or to you as a researcher?

What can you tell me about ancillary care provision in your study? or What is you experience on the provision of ancillary care to study participants in your current or previous research?

7. What are some of the common ancillary care health needs identified among research participants? And how do you respond to them?

**Ancillary care practices**

8. What ancillary health needs do you expect, or you have experienced in your participants?
9. What guidance do you provide in your study on supporting the provision of ancillary care during the conduct of your research?
10. What do you think about the provision of ancillary care to study participants in biomedical research in Malawi?
    - Probe for reasons
        - benefits
        - concerns / risks / challenges
11. In general, what are your views on access to care for non-study related condition for research participants in medical research?
12. During the designing phase of your studies, what ancillary care plans did you include in your study protocol or when applying for grants, if any? And how did that go with the ethics review?
13. Under what conditions are supported referrals of research participants with ancillary care needs made, and what are the outcomes? Or to what extent would ancillary care be provided?
14. If ancillary care is to be made available to study participant in Malawi or in RCS in general, what do you think would be the important things to put in place or what need to be considered?
15. What ethical issues do you (as a researcher) or researchers encounter regarding provision of care or support outside the study to their participants?
16. What are your views on researcher's responsibility of planning and responding to ancillary care needs during research?
    - Probe for
        - What obligations do researchers have to participants?
        - What role does context and circumstance play in determining obligation?
        - How do ideas of fairness and reciprocity play out in the context of

limited research funding and inadequate national health systems?

17. What if anything, should be provided to research participants (both as individuals and groups), and by who, after their participation, and what, if anything, should be made available to others in the host community or country during the research”
18. How could provision of ancillary care in Malawi or RCS generally likely impact on the research study objectives?
    - Probe for
        - Increased demand
        - Resources (finances and other study materials)

**Suggestions for ancillary care in future studies**

19. What are your thoughts on including plans for ancillary care in the study design?
20. What would be the necessary steps to follow if ancillary care is to be planned and provided to study participants in Malawi and other RCS more generally?
21. What do you think about the idea of ancillary care (care and treatment) in medical research?

Thank you for your time and participation in this study.

## B. Research ethics committee members (COMREC and NHSRC)

Interview questions focused on interviewee's familiarity with the concept of ancillary care and the description of the current ethical guidelines.

### Introduction

1. To start, just tell me about your role. What position, involvement with (own) research?
2. How long have you been involved in the committee?

### Views on ancillary care

3. How do you describe ancillary care? or What would you describe as ancillary care in biomedical research? What do you understand ancillary care in medical research?
4. What do you think about provision of ancillary care to study participants in biomedical research in Malawi?
    - Probe for reasons
        - benefits
        - concerns / risks / challenges
5. What are your views on researcher's responsibility of planning and providing access to care for non-study related conditions for research participants in medical research?
    - Probe for
        - What obligations do researchers have to participants?
        - What role does context and circumstance play in determining obligation?
        - How do ideas of fairness and reciprocity play out in the context of limited research funding and inadequate national health systems?

### Research ethics guidance

6. Does the NCST have existing guidance available on supporting the provision of ancillary care during medical research, particularly on research conducted in our resource- constrained settings?

In the CIOMS guidelines, they describe some consideration for the provision of care to study participants during research using terms such as being morally praiseworthy, as necessary – but not calling it as an obligation until recently in the 2021 CIOMS guidelines where it is now being referred to as an obligation.

7. What do you think of such guidance statements to researchers conducting research in RCS?

8. What do you think about the idea of ancillary care (care and treatment) in medical research?

In the COMREC general guidelines 2010– adopted from NCST- we did not find any information that supports the provision of care to study participants including the study related. Such information is not included in the NHSRC general guidelines as well.

9. As a member of the research ethics committee, I understand you have been involved in reviewing several protocols. When reviewing these protocols, what ancillary care plans, if any, have you come across or do medical researchers include in their research protocols?
10. When reviewing protocols for health-related studies, how do you determine what researchers can provide to their participants during research?

    Is any consideration made during protocols review for research when it is with participants who may have additional health needs besides those which are related to the study?

11. What ethical guidelines does REC provide to support researchers providing for the study participants additional health needs in Malawi?

12. How could provision of ancillary care in Malawi or RCS generally likely create ethical concerns in the conduct of biomedical research?

    Coercion
    Therapeutic misconception

13. Would NHSRC expect to see researchers setting out ancillary care plans in the researcher's ethics approval applications?

**Suggestions for ancillary care in future studies**

14. What would you suggest to funders of research on considerations for additional funding for ancillary care?

## C. Grant officers from international funding institutions

Interview questions focused on interviewee's familiarity with the concept of ancillary care and the description of the current research funding guidelines for RCS.

### Introduction

1. To start, just tell me about your role. What position or involvement with research funding or grants?

### Views on ancillary care

2. What type of research do you provide funding for?
3. What are your thoughts or opinions on the considerations for ancillary care?
   - What plans do you have (as funders) for ancillary care to study participants in RCS?
   - What position does your funding organisation have on supporting the provision of ancillary care
4. What specific guidelines, if any, do you provide (or do researchers follow) to researchers when applying for research grants?
   - How do they address issues of differences in study contexts? Of particular interest are studies conducted in RCS where its participants are vulnerable.
   - What funding considerations are there for participants additional health needs besides a condition under investigation?

   We saw that in some of the policies and guidelines for Wellcome funding refer to CIOMS, Declaration of Helsinki and other international ethics guidelines on the conduct of research. These guidelines contain some statements on consideration for the provision of care to study participants – as morally praiseworthy or if necessary – however these terms are not explicit. The 2021 CIOMS explicitly calls ancillary care as an obligation of researchers.

   - How does that reflect on the funding that you provide for research in RCS where we expect that these needs will arise?
   - How does the research funding provided by your organisation reflect the international ethics guidance which recommends that medical researchers can provide ancillary care to their participants if necessary or because is something praiseworthy?

   Collateral benefits - provision of healthcare benefits to communities during a research study

   - What are your thoughts on such guidance statements?

5. How much ancillary care plans do you see in the grant's application? What do researchers include in their grant application regarding the support with provision of ancillary care to the study participants?
    - What do you do when you find that researchers have included a budget for the ancillary health care of their participants?
    - How does Wellcome accommodate what researchers plans as budget for other additional health care to their participants?
6. What are your views (or the stand of Wellcome) on researcher's responsibility of planning and responding to ancillary care needs during research?
    - Probe for
        - Some research stakeholders with whom we have spoken have said that researchers gain a great deal from the information that they get from their participants. In this particular example, they are looking at the people that volunteer to participate in research in RCS, who are deemed vulnerable in a variety of aspects of their lives including on health. How do ideas of fairness and reciprocity play out in the context of limited research funding and inadequate national health systems?
        - What do you think of this obligation of researchers have to participants?
        - What role does context and circumstance play in determining obligation?
        - What happens with funding or what would happen to funding if researchers have exhausted their funds to take care of the ancillary health needs of their participants?
7. What are your thoughts on the ethical implications (on funding) of researchers supporting ancillary care provision to study participants in RCS?

**Suggestions for ancillary care in future studies**

8. What are your thoughts on researchers including plans for ancillary care in the study design?
    - When researchers are applying for funding from your organization.
9. What would you say would be the necessary steps researchers should follow when deciding and considering provision of ancillary care to study participants in Malawi and other RCS more generally?

## D. Health officials (Ministry of Health and District Health Offices)

Interview questions focused on interviewee's familiarity with the concept of ancillary care and the description of the current ethical guidelines.

### Introduction

1. To start, just tell me about your role. What position, involvement with (own) research?

### Views on ancillary care

2. What is your relationship with researchers like?
3. In what way would you need help from the researchers when they conduct their studies in your facilities?
4. Does the ministry have existing guidance available on supporting the provision of ancillary care during medical research?
5. What do you think about the idea of ancillary care (care and treatment) in medical research?
6. Is any provision made during the time of your considerations (**when giving permission for research**) for research when it is with participants who may have additional health needs besides those which are related to the study?
7. What do you think about provision of ancillary care to study participants in biomedical research in Malawi?
    - Probe for reasons
        - benefits
        - concerns / risks / challenges
8. What are your views on access to care for non-study related conditions for research participants in medical research?
    - Probe for
        - Trials
        - Observation studies
        - cross-sectional studies
        - social sciences studies
9. What are your views on researcher's responsibility of planning and responding to ancillary care needs during research?
    - Probe for
        - What obligations do researchers have to participants?
        - What role does context and circumstance play in determining obligation?

- How could you relate ancillary care and ideas of fairness or justice and reciprocity play out in the context of limited research funding and inadequate national health systems?

10. What guidelines does MoH have in place for biomedical researchers on provision of ancillary care to study participants in Malawi?
11. What are your views and experiences on ancillary care provision in Malawi?
12. How could provision of ancillary care in RCS likely create additional burden to health care workers and hospitals relative to regular care?
13. What impact does provision of ancillary care to individuals participating in biomedical research have on the health care system?
14. How do medical researchers who conducting biomedical research support with health care services within the system?
15. What do you think are the researchers' ancillary care responsibilities?

**Suggestions for ancillary care in future studies**

16. What are your thoughts on researchers including plans for ancillary care in the study design?
17. What would be the necessary steps to follow when deciding and considering provision of ancillary care to study participants in Malawi and other RCS more generally?

## E. Research participants from selected studies

Interview questions focused on interviewee's familiarity with the concept of ancillary care and the description of the current research funding guidelines for RCS**.**

**Experience with research participation**

What research studies have you been invited to take part in?

What was your decision about participation?

**Views on ancillary care**

How can you describe ancillary care? or What would you describe as ancillary care in biomedical research?

**Vignettes**

Vignettes will be presented to participants using different scenarios to make the topic being explored clearer to participants. For each of the given vignettes, we will ask participants what they see as ancillary care and why?

It is well known that when individual volunteers decide to take part in a research study, they usually think about benefits they might obtain from their participation, as well as the risks involved.

- Can you tell me what things you would consider important to think about before consenting to take part in a study?

On the one hand, if we think about the same considerations in terms of deciding to participate in a large research trial, such as an Covid-19 vaccine trial.

- If someone asked you if you wanted to volunteer to be part of an Covid-19 vaccine trial, what are the things that you would consider before making your decision?

If ancillary care should be provided to the study participants:

- Who should provide the care?
- What should be included as ancillary care?
- How and why should ancillary care be provided?

What are your views on the researcher's responsibility to provide ancillary care? Or what do

researchers owe individual participating in biomedical research?

What obligations do researchers have toward their study participants?

## Appendix 2: MLW Support letter

Malawi-Liverpool-Wellcome Trust
Clinical Research Programme
P.O Box 30096, Chichiri, Blantyre 3, Malawi.
Tel. +265 1 876444 Fax +265 1 875774

23rd December 2020

Dr Erik Umar
COMREC Chairman
College of Medicine
P Bag 360
Blantyre

Dear Dr Umar,

**Re: Letter of Support - The Social and Ethical Implications of Data-Prompted Ancillary Care in Southern Africa, Malawi**

I write to support the submission of Doctoral Research Project to COMREC for ethical review. The project will be led by Blessings Kapumba, within the Community Engagement & Bioethics group supervised by Dr Deborah Nyirenda and is funded by the Global Health Bioethics Network - Wellcome Trust funded. The doctoral research project is entitled **"The Social and Ethical Implications of Data-Prompted Ancillary Care in Southern Africa, Malawi"**

Data-driven Ancillary Care is increasingly emphasised as an ethical approach in medical research. It, however, raises complex ethical concerns when research is conducted in resource-constrained settings (RCS) where participants may have additional health care needs outside the scope of the research, not usually provided by the local health care system. Limited information is available on observational research findings and understanding on practices of ancillary care provision during research, particularly in RCS. This research project aims to explore research stakeholders' views and perspectives on the provision of ancillary care, if any are encountered by researchers in Malawi, and how they respond to them. We will conduct qualitative in-depth interviews with key research stakeholders in Blantyre and Chikwawa, Malawi, including researchers, ministry of health officials, research ethics committees (REC) members, and research participants; and grant officers from international research funding institutions, to understand their views and perspectives on the provision of ancillary care.

Findings from this study will underpin the development of relevant and acceptable standard guidelines and recommendations for the ethics of ancillary care during medical research in Malawi and other RCS.

Many thanks for your consideration of this protocol. We look forward to your feedback.

Yours sincer[redacted]

Professor Stephen Gordon
MA MD FRCP FRCPE DTM&H
Director, MLW

## Appendix 3: Permission letter – Blantyre District Council

Telephone: Blantyre 01 875 332 /01 877 401
Fax: 01 875 430 / 01 872 551

Communication should be addressed to :
Blantyre District Council
Director of Health and Social Services
0882002533 : ekawalazira@yahoo.co.uk

In reply please quote No. .....

DISTRICT HEALTH OFFICE
P/BAG 66
BLANTYRE
MALAWI

17 December, 2020

The chairperson
College of Medicine Research Committee
College of medicine
P/Bag 360
Chichiri
Blantyre 3

Dear sir/madam

**Support letter for the study entitled; The Social and Ethical Implications of Data-Prompted Ancillary Care in Southern Africa**

My writing of this letter to give an approval for the above-mentioned study. The broad objective of the study is to explore research stakeholders' views and perspectives on the provision of ancillary care, if any are encountered by researchers in Malawi, and how they respond to them.

Your usual support rendered to the office is always appreciated.

Yours faithfully,

Blantyre District Council
Director of Health & Social Services
18 DEC 2020
Private Bag No
Blantyre

[redacted]

Dr Zaziwe Fatsani Gundah
**FOR: DIRECTOR OF HEALTH AND SOCIAL SERVICES**

## Appendix 4: Support letter – Chikwawa District Council

Telephone: (+265) 01420266
Fax: (+265) 01420264
Email: chikwawa-hmis@malawi.net

Communications should be addressed to:
The District Health officer
Chikwawa District Hospital
P.O Box 32
Chikwawa

5th January, 2021.

The Chairperson
College of Medicine Research and Ethics Committee
P/Bag 360
Chichiri
BLANTYRE 3

Dear Sir/Madam,

**SUPPORT LETTER FOR THE STUDY 'THE SOCIAL AND ETHICAL IMPLICATIONS OF DATA - PROMPTED ANCILLARY CARE'**

I have sent this letter in support of the above study that is planned to take place in Chikwawa. The study investigator presented the study before the Chikwawa health research committee which has approved it.

The office of the Director of health and social services in Chikwawa expects to be kept aware of the progress of the study and study results.

I look forward to your assistance.

[redacted]

THE DISTRICT HEALTH OFFICE
CHIKWAWA DISTRICT
2021 -01- 05
CHIKWAWA

Dr Marriam Mponda
FOR:THE DIRECTOR OF HEALTH AND SOCIAL SERVICES

**Appendix 5: Ethics approval certificate - COMREC**



# CERTIFICATE OF ETHICS APPROVAL

This is to certify that the College of Medicine Research and Ethics Committee (COMREC) has reviewed and approved a study entitled:

P.01/21/3242 - The Social and Ethical Implications of Data-Prompted Ancillary Care in Southern Africa, Malawi by Blessings Kapumba

*On 04-Mar-21*

*As you proceed with the implementation of your study, we would like you to adhere to international ethical guidelines, national guidelines and all requirements by COMREC some of which are indicated on the next page for your study*

[redacted]

04-Mar-21

Prof. E. Umar -Chairperson (COMREC) Date

Approved by College of Medicine 04-Mar-2021 (COMREC) Research and Ethics Committee

## Appendix 6: Ethics approval certificate - LSHTM

**London School of Hygiene & Tropical Medicine**
Keppel Street, London WC1E 7HT
United Kingdom
Switchboard: +44 (0)20 7636 8636

**www.lshtm.ac.uk**

**Observational / Interventions Research Ethics Committee**

Mr Blessings Kapumba
LSHTM

10 June 2021

Dear Mr Blessings Kapumba

**Study Title:** The social and ethical implications of data-prompted ancillary care in east and southern Africa, Malawi

**LSHTM Ethics Ref:** 22890

Thank you for responding to the Observational Committee's request for further information on the above research and submitting revised documentation. The further information has been considered on behalf of the Committee by the Chair.

**Confirmation of ethical opinion**

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

**Conditions of the favourable opinion**

Approval is dependent on local ethical approval having been received, where relevant.

**Approved documents**

The final list of documents reviewed and approved by the Committee is as follows:

| Document Type | File Name | Date | Version |
|---|---|---|---|
| Other | Blessings_Kapumba_GCP_Certificate_R2_January 2019 | 18/01/2019 | 1 |
| Other | Deborah_Nyirenda_GCP_Certificate_R2_May 2019 | 17/05/2019 | 1 |
| Other | Nicola_Desmond_GCP_R2_Nov 2019 | 27/11/2019 | 1 |
| Other | Janet_Seleey_GCP_Certificate_R2_May 2020 | 11/05/2020 | 1 |
| Investigator CV | Janet Seeley-cv-2020-September | 30/09/2020 | 1 |
| Investigator CV | Nicola Desmond CV | 01/12/2020 | 1 |
| Investigator CV | Deborah Nyirenda CV | 09/12/2020 | 1 |
| Advertisements | Ancillary care study introductory email_English | 24/12/2020 | 1 |
| Local Approval | Kapumba 3242_Ethics_approval_certificate | 04/03/2021 | P.01/21/3242 |
| Investigator CV | Blessings_Kapumba_CV | 08/04/2021 | 1 |
| Information Sheet | Participant Information Sheet | 08/04/2021 | 1 |
| Information Sheet | Consent Form | 08/04/2021 | 1 |
| Protocol / Proposal | LEO Ancillary care study protocol V 1.0 08042021 | 08/04/2021 | 1 |
| Covering Letter | Cover Letter | 02/06/2021 | 1 |
| Protocol / Proposal | LEO Ancillary care study protocol V 2.0 02062021 | 02/06/2021 | 2 |
| Information Sheet | Participant Information Sheet V 2.0 02062021 | 02/06/2021 | 2 |
| Information Sheet | Participant Informed Consent Form V 2.0 02062021 | 02/06/2021 | 2 |

### After ethical review

The Chief Investigator (CI) or delegate is responsible for informing the ethics committee of any subsequent changes to the application. These must be submitted to the Committee for review using an Amendment form. Amendments must not be initiated before receipt of written favourable opinion from the committee.

The CI or delegate is also required to notify the ethics committee of any protocol violations and/or Suspected Unexpected Serious Adverse Reactions (SUSARs) which occur during the project by submitting a Serious Adverse Event form.

An annual report should be submitted to the committee using an Annual Report form on the anniversary of the approval of the

study during the lifetime of the study. At the end of the study, the CI or delegate must notify the committee using an End of Study

form.

All aforementioned forms are available on the ethics online applications website and can only be submitted to the committee via the website at: http://leo.lshtm.ac.uk

Additional information is

available at:

www.lshtm.ac.uk/ethics

Yours sincerely,

**Professor Jimmy Whitworth**
**Chair**

ethics@lshtm.ac.uk
http://www.lshtm.ac.uk/ethics/

---

**Improving health worldwide**