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**CARE IN HIV DRUG TRIAL CLOSURE: PERSPECTIVES OF RESEARCH
PARTICIPANTS AND STAFF IN UGANDA**

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Thesis submitted to The University of Nottingham for the degree of Doctor of Philosophy

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To my family

ABSTRACT

Background: After three decades, Human Immunodeficiency Virus (HIV) continues to pose significant threats globally. The efforts to curb the HIV epidemic have required investment in research, with clinical trials being a major focus, to develop HIV prevention, treatment, and cure interventions. A large portion of such research has been undertaken within low income settings, due to the high burden of HIV and the availability of willing volunteers within this setting. HIV research calls for the implementation of ethical research practice which is informed by policy guidelines. However, current policies are largely informed by inputs from high income countries, and lack the voices of those closely involved in research implementation. In order to contribute to ethics policy development in HIV research, it is essential to involve different stakeholders by exploring their experiences/views on the issue. Existing research in this field has mainly explored experience of recruitment and trial conduct, while very little has been done on trial closure, indicating a significant evidence gap worth exploring. This research therefore sought to illuminate, explore and understand the significant issues regarding the care of HIV positive drug trial participants during closure of HIV clinical trials, within a low income setting, specifically, Uganda.

Study aim: The study aimed to explore how care is perceived and enacted in HIV drug trial closure in Uganda, by addressing the following specific objectives:

1. From the perspective of research participants and research staff, to explore the views, opinions and understandings of the ethical/legal/moral post-trial obligations in HIV drug trials.
2. From the perspective of research staff, to explore the experiences, practices and processes related to care for HIV drug post-trial participants in a low income setting.
3. From the perspective of research participants, to explore the experiences of care at trial closure.
4. From the perspective of research participants, to explore the experiences of transitioning from HIV research to care/community.

Methodology: The study adopted an interpretive-constructivist approach, and employed a social constructivist grounded theory methodology. The study included a total of 21 trial participants and 22 research staff from three different HIV drug trials, in two Ugandan research institutions. In addition, relevant ethical documents were reviewed from two of the included trials. Data collection and analysis followed the principles of grounded theory, with data collection and preliminary analysis being undertaken concurrently, and earlier data informing subsequent data collection. Data collection

strategies included individual interviews, focus group discussions, and key informant interviews. Data was collected over a period of 10 months, from October 2014 to August, 2015. NVivo10 software was used to manage the data. Ethical approval was received from the University of Nottingham UK and The AIDS Support Organization (TASO) Uganda, Research Ethics Committees (RECs). The study was registered with the Uganda National Council for Science and Technology (UNCST), as SS 3608. Permission to conduct the research was granted by the respective research institutions, and written informed consent was received from all respondents.

Findings: The findings showed that trial closure was often stressful for HIV positive participants in Uganda, and often resulted in negative psychological, socio-economic and health impacts. The negative effects mainly resulted from being stopped from accessing research related health care, which was of a significantly higher quality, and the inability to find alternative care to match the research standards. The main concerns which arose during the transition process of participants from HIV drug trials to usual care facilities include: the loss of the quality care and valued relationships in research, the need to find and link to alternative care facilities, the need to meet the increased financial needs, and worries about the effects/outcomes of research participation. These concerns demanded a range of additional care and supportive strategies from researchers (and other stakeholders).

A conceptual model, the model of 'Facilitated Transition' was developed, which summarises the findings of this research and provides a diagrammatic representation of the research findings, showing the links and relationships between the different elements. The research established that the transition of HIV positive trial participants from research to usual care facilities is a process, which appears to consist of three overlapping phases. These phases include: The pre-closure phase which represents events occurring before the actual trial closure but that underpin post-trial care, the trial closure phase which is the active phase of the closure, in which trial participants are prepared and exited from the trials, and the post-trial phase which represents the events occurring after trial participants have been linked to post-trial care facilities until 12 months later. These phases are demarcated by specific time points, which reflect how the transition process evolves, proceeds and concludes. At the various phases of the process, specific concerns (care needs) arise, being influenced by the participants' previous care experiences and perceptions, plus their health and socio-economic positions. Specific actions are required to proactively facilitate trial participants during these phases. These actions are underpinned by the perceived ethical and moral responsibilities of the researchers, and are principally aimed at establishing a continuum

of HIV care and treatment after trial closure, promoting positive care experiences for trial participants during the transition, and enabling the settlement and adaptation of trial participants to care in the public healthcare system.

Conclusions: This is the first known study to investigate perspectives on post-trial care among HIV positive trial participants in a low income setting, from those closely engaged in the research process. This study has provided novel contributions in the area of HIV research ethics and post-trial care in general. The study has established that trial closure involving HIV positive participants raises significant ethical, moral and practical concerns in the Ugandan context. The findings further demonstrated that current post-trial care practice does not meet all the care needs of the HIV positive trial participants. Existing ethical recommendations on post-trial care place an emphasis on the need to ensure access to trial drugs and provision of trial results, where as less attention is given to other important aspects, as revealed in this research. To meet the post-trial care needs of HIV positive participants in Uganda, a comprehensive trial closure strategy is required. In addition to the already existing aspects of post-trial care, the new strategy should aim to: (i) address the financial needs of trial participants through financial assessment, support and empowerment, (ii) provide practical support during linkage to post-trial care, and (iii) offer post-trial follow-up to monitor and support the participants. Implementing these recommendations may require involvement of various stakeholders, including researchers, ethics authorities, research funders and donors, public healthcare workers, families, trial participants, and the community.

Recommendations for future research: Further research is required to ascertain the rates of linkage to care, and to assess the health outcomes of post-trial participants following trial exit. In addition, a study to target the views of other stakeholders, such as the public healthcare facility workers, the family, and ethics authorities on post-trial care may be essential to understand better the ways in which to support HIV positive trial participants in Uganda. Furthermore, a longitudinal prospective study on a larger sample is required to test the model proposed in this research. And finally, there is need to deliberate more on the ethical and moral implications of financial benefits in HIV research involving HIV positive participants in a low income setting.

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Conferences

Experiences of HIV infected people within their first year of leaving HIV clinical trials in Uganda: a grounded theory assessment. Poster presentation at the 21st International AIDS Conference (AIDS 2016), Durban South Africa, (17th -22nd July, 2016)

Ethical and practical considerations in HIV drug trial closure: perspectives of researchers in Uganda. Poster presentation at the 21st International AIDS Conference (AIDS 2016), Durban South Africa, (17th -22nd July, 2016)

'Moving to another world': understanding the impact of clinical trial closure on HIV positive participants in Uganda. Poster presentation at the University of Nottingham, School of Health Sciences' researchers away day, (15th June, 2016)

'Moving to another world': understanding the impact of clinical trial closure on HIV positive participants in Uganda. Poster presentation at the 22nd Annual conference for the British HIV Association (BHIVA) (19th-22nd April, 2016)

'Moving to another world': understanding the impact of clinical trial closure on HIV positive participants in Uganda. Poster presentation, University of Nottingham, Doctoral Research Saturday seminar, (April, 2016).

Participant views and experiences of participating in HIV research in sub-Saharan Africa: a qualitative systematic review. Oral presentation *at the Aga Khan University, School of Nursing and Midwifery Regional Alumni Conference, Kampala, Uganda* (30th-31st July 2015)

The experiences of HIV research participants in Sub-Saharan Africa: a qualitative systematic review. Poster presentation *at the 9th Biennial Joanna Briggs International Colloquium, Singapore* (10th -12th November 2014)

The experiences of HIV research participants in Sub-Saharan Africa: a qualitative systematic review. Oral presentation *at the National HIV Nurses Association (NHIVNA) 16th Annual Conference, Cardiff, UK* (25th-27th June 2014)

The experiences of HIV research participants in Sub-Saharan Africa: a qualitative systematic review. Poster presentation *at the Royal College of Nursing (RCN) International Nurses Conference, Glasgow, UK* (2nd -4th April 2014)

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ABBREVIATIONS AND ACRONYMS

Table 1: Abbreviations

AIDS	Acquired Immunodeficiency Syndrome
ART	Antiretroviral Therapy
CAB	Community Advisory Board
CAHR	Canadian Association for HIV Research
CBER	Center for Biologics Evaluation and Research
CDER	Center for Drug Evaluation and Research
DoH	Department of Health
DSMB	Data and Safety Monitoring Board
EC	Ethics Committee
eMTCT	Elimination of Mother to Child Transmission of HIV
FDA	U.S. Food and Drug Administration
FGD	Focus Group Discussion
GDP	Gross Domestic Product
HAART	Highly Active Antiretroviral Therapy
HIV	Human Immunodeficiency Virus
IBC	Institutional Bio-safety Committee
IDI	Infectious Diseases Institute
IDRC	Infectious Diseases Research Collaboration
IRB	Institutional Review Board
IRC	Institutional Review Committees
JBI	Joanna Briggs Institute
JCRC	Joint Clinical Research Centre
MARPs	Most at Risk Persons
MJAP	Mulago-Mbarara Teaching Hospitals Joint AIDS Program
MOH	Ministry of Health
MRC/UVRI	Medical Research Council/Uganda Virus Research Institute
MUJHU	Makerere University-John Hopkins University
NDA	National Drug Authority
NGOs	Non-Government Organisations
NIH	National Institutes of Health
OI	Opportunistic Infection

PEPFAR	President's Emergency Plan for AIDS Relief
PFP	Private for Profit
PLHIV	People Living with HIV
PMTCT	Prevention of Mother to Child Transmission of HIV
PNFP	Private Not for Profit
POSTNOTE	Parliamentary Office of Science and Technology
PrEP	Pre-Exposure Prophylaxis
REC	Research Ethics Committee
SCs	Scientific Committees
TASO	The AIDS Support Organisation
TCMP	Traditional and Complementary Medicine Practitioner
TED	Technology Entertainment Design
UAC	Uganda AIDS Commission
UN	United Nations
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNCST	Uganda National Council of Science and Technology
UVI	Uganda Virus Institute
WHO	World Health Organisation

OPERATIONAL DEFINITIONS

Table 2: Definition of key terms

Trial participant (s) or participant(s)	HIV post-trial participant(s) who participated in the current research
Research staff or staff	Research (trial) staff who were interviewed in the current study
Respondents	This term is used when post-trial trial participants and research staff who took part in the current study are talked about together
Healthcare staff or facility staff	These refer to healthcare workers from non-research institutions
Pre-trial care facility or previous care facility or primary care facility or former care facility	These terms refer to the care facilities where trial participants attended care before joining the included trials
Post-trial care facility	These are care facilities where trial participants attended their care after exiting from the included trials

CHAPTER 1: INTRODUCTION

1.1 Introduction to the thesis

This thesis presents a study, which sought to explore how care in HIV drug trial closure in Uganda is perceived, enacted and experienced among HIV positive research participants and research staff. The thesis is composed of 11 chapters. The first chapter provides an introduction to the thesis, sets out the background, and provides the rationale for the current study. The second chapter provides an introduction to research ethics, by examining the key debates, recommendations, and guidelines on research conduct, and by discussing the ethical and theoretical perspectives in research, and how these relate to the current study.

Chapter three presents a review of the literature related to the research area. The chapter first explores the concept of stigma, focusing on experienced stigma and self stigma. Secondly, issues around closure of health related programs with a focus on the termination of close relationships in health related settings are explored. Furthermore, literature about termination of healthcare services is explored. Specific concerns about closure of research programs and HIV research in particular are examined, with an interest on the researchers' obligations and participants' needs. Evidence gaps are highlighted and the chapter concludes by providing the research aim and objectives, emerging from the identified evidence gaps.

Chapter four presents the methodology adopted for this study. The chapter presents the philosophical underpinning of the research, followed by the research design, under which the study sample, data collection, and data analysis procedures are described. The chapter concludes with a discussion about how the rigour of the research was maintained, how reflexivity concerns were addressed, and the ethical considerations for the research.

Chapter five presents a summary of the study findings. The chapter begins with a description of the socio-demographic characteristics of the respondents and the contextual characteristics of the included trials. The chapter further presents an introduction to the main findings of the research, highlights how various trials contributed to the key findings of the study and presents a summary of each of the main findings' chapters.

Chapter six presents the first main theme of the research findings, which relates to the perspectives of trial participants about trial closure. This chapter describes how HIV

post-trial participants experienced care as they navigated through the psychosocial and practical complexities associated with trial closure and re-establishing into usual care facilities in Uganda.

Chapter seven presents the second main theme of the study findings. This chapter presents findings related to the post-trial phase of the trial closure process, and describes how trial participants experienced and adapted to the post-trial contexts following trial exit. The chapter describes trial participants' accounts of how they negotiated through the complexities associated with accessing routine HIV care and treatment in the Ugandan public healthcare system, within a context of constrained financial abilities, ill health, and other domestic needs and responsibilities.

Chapter eight presents findings related to the perspectives of research staff on post-trial care. The chapter provides an account of how research staff engaged in various activities to provide post-trial care to trial participants, and highlights their views on some aspects of post-trial care where improvement is required.

Chapter nine presents a discussion of the study findings. This chapter presents a discussion of the ethical, moral, and practical considerations during closure of HIV clinical trials involving HIV positive participants in Uganda. The chapter deliberates on the main issues arising from this research, in light of the existing policy recommendations in HIV research and trial closure, and of the wider literature and debates in research ethics.

Chapter 10 presents a conceptual model based on the findings of the research, the Facilitated Transition model, which represents the process by which HIV positive trial participants transition from research to usual care facilities. The chapter also presents a theoretical interpretation of the research findings, in light of existing models of care and theories in research ethics.

Chapter 11 is the concluding chapter of this thesis. This chapter provides a summary of the study findings by highlighting the key contributions made in the area of HIV drug trial closure in Uganda, and by presenting the implications of the research findings to policy, practice, the role of the research nurse, education and training, and for future research. The chapter concludes by explaining the study limitations and strengths.

1.2 Rationale for the choice of the research topic

After three decades, HIV continues to pose significant threats globally (The Joint United Nations Programme on HIV/AIDS (UNAIDS, 2012b), Global Burden of Diseases (GBD) 2015 HIV collaborators, 2016). Whilst efforts to curb the epidemic have yielded considerable results, the innovations also come with some unintended/unforeseen challenges. For example, HIV drug treatments may cause unwanted effects, while the long term effects of HIV vaccines and new drugs may be unknown (Thomas, 1998). It has therefore become important to continuously evaluate HIV care and research programs, to elicit the experiences and/or concerns of those who partake of these programs and use this understanding to enhance the care and support offered to those who participate in this kind of clinical research.

In HIV clinical trials, the main ethical debates and concerns have been around the risk of people becoming HIV infected in HIV prevention trials, and the possible harmful effects of HIV treatment and/prophylactic interventions for participants in HIV treatment and prophylaxis trials, some of which may be long term. Such concerns have ethical implications for the researchers e.g. of caring for the people who become infected during prevention trials, and provision of the proven effective treatment (or prevention) interventions to research participants and the general public. More recently, the search for an HIV cure has seen more drug trials being conducted on individuals infected with HIV. Similar to prevention trials and trials for treatments, HIV cure research poses significant ethical concerns. Importantly, in addition to the above, HIV cure research may also pose concerns of the likely effects of drug holidays and interruptions (CDER, CBER, & FDA, 2014; Sylla & Garner, 2016). Such concerns raise the need to undertake qualitative studies, to evaluate the concerns, needs, and experiences of the different stakeholders, and of identifying good approaches for caring for those who may be affected.

However, although increasingly qualitative studies have been undertaken to assess the perspectives of stakeholders involved in HIV related research, the majority have involved hypothetical scenarios instead of actual HIV trial participants, while other studies have included other stakeholders such as members of the community, and have often left out those closely involved in the research process. For studies which have assessed real experiences of actual research participation, these have also mainly focused on the motivations for research participation or experiences during study conduct. To date, no known study has assessed the post-trial experiences of those involved in HIV drug trials in low income settings (Nalubega & Evans, 2015).

Having practiced in HIV research, I noticed that HIV drug trials could pose peculiar concerns which may necessitate post-trial care. For example; the need for continuity of HIV care and treatment may raise a concern as to how individuals access HIV services after leaving a trial while concerns associated with unknown side effects of trial drugs, especially those which may come up later in life, raise a concern as to how long participants should be monitored post-trial. In addition, since normally in low income settings research provides better health care than the usual care (Mano, Rosa, & Dal Lago, 2006), what does stopping research participation mean to an individual from a low income setting?

Although research conduct is carefully regulated, current debates and policies tend to be general, lacking specific guidance and regulation for HIV trials. Moreover, the available guidelines tend to be generic and applicable to global rather than contexts (Ananworanich et al., 2004). Whilst some guidelines have paid considerable attention to HIV research, these have majorly focused on areas such as informed consent, monitoring for side effects during trial conduct, compensation issues and research benefits, and provision of trial feedback. It is noteworthy that very limited guidance exists on how closure of HIV drug trials should be managed.

In order to contribute to policies in research, it is also very relevant to involve different stakeholders. Evidence has indicated that current debates and guidelines in research have mainly involved policy makers (Clouse et al., 2010), while very little is contributed by those actually involved in the research process, such as research participants and research staff. Contributions of stakeholders can be achieved by exploring their perspectives on the issue. Therefore, it is important that various voices are involved in contributing to policies which govern HIV research conduct. Doing this will hopefully improve our approach to HIV trial closure practice in Uganda and other related contexts.

1.3 Research context

1.3.1 Demographic characteristics

Uganda is a landlocked country, located in the Eastern part of Africa, in the sub-Saharan region. It is bordered by Kenya in the east, Sudan in the north, Democratic Republic of Congo in the west, and Rwanda and Tanzania in the south (MoH Uganda, 2012b; Uganda Bureau of Statistics, 2016) (Figure 1 below). The country has an area of 241,551 km², and is highly populated with approximately 34.6 million people (2014 estimate) (Uganda Bureau of Statistics, 2016) and a population growth rate of approximately 3.4% pa, which is mainly contributed to by the high fertility rate (of 5.89%) (MoH Uganda, 2012b;

The World Fact Book, 2015), short birth intervals, and high teenage pregnancies (Kamwesiga, 2011). The population pyramid is characteristic of a developing country, indicating high fertility and high mortality rates (Figure 2 below). The effects of the AIDS pandemic has contributed to lower life expectancy, higher infant mortality, higher death rates, lower population growth rates, and changes in population distribution, contrary to what would be expected (The World Fact Book, 2015). Despite this, Uganda's population continues to grow rapidly and is predicted to increase to 44 million by the year 2020 if the current fertility and annual growth rates are maintained (Kamwesiga, 2011).

Figure 1: Map of Africa showing Uganda

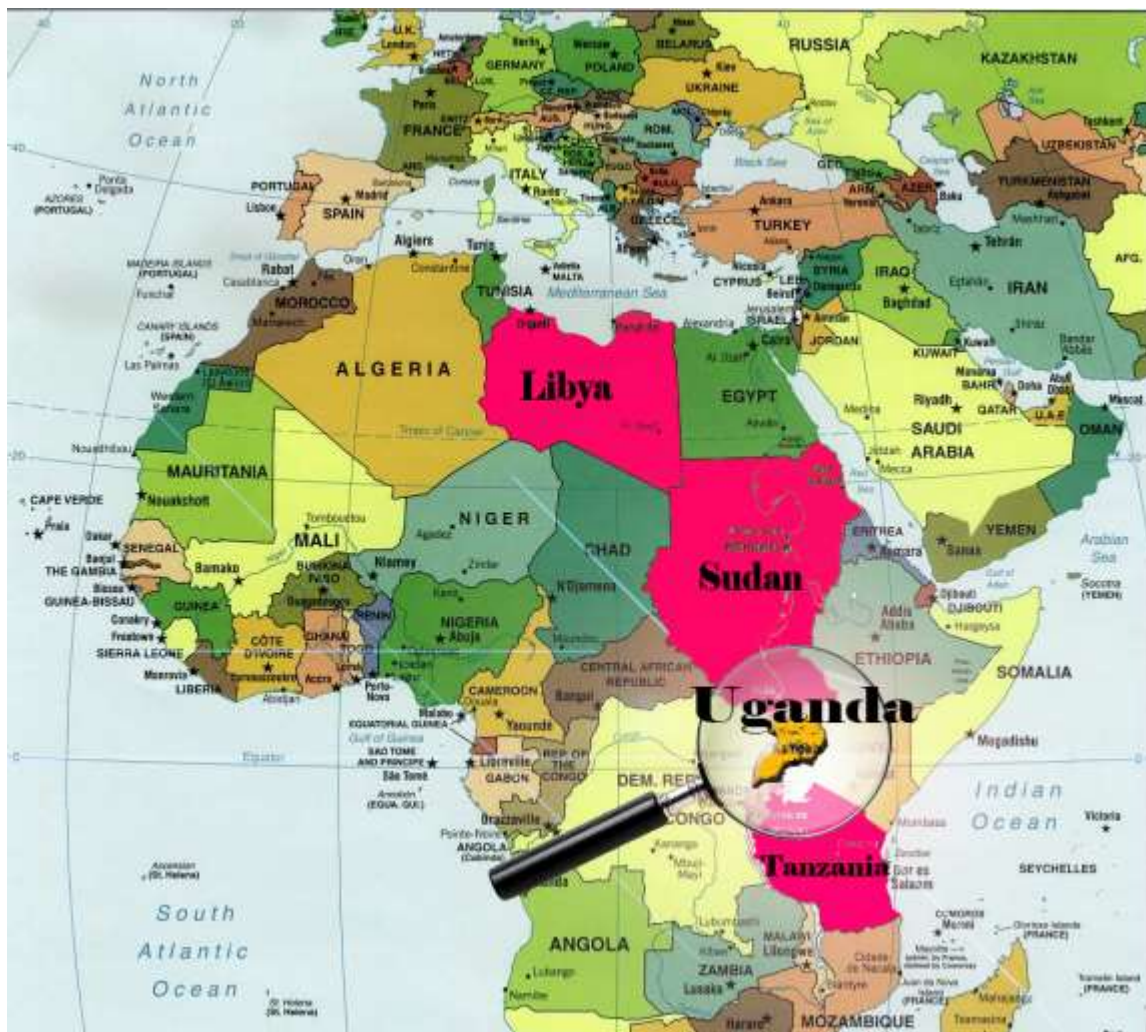


Image from google images free to use and share

Uganda is comprised of 111 districts, and consists of diverse ethnic groups and cultures, which are distinct from each other by their languages, food, cultural norms and traditions, and geographical locations (Uganda Bureau of Statistics, 2016). The country comprises of 3 main groups of people i.e. Bantu, Nilotics and Nilo hamites. The Bantu comprise of the majority of the population with approximately 50% of the total

population, and are the majorly located in the central, southern and eastern parts of the country (The World Fact Book, 2015). As previously mentioned, each tribe tends to have their own language; however, there are mainly three languages spoken in the country. i.e. Luganda, English, and Swahilli, with English being recognised as the official national language, while Swahili is slowly being promoted as a language to unify East Africans, with the new establishment of the East African Community (EAC) (The World Fact Book, 2015; Uganda Bureau of Statistics, 2016). Although 78.4% of the population are considered literate by their ability to read and write, very few people (approximately 30%), in Uganda are fluent in English, making communication within the country quite a challenge (The World Fact Book, 2015). The majority of the population (approximately 90%) stay in rural settings, and access to clean water and adequate toilet facilities still remains a challenge (MoH Uganda, 2012b).

Figure 2: Uganda 2014 population pyramid

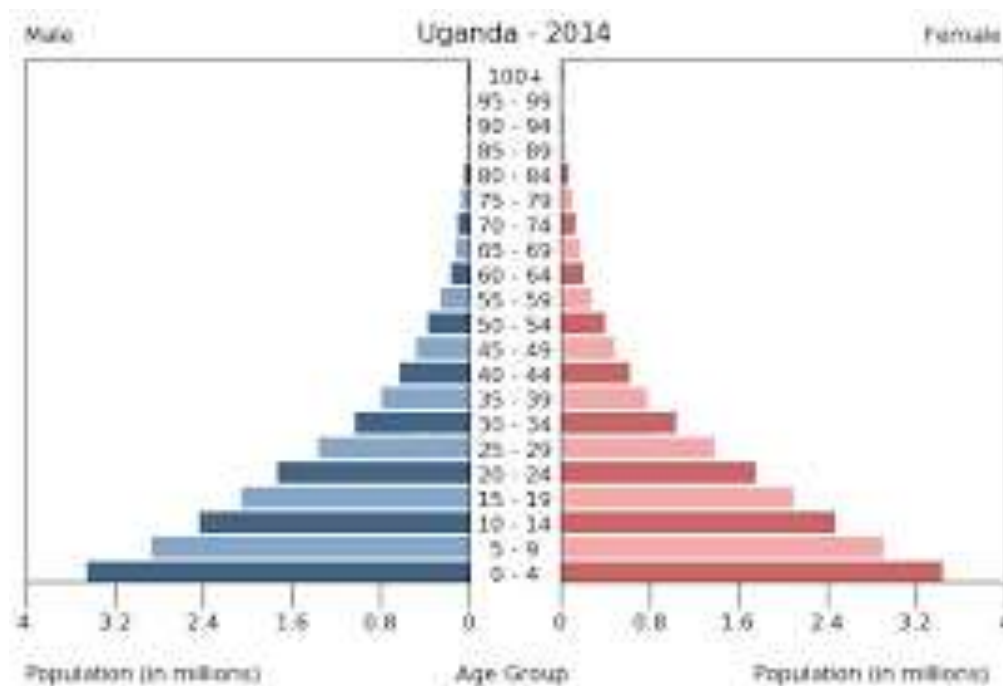


Image from google images free to use and share

Uganda gained its independence in 1962 under the reign of Milton Obote. The country has had series of political conflicts since its independence under different presidents, with the worst regime remembered being of Idi Amin Dada, who came to power in January 1971 (The World Fact Book, 2015). The political instability greatly contributed to under development of the nation and has grossly affected the health sector and other related systems (MoH Uganda, 2012b; The World Fact Book, 2015). President Yoweri Kaguta Museveni, the current president of the Republic of Uganda came to power in 1986, and during his reign, the country has experienced a period of political stability

compared to earlier regimes (The World Fact Book, 2015). However, the northern region has experienced a prolonged period of civil war, under a notorious rebel group of the Lord's Resistance Army (led by Joseph Kony). With the help of different international bodies, it was possible to negotiate for a cease fire, which saw some stability in the region.

The country is low income with a Gross Domestic Product (GDP) per capita of US\$ 501, and an economy growth rate of 5.1%. The country encourages foreign investors, and the private sector remains the main source of productivity (MoH Uganda, 2012b).

Approximately 70% of the employed population is within the Agricultural sector, while many other Ugandans engage in small scale businesses (MoH Uganda, 2012b). In the past 10 years, a gradual improvement in the country's economy is being realised, which is attributed to the sustained political stability in the country. In addition, Uganda's economic growth has been attributed to the aid from Western institutions and other financial institutions such as the World Bank (The World Fact Book, 2015), which has enabled many Ugandans to embark on a number of income generating activities. As a result, the livelihood of many citizens has been uplifted, and a great proportion of the population now lives above the poverty line from (MoH Uganda, 2012b). Uganda's National Development Plan (NDP II) is now aimed towards achieving a middle income status by 2020 (Uganda Bureau of Statistics, 2016).

However, at the present, unemployment still remains a key challenge to Uganda's economy, affecting many people especially the youth. For example, in 2009/2010, Uganda's unemployment rate was 4.2 percent compared to 1.9 percent observed in 2005/2006. Unemployment remains predominantly an urban problem as the unemployment rate in urban areas is more than three times that of their rural counterparts. In Kampala for example, unemployment was rated at approximately 10% in 2010 and was the greatest in all regions of the country (Uganda Bureau of Statistics, 2010). In the recent past, Uganda's economy has also been affected by the political instability in South Sudan, since Uganda is a key destination for Sudanese refugees and South Sudan is Uganda's main export partner. Unreliable power, high energy costs, inadequate transportation infrastructure, and corruption are also contributors to the poor economic development and investor confidence in the country (The World Fact Book, 2015). The country's challenging socio-economic situation is reflected in some of the key indicators such as the high mortality and morbidity rates, and the low life expectancy as shown in table 3 below.

Table 3: Uganda's key indicators compared to other countries

Adapted from: Ministry of Health (MOH) (2012), Uganda Health System Assessment 2011

Selected Indicators	Uganda	Sub-Saharan African Countries' Average	Low-Income Countries' Average
Total population	33,424,683	17,598,890	22,750,325
Population growth (annual)	3.21	2.50	2.10
Rural population	86.70	62.57	71.72
Fertility rate	6.24	5.00	4.70
Contraceptive prevalence rate	23.70	20.97	33.00
Life expectancy at birth	53.07	53.75	58.44
Under-five mortality ratio (per 1,000 births)	98.90	121.23	107.87
Maternal mortality ratio (per 100,000 births)	430	640	590
Adult literacy rate	73.21	N/A	N/A
Population with sustainable access to improved drinking water sources	67.00	59.72	63.11
Population with access to improved sanitation facilities	48.00	31.36	35.47
Prevalence of underweight among children under five	16.40	24.57	28.33
Prevalence of HIV total (% of population aged 15-49)	6.50	5.45	2.57

1.3.2 Healthcare delivery and systems in Uganda

Uganda's health care system is comprised of the public and private sectors. The public sector consists of national and regional hospitals, and a health centre system which is overseen by district level institutions. The national and regional hospitals offer specialised care and referral services and are managed by medical doctors and medical

specialists. The rural settings are mainly served by smaller units referred to as Health Centre II and III. These mainly offer unspecialised services such as treatment of common diseases and antenatal/maternity care, and are normally managed by registered nurses, registered midwives or clinical officers (Kamwesiga, 2011; Kavuma, 2009; MoH Uganda, 2012b). The private sector comprises of Private Not for Profit organisations (PNFPs), Private for Profit health care providers (PFPs), and Traditional and Complementary Medicine Practitioners (TCMPs) (MoH Uganda, 2012b).

The health care system especially in the public sector is characterised by a shortfall of health staff¹ (Kamwesiga, 2011; MoH Uganda, 2012b), and a lack of adequate resources such as drugs and other supplies which force patients to seek care from private facilities (Kavuma, 2009). However, the public services are free of charge and are accessible by most people within 5 kilometres on average (MoH Uganda, 2012b).

1.4 The HIV epidemic

HIV remains a significant global health threat. For nearly 30 years since the start of the epidemic, HIV/AIDS remains one of the most important health threats globally claiming the lives of millions of people worldwide. Globally, nearly 34 million people were living with HIV by the end of 2011 (UNAIDS, 2012b), while in 2012, the number increased to about 35.3 million people (UNAIDS, 2013). By the end of 2015, the global prevalence had raised to nearly 38.8 million people (GBD 2015 HIV collaborators, 2016) an indication of a steady global increase, although the distribution of these cases considerably varies among countries and regions of the world. This increase is not a bad indicator however, as it may reflect that more people live longer with HIV due to treatment measures such as Antiretroviral Therapy (ART). A report by UNAIDS (UNAIDS, 2012c, 2013) indicates that a majority of the people living with HIV, even in the developing world are now receiving ART which is helping them to live longer and healthier lives. This has been reflected in the steady decrease in the number of deaths over the years, which dropped from 2.3 million in 2005 to about 1.6 million in 2012 (UNAIDS, 2013), and further dropping to 1.2 million people in 2015 (GBD 2015 HIV collaborators, 2016).

HIV incidence is reportedly reducing in many countries. In 2013, UNAIDS (2013) reported a decline in the number of new infections of 33% from 2001 to 2012. A recent report by the United Nations (UN, 2014) indicated that there is a remarkable reduction of HIV infection in sub-Saharan Africa, evidenced by a reduction in new infections among

¹ Uganda has approximately a doctor to patient ratio of 1:24,000 and a nurse to patient ratio of 1:1,700

children of approximately 50% or more in seven countries in sub-Saharan Africa by 2013, while UNAIDS (2013) also reported a reduction in the annual number of new infections among adults and adolescents of 50% or more in 26 countries between 2001 to 2012.

The decrease in the HIV incidence has been attributed to a number of initiatives such as the Global Fund (Nahlen & Low-Beer, 2007), the President's Emergency Plan for AIDS Relief (PEPFAR), and the International Mobilisation to Combat HIV/AIDS (Coggin, Ryan, & Holmes, 2010; Vitoria et al., 2009), which have scaled-up various HIV/AIDS interventions, to reduce infection, illness, and death among communities mostly at risk, especially the developing countries (Nahlen & Low-Beer, 2007; UNAIDS, 2012c). These initiatives have led to an increase in the coverage of Antiretroviral Therapy (ART), and also to the implementation of various HIV preventive strategies such as eMTCT (Elimination of Mother to Child Transmission of HIV), ABC (Abstinence, Being faithful, Consistent and correct condom use), PrEP (Pre-exposure prophylaxis, and SMC (Safe Male Circumcision) (GBD 2015 HIV collaborators, 2016; UNAIDS, 2014).

Sub-Saharan Africa remains the most affected region by the HIV epidemic (Howard & El-Sadr, 2010; Mystakidou, Panagiotou, Katsaragakis, Tsilika, & Parpa, 2009; UNAIDS, 2012b; WHO, 2012), with approximately 25 million people currently infected. In 2015 alone, 1.8 million people (75.4% of all new cases) were in sub-Saharan Africa (GBD 2015 HIV collaborators, 2016). According to World Health Organisation (WHO, 2012), the sub-Saharan region accounts for nearly 75% of AIDS global deaths. A number of factors have been blamed for the continued spread of HIV in the sub-Saharan region. The most important ones include; HIV stigma, social-economic factors such as sex trade, male dominance, and violence; individual factors such as drug abuse and multiple sexual partners, (WHO, 2012, 2016), migration (McGrath, Eaton, Newell, & Hosegood, 2015), and inadequate utilisation of HIV preventive measures (Smit et al., 2005). These factors continue to hamper HIV prevention programs, thereby slowing down the efforts put in place to combat the epidemic.

In Uganda, HIV is the 2nd leading cause of death (after malaria) (Kamwesiga, 2011; MoH Uganda, 2012b). The HIV epidemic is described as generalised and stable for the past 5 years. Since 2011, HIV prevalence in the general population in Uganda increased from approximately 6.4% in 2004/5 to 7.3% by 2011 (Uganda AIDS Commission (UAC, 2012). These figures have remained relatively stable, as the 2013 HIV estimates also showed that HIV prevalence stabilised around 7.4% in 2012/2013 (MOH Uganda, 2015). Between 2011 and 2014, the estimated number of people living with HIV increased from

1.3 million to 1.5 million (MOH Uganda, 2015; The World Fact Book, 2015). Although the increasing figures have been attributed to new infections, similar to the global scene, an increase in the coverage of ART has also been associated to the increased prevalence of HIV in Uganda, as reflected in an increase in the number of HIV infected individuals accessing ART from about 330,000 in 2011 to about 750,896 in 2014 and a reduction in AIDS related deaths (MOH Uganda, 2015).

The HIV prevalence is reported to be higher among women (8.3%) than men (6.1%), while it is reported to be lowest among children under the age of 5 years (0.6%), a factor attributed to the recent eMTCT efforts (MoH Uganda, 2012b, 2015). Regionally, the central region continues to carry the highest prevalence rate (approximately 10.6%), while the mid-eastern region carries the lowest rate (estimated at 4.1%) (MOH Uganda, 2015; UAC, 2012).

Heterosexual transmission remains the dominant mode of HIV transmission estimated at 80%, Mother to Child Transmission stands the second at 20%, and other modes account for only 1% (UAC, 2012). Some of the identified risk factors for HIV transmission among Ugandans include; involvement in multiple sexual relationships, HIV sero-discordance, being infected with other sexually transmitted infections, urban residence, older age, female gender, involvement in transactional sex, being mobile, alcohol consumption, sexual and gender based violence, and poverty (MOH Uganda, 2015; UAC, 2012). These data call for a need to intensify interventions targeted at mitigating these risk factors.

Although new infections still occur, Uganda has registered an impressive reduction in the overall HIV transmission in the general population. A recent report by the Ministry of Health Uganda (MOH Uganda, 2015) showed a progressive reduction in the number of new HIV infections among adults over the past five years, from 160,000 in 2010 to 140,000 in 2013 and to 95,000 in 2014. Similarly, the report indicated that new infections among children had been progressively reducing from 31,000 in 2010 to 15,000 in 2013 and to 5200 in 2014. Another remarkable improvement noticed was the reduction of annual AIDS related deaths from 67,000 to 63,000 in 2010 to 2013 respectively, and to 31,000 in 2014 (MOH Uganda, 2015), a trend which is consistent with the global picture.

1.4.2 HIV services in Uganda

In 2011 World AIDS Day, the Ugandan president launched a program targeted at increasing the fight against the HIV epidemic. The goals of the program were; "(a) to

reduce HIV incidence by 30% by 2015, (b) improve the quality of life of People Living with HIV (PLHIV) by mitigating the health effects of HIV/AIDS by 2015 (c) improve the level of access of services for PLHIV, and other vulnerable populations by 2015, and (d) build an effective and efficient system that ensures quality, equitable and timely service delivery by 2015" (Uganda AIDS Commission (UAC), 2012 p2-3). These efforts indicate a serious commitment by the government of Uganda to respond to the epidemic. Through the health sector, the government has intensified the effort to mitigate the impact of the epidemic, which has been achieved through the provision of care, treatment, and support services (MoH Uganda, 2012a).

Uganda implements an HIV comprehensive care package comprising of: the provision of HAART (Highly Active Antiretroviral Therapy), prevention and treatment of opportunistic infections (OIs), Home Based and Community Based care and support, and integrated sexual and reproductive health services (UAC, 2012). These services are majorly provided by public and private facilities. The public facilities include health centres and hospitals, while the private facilities include for Profit and not-for profit institutions (Moreland, Namisango, Paxton, & Powell, 2013). Social support services are also provided to HIV affected households, to empower them with livelihood skills and opportunities for coping. Such services include material and financial support, and are usually provided by Non-Government Organisations (NGOs).

Cotrimoxazole remains the recommended routine prophylactic medication against opportunistic infections such as Pneumocystis Pneumonia (PCP) among all HIV infected individuals (MOH Uganda, 2015). The provision of HAART follows the national recommendation, which provides guidelines on ART initiation, and the regimens to be considered in different situations. In Uganda, initiation of ART among HIV positive individuals is implemented in all: adults and adolescents with a CD4 of <500 cells/mm³ irrespective of the clinical stage, individuals with active TB disease, Hepatitis B Virus (HBV) co-infection with evidence of severe chronic liver disease, HIV positive partner in a sero-discordant sexual relationship, most at risk persons (MARPs) e.g. those in fishing communities, commercial sex workers and long distance truck drivers, pregnant and nursing mothers, and all HIV positive children below 15 years irrespective of their CD4 counts or WHO staging (Riolexus, 2014). Nevertheless, the 2015 WHO guidelines on when to start ART among people living with HIV recommends initiation of ART in all HIV positive people irrespective of CD4 cell count (WHO, 2015). ARV Prophylaxis is also recommended for all breastfeeding HIV exposed infants for the full duration of breastfeeding (Riolexus, 2014). There are three regimes currently recommended for adults (and adolescents), i.e. first line, second line, and third line regimens, and two

regimes for children <15 years (first and second line) which vary according to the age and weight of the child.

The country has also integrated a joint TB/HIV management strategy to ensure adequate screening of all HIV positive people for active TB and testing for HIV among all individuals with active TB (MOH Uganda, 2015). Routine monitoring for all patients on ART is recommended once every 12 months, using viral load or CD4 count measures. The implementation of the recommended ART guidelines continues to be challenged by shortage of supplies, a shortfall of staff, and loss to follow-up of the patients (MoH Uganda, 2012a; Rioplexus, 2014). Addressing these challenges requires proper planning and a combined effort among various stakeholders. To enhance adherence to HIV treatment, it has been recommended that telephone text messages (SMS) be adopted as reminders to the patients (Rioplexus, 2014).

1.5 Conclusion

This chapter has provided an introduction to the proposed research by describing the research context, and providing an overview of the current trends on the HIV epidemic, both internationally and in the Ugandan context. The next chapter will provide an examination of the key ethical and theoretical issues in research conduct, with a particular focus on post-trial care.

CHAPTER 2: ETHICAL AND POLICY ISSUES IN RESEARCH

2.1 Introduction

Tackling the HIV epidemic has required an enormous, globally coordinated research effort. Much of this research has taken place in sub-Saharan Africa. Developing countries have been targeted for HIV clinical trials for a number of reasons, such as: the high prevalence/incidence of HIV in these settings, having readily available and willing volunteers (Lairumbi, Parker, Fitzpatrick, & English, 2012; London, Kagee, Moodley, & Swartz, 2012; Silverio, 2006), and the need to help the poor countries to find interventions that can be suitable and affordable in their settings (Silverio, 2006). Additionally, people in the low income countries have been shown to easily accept HIV research participation, a situation attributed to the level of poverty and the poor healthcare systems in these settings (Silverio, 2006).

Although ethical concerns related to HIV research are of global concern, research conducted in the low income settings has been of particular concern. In low income settings, various circumstances such as the low socio-economic status, low literacy levels, and poor healthcare delivery are likely to increase the vulnerability to exploitation of the research participants in these settings (MacQueen et al., 2007). HIV research therefore requires a high level of ethical regulation globally, while a particular focus should be paid to research conducted in the low income settings.

Most of the policy guidelines have attempted to address the key issues pertaining to clinical research in general, although some have been established to address HIV-specific issues. The main areas of focus in research regulation have been on: (i) ensuring informed consent among participants, (ii) the researcher's obligations to provide treatment and care to research participants during research conduct, (iii) compensations for injuries incurred during trial conduct, and (iv) post-trial access to medications. In addition, some stakeholders have suggested the need to specifically address issues related to research in low income settings (Benatar, 2002; Ezekiel J Emanuel, Wendler, Killen, & Grady, 2004; Faden & Kass, 1998). In recent years, there has been a growing interest on general post-trial obligations of researchers to research participants, although this still remains an under researched/debated area (Nalubega & Evans, 2015).

This chapter focuses on the key ethical and theoretical perspectives in research conduct. The first section focuses on how research conduct is regulated in Uganda. The second section presents the key ethical guidelines in research conduct, with a particular focus on

post-trial care, while the third section presents the theoretical perspectives in research regulation, focusing on the universal ethical principles and key ethical theories.

2.2 Research regulation and conduct in Uganda

In Uganda, HIV research has been mainly pioneered by Non-Governmental Organisations working in partnership with overseas universities, HIV funding agencies, and research institutions. Some of the prominent institutions involved in HIV research in Uganda include: The AIDS Support Organisation (TASO), Infectious Diseases Research Collaboration (IDRC), Makerere University-John Hopkins University (MUJHU), Infectious Diseases Institute (IDI), Mulago-Mbarara Teaching Hospitals' Joint AIDS Program (MJAP), Medical Research Council/Uganda Virus Research Institute (MRC/UVRI), and Joint Clinical Research Institute (JCRC).

2.2.1 Research regulation

The research activities in the country are regulated at both the national and institutional levels and are intended to ensure that the research conducted is ethical, and that the rights, interests, values and welfare of research participants are respected (UNCST, 2014a). Uganda National Council for Science and Technology is the national regulatory body which conducts registration and approval of all research activities in all sectors (UNCST, 2014b). The Institutional Review Committees (IRCs) are the main institutional regulatory bodies, mainly located at teaching or research institutions, and are responsible for conducting initial and continuing review and approval of research projects (UNCST, 2014a). UNCST is responsible for accrediting the IRCs, usually after every 3 years, and monitoring their activities (UNCST, 2014b).

In addition, there are other regulatory bodies at institutional levels. These include; the National Drug Authority (NDA) which regulates the safety, quality, efficacy, handling and use of drugs or drug related products in research, the Scientific Committees (SCs), Data and Safety Monitoring Boards (DSMBs), the Institutional Bio-safety Committees (IBCs), and the Community Advisory Boards (CABs) (UNCST, 2014b). CABs are composed of members from local authorities such as community, peer, and religious leaders, representatives of the study populations, and the media. These boards are important forums for facilitating dialogue between community members, study volunteers and researchers.

2.2.2 Care during research participation

The health care provided to participants during research varies considerably among individual trials. Usually, this care is determined in advance of trial conduct and is guided by general principles, set by the regulatory authorities such as the RECs, the sponsors, and others. The nature of care also depends on the nature of the trials i.e. the risks, type of interventions, and the bargaining power of the local authorities, usually representing the participating communities. At the minimum, the standard of care in research should not be lower than that provided in public healthcare. UNCST, a research regulatory authority in Uganda, recommends that research participants can be provided extra care/treatment unrelated to research procedures, although this is not mandatory (UNCST, 2014a).

The main aspects of care provided in research studies include: prompt and adequate medical care and treatment for various illnesses for individuals and sometimes their families, prompt and adequate medical check-up, and financial and material incentives e.g. transport facilitation and meals (Nalubega & Evans, 2015). Although some of these are not in the real sense benefits, previous research has shown that many participants regard these as research benefits. In many research studies, the quality of health care provided in research has been a major motivation for research participation (MacPhail, Delany-Moretlwe, & Mayaud, 2012; Nalubega & Evans, 2015).

In low income settings such as Uganda, the care provided in research is often of a higher standard compared to the one provided in the public healthcare facilities. This sometimes may be feared to cause ethical conflicts, as it may unduly influence or coerce potential participants into accepting to participate in the current study or in future research (Largent, Grady, Miller, & Wertheimer, 2012; Roche, King, Mohan, Gavin, & McNicholas, 2013).

2.3 Policy and regulatory guidelines on post-trial care

Post-trial obligations have become an issue of concern in research ethics. The main concern in this area has been to establish the need for, and extent to which, researchers may be obligated to research participants after research closure. Although still an under researched (and also under debated) area, in recent years, there has been a growing interest in post-trial care. Sukovski (2003), argues that post-trial considerations must not be neglected as they also constitute a part of the clinical trial.

Schroeder (2008) refers to post-trial obligations as “a duty by research sponsors to provide a successfully tested drug to research participants who took part in the relevant clinical trials after the trial has been concluded” (Schroeder, 2008 p.63). However, in some types of research especially those involving chronic conditions such as HIV, post-trial obligations may necessitate going beyond the provision of trial products. For example, in HIV research, some research participants are HIV positive (or have become HIV positive during the trial) and will require continued lifelong HIV care. These people may also need long term support to deal with other potential HIV related risks or harms (e.g. the social consequences of HIV stigma). Therefore, in such groups, there is a need for continued/lifelong provision of HIV treatment, care and support, which requires referral and adequate linkage to alternative care facilities, and follow up beyond the period of trial closure. In addition, the need for monitoring and compensation for unwanted adverse effects from trial interventions, and provision of trial feedback have been key concerns in post-trial ethics. These issues are elaborated on in the following sections.

2.2.1 Linkage to care (referral)

For the majority of HIV trials, participants will receive all their care and treatments within the research facilities. Appropriate linkage to alternative services after trial closure is therefore important to facilitate continuation of the required treatments for HIV infected participants. Uganda National Council for Science and Technology (UNCST, 2007, 2014a) recommends that for participants who require further care after research participation, referral and follow-up mechanisms should be instituted to ensure quality case management services. UNCST maintains that investigators are responsible for referrals to local services that provide an acceptable level of care, while Rennie and Sugarman (2009) suggest that when no adequate referral units currently exist, investigators should work together with local health authorities to try and build the local capacity where clients can be referred. This however may have political and logistical implications which may be a key concern in low income settings.

2.2.2 Provision of trial interventions

The World Medical Association states that study participants are entitled to share any benefits that issue from research, including interventions identified as beneficial (Rennie & Sugarman, 2009; World Medical Association, 2013). Similarly, Uganda National Council of Science and Technology (UNCST, 2007, 2014a) underscores the importance of continued post-trial care of trial participants following trial closure. Whilst this is accepted as an important general principle, there is ongoing debate regarding who

should provide these benefits and for how long this should be done. The Parliamentary Office of Science and Technology (POSTNOTE, 2008), a governing body of public policy issues related to science and technology in the UK, recommends the sharing of this responsibility among different stakeholders such as the drug companies/funders, governments, Non-Government Organisations (NGOs), and researchers. However, most commentators argue that the biggest responsibility rests on the researchers (Barsdorf, Maman, Kass, & Slack, 2010; Dainesi & Goldbaum, 2012; Essack et al., 2010; Schuklenk, 2010). Although UNCST supports this notion, they recommend that sponsors are not obligated to provide lifelong care and treatment for chronic illnesses (UNCST, 2007, 2014a).

2.2.3 Monitoring and compensation for research related injuries

Biomedical research has been associated with a number of unknown risks. The key risks associated to HIV research have been identified as: physiological effects (e.g. vaccine induced sero-positivity), physical effects (e.g. adverse effects of trial interventions and pain due to research procedures), psychological effects (e.g. fear of unknown trial effects), social effects (e.g. facing stigma and discrimination resulting from trial participation), and economic effects (e.g. costs incurred in research such as transportation costs or loss of work due to clinic attendances) (Dhalla & Poole, 2011). Therefore, in addition to compensation for trial-related biological/medical injuries as many commentators recommend, UNAIDS (2012a) argues that HIV research should also consider appropriate compensation for social, psychological or economic harms. In addition, UNAIDS argues researchers to specifically indicate in the research protocols the nature and extent of all suspected/potential harms from HIV prevention trials and indicate the measures put in place to mitigate these (UNAIDS, 2012a).

Regarding the care for injuries incurred during research participation, UNCST (2007, 2014a) argues that participants should be provided with the highest attainable standard of care within the country, and that researchers are obliged to ensure that all adverse events related to the study are fully resolved. For participants who suffer from social/psychological harms, it is recommended that these should be referred for ongoing psycho-social services, including counselling, social support groups, and legal support (UNAIDS, 2012a). The Canadian Association for HIV Research (CAHR), (2008), argues that it is the responsibility of all researchers to ensure that foreseeable harms do not outweigh the anticipated research benefits, necessitating researchers to have knowledge of possible adverse effects from the respective trials.

2.2.4 Providing trial feedback

Many regulatory bodies and commentators (E. J Emanuel, Wendler, & Grady, 2000; Fernandez et al., 2012; Rennie & Sugarman, 2009; UNAIDS, 2012a; World Medical Association, 2013) recommend that researchers inform trial participants and their communities of the trial results. These observe that the formal dissemination of research results expresses the values of respect for persons and communities who contributed to the research. Whether and how this aspect is implemented in practice still remains an important question, especially with regard to HIV related research.

Whilst recommendations for ensuring ethical research conduct have been made, it has been argued that many debates have taken place without adequate participation of low income countries (Ananworanich et al., 2004). Moreover, existing research guidelines tend to be generic and offer little detail to guide practice in the specific context of HIV drug trial closure. Several authors (Ciaranello et al., 2009; Dainesi & Goldbaum, 2011; Sofaer & Strech, 2011; Wang & Ferraz, 2012) have called for more debate to develop appropriate guidelines, in order to address the pertinent issues in the field, focusing on the needs of the individuals in these settings. Research is needed to inform the development of such standards.

2.4 Ethical and theoretical perspectives in research conduct

The above section has focused on the regulatory and policy guidelines regarding post-trial care. Action on these issues requires a theoretical understanding of research ethics. This section examines the concepts of morality and ethics, presents the ethical principles that guide research conduct, and discusses how the implementation of the ethical principles can be achieved through the application of ethical theories.

2.4.1 Morality and Ethics

Though difficult to independently define and generally used interchangeably, the concepts of ethics and morality do carry different meanings in society and have significant differences (Butts & Rich, 2013; Sproul, 2015). Broadly, these two concepts relate to what is considered right and wrong or good and bad conduct or behaviour of individuals in society (Sproul, 2015).

The concept of ethics can be explained as the rules provided (by an external source, as opposed to an internalised code of conduct), which enable one to distinguish what is right from wrong, and aim to guide conduct/behaviour in society (Butts & Rich, 2013; Surbhi, 2015). Conversely, morals refer to generally accepted standards of behaviour in

a particular society, that individuals tend to adopt and accept as their own, which eventually shape their character while trying to make sense of what is right or wrong (Surbhi, 2015). Hinde (2004) explains that ethical standards are more related to the laws governing society, while morality tends to relate more to the interpersonal, cultural and societal norms which shape character. While ethics tend to define the code of conduct that a society should adhere to, morality stems from a deeper-internal level, shaped by both personal and spiritual standards (Sproul, 2015). Some authors have suggested that emotions have a great role to play in shaping one's moral perspectives (Bankard, 2015; Ugazio, Lamm, & Singer, 2012), implying that one's moral standards can be shaped by how an individual feels about a particular situation. This may also be viewed however as a weakness in shaping character, as some argue that emotions are so personal and can be misleading (Bankard, 2015).

In trying to clarify the meaning of the concepts of ethics and morality, authors have explained how the two concepts differ. One difference, as explained by Surbhi (2015), relates to the flexibility in application of the principles related to the two concepts. According to Surbhi (2015), ethical principles are more stable (rigid) standards and generally take a long time to change. As opposed to ethics, moral principles, while they may be broadly accepted by the majority in society, can be flexible in their application at an individual level and can change over short periods of time.

Another dimension in which authors have identified a significant difference between the two concepts, relates to how they apply to gender. Dawson (1995), in her paper entitled 'Women and Men, Morality and Ethics', concluded that women may tend to make more moral decisions while men may make more ethical decisions on a similar subject. For example, while making decisions, men are likely to consider the set organisational standards, rules, values, rights and impartiality, while women are more likely to put into consideration how others may feel about their decisions and who their decisions may hurt. Women are also more likely to be guided by emotions and try to make decisions which minimise harm, even if these decisions may contradict authority.

Saxen (2017) also explained an important dimension relating to how ethics and morality can differ, which relates to how ethics and morality can influence professionalism in the medical and nursing professions. According to the author, physicians tend to base their practice on the universal ethical standards, which are more rigid and support objectivity. Nurses on the other hand are seen to align more with flexible and sometimes subjective standards, which are more akin to moral standards.

Nevertheless, despite the differences, there is a connection between these two concepts. This connection mainly lies in how the two concepts can influence one another. Butts and Rich (2013) explain that moral standards are often judged through an ethical lens. For example, some behaviours which may have been accepted as moral in some societies (such as slavery), after undergoing an ethical check, have been declared (and accepted) as immoral in modern day society. Hence, ethics is generally the standard unto which morality can be judged; and while both standards are important in society, ethics appears to be more acceptable in shaping behaviour.

2.4.2 The ethical principles in research

There are four well recognised ethical principles that are used to guide research conduct. These are autonomy, beneficence, justice and non-maleficence and are described in table 4 below. The ethical principles are an obligation for all researchers to fulfil in research involving human subjects. However, as general principles, they may not be applicable in exactly the same way in all contexts. For example, the meaning of 'informed consent' may differ according to the stakeholders involved and the socio-cultural context (Beauchamp & Childress, 2001). Thus whilst application of ethical principles is considered essential for good research conduct, the process of implementation may, in reality, be quite challenging. Hence, it has been argued that use of ethical theories may provide a useful perspective with which to consider the implementation of ethical research principles (Held, 2005). The following section provides an overview of some ethical theories and how they can be used to guide the implementation of ethical principles.

Table 4: The four fundamental ethical principles

Adapted from: Beauchamp and Childress (2001). Principles of biomedical ethics. Oxford, University Press

Principle	Description
Autonomy	This principle requires researchers to ensure that each individual makes an informed decision regarding participation in research. The principle underpins the meaning of informed consent, which entails giving as much information as possible about the research so that prospective participants can make an informed decision about their involvement. This principle also requires that research staff are made fully aware of the proposed research and its potential risks to them.

Beneficence	This principle requires researchers to maximize benefits for research participants and/or society while minimizing the risk of harm.
Justice	This principle demands equitable selection of research participants and ensuring that participant populations that may be unfairly coerced into participating are avoided.
Non-maleficence	This principle ensures that researchers first of all do no harm. This is similar to beneficence, but deals with situations in which neither choice is beneficial. In this case, a person should choose to do the least harm possible and to do harm to the fewest people.

2.4.3 Ethical theories

Ethical theories are often represented as falling into two main categories (Beauchamp & Childress, 2001), the traditional/dominant moral theories (e.g. Consequentialism, Deontology and Virtue ethics), and the ethics of care theory. These are described in table 5 below.

Table 5: The ethical theories

Adapted from: Beauchamp and Childress (2001). Principles of biomedical ethics. Oxford, University Press and Held (2005). The Ethics of Care, Personal, Political, and Global. Oxford Scholarship Online

Theory	Description
Consequentialism	This theory is concerned with the outcomes of actions. It believes that the right action is the one that has the best overall consequences for individual welfare. Thus if the overall research benefits outweigh the harm, the research would be considered ethical.
Deontology	This theory is concerned with the fulfilment of duties, and believes that an action is right only if it complies with universal rules/principles. It also puts emphasis on individual rights such as autonomy, confidentiality, privacy and respect.
Virtue (ethics) theory	This theory is concerned with the character or nature of the agents. It assumes that the right action is the one that would be performed by a virtuous (respected) person (e.g. doctor, researcher, graduate student).
Ethics of Care Theory	This theory puts emphasis on contextual factors in implementing research ethics, and considers care as a responsibility informed by social values, dialogue and

	negotiation; acknowledgement of power relations, and recognition of the self within the ethical negotiations.
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All ethical theories strive to achieve the ethical principles by providing a framework under which the principles can be implemented (Held, 2005). The traditional moral theories believe that to be morally acceptable, the ethical principles should be applicable universally and impartially (Bloch & Green, 2006; Held, 2005). This can be problematic. For example, in research, although it is possible to produce generalisations about how a given research situation may be approached, these may not be exhaustive enough to provide helpful guideline to all cases (Beauchamp & Childress, 2001).

On the other hand, whilst trying to maintain universal ethical standards, the Ethics of Care Theory, in addition, emphasises the importance of relationships, the role of emotions, and putting contextual factors into consideration while implementing the ethical principles (Beauchamp & Childress, 2001). Proponents of the Ethics of Care Theory argue that it is paramount to have an insight into the needs of people and to attentively consider the different circumstances facing them while meeting the ethical standards (Fry, 1989; Green, 2012). For example, while trying to ensure autonomy, one may need to think of situations in which the right to autonomy may be compromised. Situations such as ill health, poverty, and/or a culture where patients entrust their lives to health care professionals may significantly affect how the principle of autonomy will be achieved. These situations are likely to be true for HIV research involving HIV positive individuals and conducted in low income settings. In another example, the Ethics of Care approach will suggest that providing informed consent in a low literate population may require more explanations or use of translators, which will improve the understanding of the research and contribute to a more informed decision for such participants. It can be argued that the Ethics of Care theory therefore allows a more patient (participant) centred approach to research ethics (Green, 2012), which can lead to a more culturally appropriate and contextually relevant and acceptable research practice.

Carol Gilligan, a proponent of the Ethics of Care theory, expressed in an interview that the Ethics of Care theory helps one to make ethical judgements/decisions, in consideration of the contexts in which such decisions are made (Gilligan, 2011). According to Fry (1989), caring ought to be the foundational value for any ethical theory, and as such, caring as a moral value should be the foundation for research ethics. Although the understanding of care might include a diverse range of opinions, there are common features which are recognised by different commentators. For example, care strongly involves relationships, a need to alleviate another person's vulnerability, and

showing concern, empathy and responsibility for others. These should also be undertaken within an environment of culture, and society, shaped by political and structural realities (Green, 2012; Lachman, 2012 ; Paulsen, 2011), and also acted (Held, 2005; Paulsen, 2011).

With a personal interest in caring mainly attributed to my nursing background, the Ethics of Care Theory appears particularly relevant to my research inquiry. The theory offers a useful perspective of looking at the findings of the current study, given the nature of the target group for this research, which is essentially a vulnerable group. The approach adopted for this study also aligns well with the Ethics of Care theory, as it seeks to generate theory inductively, basing on the perspectives of the respondents. Generating theory this way will be helpful in uncovering the key issues which are important to the population under study, which will be a basis for recommendations on improving post-trial care among HIV positive trial participants in Uganda. This will hopefully offer a new way of looking at some of the gaps in our existing understanding of research practice, with a particular focus on how individual care needs of an HIV positive trial participant in a low income setting can be met.

2.5 Conclusion

This chapter has presented some of the key issues related to research ethics and regulation, with a special focus on post-trial care. An overview of the theoretical perspectives in HIV research ethics has also been presented. The following chapter provides relevant research literature related to the proposed study, to highlight the important gaps existing in the area of HIV post-trial care.

CHAPTER 3: LITERATURE REVIEW

3.1 Introduction

The previous sections have set out the background for this research. Information on the current HIV general and research related issues have been presented. In addition, important regulatory, ethical, and theoretical issues in research have been presented. This chapter will provide a review of existing literature on the views, experiences, and/or practices related to post-trial care.

In July 2013, as part of my MSc dissertation, a comprehensive systematic literature search was conducted on several data bases, to identify research articles related to the experiences/perspectives of HIV research participants in sub-Saharan Africa. The databases included; CINAHL, MEDLINE, Pub-med, ASSIA, PsychInfo, Web of science, EMBASE, The Cochrane library, Joanna Briggs Institute library and African Index Medicus. The search strategy developed for this search is presented in table 8 below. In addition, hand searching was done to identify relevant literature from books, journals, and other internet sources such as Google web and Google scholar. The search for published literature yielded a total of 8344 articles which were screened on title, abstract, and on full text, to identify papers which met the inclusion criteria for the systematic review. Seventeen papers met the inclusion criteria from the systematic search and four more papers were added from grey literature, making a total of 21 papers included in the systematic review. A synthesis of qualitative literature was then undertaken to identify the views and experiences of HIV research participants in sub-Saharan Africa, in which five main themes were generated as shown below:

- (i) Individuals are motivated to participate in HIV research due to a range of perceived benefits for themselves and others
- (ii) Participation in HIV research can be associated with considerable fear and uncertainty
- (iii) Participation in HIV research is strongly influenced by social relationships (e.g. support or disapproval of family or friends) and social-economic and domestic factors (such as time or finances)
- (iv) The meanings of research programs and processes are constructed within a context of existing lay beliefs, experiences and social relations associated with HIV and biomedical interventions in general. This means that local people may understand research and its processes very differently to health professionals

- (v) Participants' research experiences and their continued participation in HIV research are influenced by the research clinic context and the nature of their interactions with research staff

The review identified a gap in the knowledge of post-trial care, which informed the focus for the current study. The findings of this systematic review were published in 2015 (Nalubega & Evans, 2015).

An update of the literature based on the search strategy presented in the table below, was constantly done throughout the course of the PhD study. The subsequent literature searches did not identify any studies related to participants' experiences of post-trial care in HIV research in low income settings. Due to the lack of evidence on the studied topic, a broader literature search was also undertaken to identify the key conceptual information on the studied area, and to set the background for the research. This search generated two main themes which included 'termination of close relationships', and 'termination of healthcare programs', which, together with the literature generated through the systematic search, formed the literature review chapter.

Table 6: Search strategy

Key concept	Synonyms/ related terms/alternative forms for key words
Views and experiences	View*, experience*, understand*, comprehen*, concern*, opinion*, attitude*, perspective*, belie*, knowledge, perception*
Research Participants	Research participant*, research subject*, study participant*, study subject*, healthy volunteer*, trial participant*, trial subject*, lay people, community member*, public, opinion leader*, stake holder*, client*, patient*, family member*
HIV research	HIV, HIV? AIDS, AIDS, malaria, TB, tuberculosis, vaccine trial*, health? related research, health research, health service* research, biomedical research, research, clinical research, medical research, clinical trial*, social science research, health survey*, experimental stud*
Sub-Saharan Africa	Sub? Saharan Africa , Africa, African countries, low income countr*, resource limited countr*, resource limited setting*, developing countr*, non? Western countr*, developing world, under? developed countr*, poor countr*, low resource setting*, third world nation*
Informed consent	Informed consent, consent*, ethic*, bioethic*, participation

This chapter is presented in five main sections. The first section examines the concept of stigma, with a focus on experienced stigma and self stigma. The second section reviews research evidence related to termination of close relationships. The third section reviews literature related to termination of healthcare programs. The fourth section presents literature pertaining to the termination of research programs, and highlights the key issues in post-trial care. The fifth section presents the conclusions and the research gaps

identified in existing literature. The aim and objectives of the current study are also presented in the last section.

3.2 Stigma: Self-stigma and experienced stigma

Broadly, stigma can be understood as a negative phenomenon in which an individual or a group is treated differently or is excluded from society. Social (experienced) stigma refers to extreme disapproval of (or discontent with) a person or a group based on certain social characteristics or behaviours that are perceived, and serve to distinguish them, from other members of a society (Catona, Greene, Magsamen-Conrad, & Carpenter, 2016; Crocker & Major, 1989; Goffman, 1963). Individual society members may hold negative attitudes, stereotypes, and beliefs, against members thought to possess particular characteristics different from the mainstream society, which results in discrimination against such members (Crocker & Major, 1989).

Hence, social stigma occurs when individuals or certain minority groups are excluded or treated differently from others, which might deny such individuals their rightful opportunities, such as employment, housing, and even health-care (Catona et al., 2016; Parker & Aggleton, 2003). Attributes associated with social stigma often vary depending on the geographical, political and socio contexts, although some characteristics have been associated with this type of stigma. Individuals with mental disorders, physical disability, and various diseases such as HIV, TB, and leprosy have commonly been stigmatised in society (Arrey, Bilsen, Lacor, & Deschepper, 2015; Crocker & Major, 1989; Goffman, 1963). Other important characteristics which may predispose an individual to social stigmatisation can include their: sexual orientation and gender identity, nationality and ethnicity, social class and wealth, religion, and physical outlook or beauty (Crocker & Major, 1989).

Self-stigma

Self-stigma is a personal response to a perceived negative situation. It is an internalised stigma that destroys one's self esteem, by individuals believing that they are not good enough to fit in society (Hing & Rusell, 2017). Individuals experiencing self-stigma possess feelings of shame and guilt when they (are made to) believe they do not fulfil certain criteria, to be full members of a society (Catona et al., 2016; Hing & Rusell, 2017). These individuals may lose hope of trying out new opportunities or pursuing goals, often as a protective mechanism from painful experiences of social stigma (Hing & Rusell, 2017). Thus, self-stigma is likely to be influenced by experiences of social stigma and discrimination. Indeed, according to the findings of a study by Hing and Rusell (2017) which assessed the effect of anticipated and experienced stigma on self-stigma,

authors established a strong positive influence of anticipated and experienced stigma on self-stigma. These authors concluded that self-stigma arises from an internalisation of anticipated or experienced stigma, findings which other authors (Catona et al., 2016; Crocker & Major, 1989) support.

When individuals experience self-stigma, they manifest particular characteristics such as: setting unrealistic goals, feeling shame and guilt, allowing negative feelings take control of them, resort to avoidance tactics, lose confidence and motivation, start to withdraw from others, and eventually may become isolated and lonely (Hing, Nuske, Gainsbury, & Russell, 2015). In addition, self-stigma can result into secrecy, which eventually may lead to failure to seek healthcare, in fear of disclosure of their situation (Hing et al., 2015; Neuman et al., 2013).

In an attempt to challenge and overcome self-stigma, it is recommended that individuals: identify and interact more with supportive people, try to avoid those who bring them down, try to identify, acknowledge and value their strengths, make an effort to engage in positive and beneficial activities, and notice their negative feelings and challenges (Dowshen, Binns, & Garofalo, 2009; Neuman et al., 2013).

HIV stigma

Although various interventions have been geared towards minimising HIV related stigma, people living with HIV (PLHIV) still experience stigma and discrimination in this era. HIV stigma emanates from factors associated with the sexual nature of its transmission and the perceived transgression of moral boundaries. As various authors note, the stigma associated to HIV is driven by factors such as the public negative feelings of the condition, the chronicity and incurable nature of the condition, and associated factors to its transmission such as promiscuity, being gay, injectable drug use, and sex work (Arrey et al., 2015; Parker & Aggleton, 2003). These associated factors may also be socially unacceptable and/or may carry their own stigma which worsens HIV stigmatisation (Parker & Aggleton, 2003).

The manifestations of HIV stigma have been found to take various dimensions. Parker and Aggleton (2002) observe that policies related to HIV and some behaviours directed towards HIV positive individuals reflect stigmatisation. For example, HIV criminalisation, mandatory HIV testing, exclusion of people from certain jobs due to their HIV positive status, prohibition of travel, and compulsory screening/treatment of HIV infected people may carry stigma implications. It is also noted that HIV stigmatisation is widespread and reported in many social settings such as community gatherings, workplaces, schools,

places of worship, in the family context, and even health care settings (Donnelly et al., 2016; Dos Santos, Kruger, Mellors, Wolvaardt, & van der Ryst, 2014; Neuman et al., 2013; Parker & Aggleton, 2002). For example, in a study by Neuman et al. (2013), which investigated stigma related experiences among HIV positive people and their access to health care in four sub-Saharan African countries, reported a 10.4% prevalence of health care discrimination of the affected people. In another study to establish the experiences of HIV-related stigma among gay men, Dowshen et al. (2009) reported that individuals experienced stigma in various ways, which included both social and self-stigmatisation.

The impacts of HIV stigma experiences, (both social and self-stigma), still pose a significant challenge towards HIV treatment adherence. The main impacts reported in literature include low self-esteem, social exclusion, depression, and loneliness (Arrey et al., 2015; Dowshen et al., 2009). These impacts reinforce concealment of HIV status, resulting into reluctance to seek treatment/care, and undermining social support (Arrey et al., 2015; Catona et al., 2016; Donnelly et al., 2016; Dos Santos et al., 2014; Dowshen et al., 2009). Efforts to reduce HIV stigma and discrimination remain relevant in the management of HIV/AIDS in order to enhance positive treatment outcomes (Donnelly et al., 2016; Mhode & Nyamhanga, 2016). Such strategies should aim to implement socially/culturally-adapted stigma reduction strategies, that will improve support services for affected individuals (Arrey et al., 2015; Parker & Aggleton, 2003). Parker and Aggleton (2003) recommend that understanding and approaching HIV stigma as a social problem will go a long way in addressing it, while Dowshen et al. (2009) recommend that service providers should aim to address disclosure concerns.

3.3 Termination of close relationships

Because closure of research studies involves termination of a researcher-participant relationship which may be close (Unguru, Joffe, Fernandez, & Yu, 2013), it is relevant to review literature that has focused on termination of close relationships. This section examines research evidence related to the effects of termination of close relationships in various care settings.

The relationship developed between a patient and a health worker² can be strong, and as such its termination may involve strong emotions which may be both negative and/or positive (Fortune, 1987; Wilson, Elkan, & Cox, 2007). The negative reactions may include fear, sadness, anger, feelings of loss, and mourning (Fortune, 1987; Fortune,

² To be consistent, the term health worker will be used to mean a health worker, doctor, physician, nurse, therapist, etc.

Pearlingi, & Rochelle, 1992; Orgel, 2000), while the positive ones may include feelings of happiness, confidence and satisfaction due to completion of a therapy (Fortune, 1987; Wilson et al., 2007).

According to Fragkiadaki and Strauss (2012), the development of a therapeutic relationship determines the experience of termination. It appears therefore that the longer/closer the relationship, the more difficult the termination process is likely to be. For example, in research, Sofaer et al. (2009) assert that trials which run for one year or more tend to create relationships between researchers and participants which may become difficult to break. Relationships that are terminated abruptly or without prior knowledge or preparation (forced termination) have been attributed to constitute an even more complex termination scenario (Fragkiadaki & Strauss, 2012; Mirabito, 2006). For example, in a study by Peck (2007), which examined 12 patients' experiences following the unplanned and unexpected termination of their healing touch treatments, results indicated that six patients had negative experiences, including increased pain, impaired functional ability, and sleep and emotional disturbances. Some authors therefore advise that the process of termination in healthcare relationships should be taken with thoughtful consideration (Harrigan & Walsh, 2003; Wilson et al., 2007), with a need for health workers to have competence in clinical, practical, and ethical knowledge, in order to effectively manage this stage of care (Davis & Younggren, 2009).

Despite the above recommendations, how the termination of close relationships is handled in practice still remains unclear. For example, in a qualitative study by Mirabito (2006) which sought to explore clinicians' perceptions about unplanned terminations from mental health treatment among economically disadvantaged inner city adolescents, it was revealed that although clinicians were aware that termination was a significant phase of the treatment process, they did not show any concern in planning for this time. According to Mirabito (2006), this could have resulted from a lack of administrative and theoretical guidelines to termination of such a group of clients. This study suggested that prior planning and use of established guidelines can be effective in handling the termination process and can help health workers to effectively engage and manage difficult cases, identify when and how termination should be handled, and manage their own and their patients' reactions to termination. Similarly, a review by Wilson et al. (2007) about closure of a cancer clinical trial, established that despite termination being an important part of care, it is often neglected by health workers. They argued that health workers should devise mechanisms of ensuring the provision of post-treatment care, to enable patients to cope with the termination. This literature suggests a need for

more research focusing on how termination of close relationships is enacted and experienced in research situations.

Although some of the literature reviewed in this section focused on termination within a healthcare environment, the issues presented mainly focused on termination of the health worker-patient relationship. The following section provides literature focusing on the specific issues about termination of healthcare programs.

3.4 Termination of healthcare programs

In addition to concerns about termination of the health worker-patient relationships, most HIV drug trials (especially those involving HIV positive participants) will involve provision of care/treatment to participants, which might be similar to that provided in the general healthcare settings. It is therefore relevant to review literature related to termination of healthcare programs, in order to understand the phenomenon of withdrawal of care/treatment from individuals and its likely impacts.

Termination of healthcare programs³ may involve a number of players (such as patients, health workers, family members, even the community), which may demand for a more focused and thoughtful approach to termination. Furthermore, in addition to concerns about termination of the health worker-patient relationship, often, termination of healthcare programs may present other concerns such as the need to ensure continuity of care/treatment for particular groups of service users. Inadequacies have been reported in how the termination of healthcare programmes has been handled, resulting in summoning the attention of policy makers and other concerned individuals. Levine et al. (2006), studied family caregivers of stroke and brain injury patients in United States, when home care cases were opened and closed. Their findings revealed that during the closure, there was lack of adequate preparation which resulted in remarkable feelings of isolation, anxiety and depression among the caregivers. According to Hekmatpou, Mohammadi, Ahmadi, and Arefi (2010), patients consider discharge from healthcare services as the termination of professional responsibility of healthcare providers which necessitates a post discharge plan. Levine et al. (2006), recommended adequate preparation, education, and support to the involved parties, while integration of counselling services has also been identified as a good strategy to attend to the emotional needs of those involved (Williams, Netten, & Ware, 2006).

³ In this thesis, termination of healthcare programs means either discharge from or the complete closure of a healthcare program such as a hospital, care home, other care/treatment programs.

In addition to emotional concerns, some conditions/patients may require continued monitoring, treatment, or care after normal discharge, or in case of complete closure of a healthcare program. These issues may raise concerns of follow up care or identifying alternative facilities for suitable services. In a study by Williams, Netten, and Ware (2003), which assessed relatives' and residents' experiences and views of the closure process of a care home, participants' main concerns included: finding an alternative home, finding a home suitable for their needs, and maintenance of the standards of care. Participants in this study suggested that early and clear notification, support to locate alternative options, maintenance of good standards of care during the closure, offering practical help during the transfer, and mediating the transfer process by staff would be beneficial during this period. Similarly, Smith (2002) urges health workers to ensure that the discharged/terminated patients will have a safe place to go to, and also suggests soliciting of community support to facilitate the transition from healthcare to home/community. These findings highlight the importance of supporting clients who are terminated in healthcare programmes, in identifying and transferring to alternative care facilities. This strategy could be helpful in the termination of HIV research programs involving HIV positive individuals, who will require continuation of HIV care and treatments.

Although some suggestions have been made to facilitate closure of healthcare programs, there appears to be very few established guidelines to this effect, and this may have contributed to the inadequacies in handling this process. Robinson, Glasby, and Allen (2013), suggest that a policy to guide such a process should be established to ensure good practice. In addition, much as general guidelines may be helpful, establishing guidelines in accordance to the nature of the healthcare program is essential. For example, the needs of patients with chronic conditions may not necessarily be similar to those with acute/short term conditions. Mirabito (2006) recommends the use of context sensitive models/guidelines which focus on a particular patient group.

3.5 Termination of research programs

Unlike closure of general healthcare programs, closure of research programs may involve additional needs and obligations. The additional needs/obligations could be attributed to a number of factors including: (i) the fact that the tried interventions may be unknown and thus may require continued monitoring, (ii) the implications of discontinuing a trial treatment, and (iii) provision of post-trial care as an ethical/moral requirement for researchers. This section discusses literature on termination of research programs, and its implications on research participants and researchers. The literature reviewed in this section focuses more on clinical trials, since these are more relevant to the current

study. Literature addressing special contexts such as HIV related research or research undertaken in low income settings is emphasised.

The majority of concerns related to closure of research programs have focused on how post-trial obligations have been respected by researchers and on the needs of research participants arising during the closure period. Areas such as: compensation for injuries caused during research, the need for continued access to post-trial care and to the trial treatments, support during transition to post-trial care, monitoring of possible adverse effects from trial interventions, and provision of trial feedback, have been of major concern among different stakeholders such as policy makers, research volunteers, and community members (Schuklenk, 2010; Unguru et al., 2013).

In a qualitative study by Sofaer et al. (2009), which assessed current and former US chronic disease trial subjects' views of obligations to ensure post-trial access to drugs, care and information, participants' expectations included: provision of transition (short term) care, access to trial drugs, referrals to non-trial physicians, care for long-term adverse events, access to the trial products at a lower cost, and access to information about the trial drugs received. In this study, participants felt that researchers are obliged to offer post-trial benefits due to: subjects' exposure to risks, the special relationships with researchers (researcher-subject relationships), and the consent form being a "contractual arrangement". These data highlight the importance research participants place on particular aspects in post-trial care, and highlights the important post-trial care obligations from a participant's point of view.

In another study from the United States by MacQueen, Shapiro, Karim, and Sugarman (2004), which examined the views of members of an HIV-prevention research network about the ethical challenges in international HIV prevention research, the major themes which emerged relating to post-trial care were: the need to determine acceptable standards of care for post-trial participants and reducing risks related to HIV stigma. The results of this study suggested a need for establishing strategies to be incorporated into the planning and conduct of HIV trials.

It has also been shown that a proportion of participants will agree to take part in research specifically in order to access therapeutic benefits. For example, in my review which aimed to establish the views and experiences of HIV research participants in sub-Saharan Africa (Nalubega & Evans, 2015), the expectation of access to prompt and adequate medical care and treatment was expressed in 4 of the 21 included studies (Kass, Maman, & Atkinson, 2005; Pistorius et al., 2004; Reynolds, Mangesho,

Vestergaard, & Chandler, 2011; Tarimo et al., 2011). This finding suggests that many trial participants' value access to quality care and treatment, and since it is possible that the initial motivation for taking part in research may contribute to participants' overall post-trial care expectations and experiences, researchers need to pay attention to these while managing trial closure.

Some authors have also argued that researchers' obligations may increase in certain conditions such as in research conducted in resource limited settings or in research involving patients with chronic diseases (Sofaer et al., 2009; Unguru et al., 2013). For example, for some diseases such as HIV which require lifelong treatment, exacerbation of symptoms of the disease can occur if treatment is stopped (Grady, 2005a; Sofaer et al., 2009), while in some settings, trial participation constitutes the only available avenue to quality medical care (Schuklenk, 2010). In these contexts, termination of research services may have serious implications for the participants' healthcare needs, and therefore may call for special considerations. Similarly, in therapeutic clinical trials, Unguru et al. (2013), suggest that researchers may have more ethical obligations since these carry more risks to participants than non-therapeutic trials. This literature suggests that contextual factors are important in the implementation of post-trial care.

The key issues identified in literature pertaining to post-trial care have been explored in more details in the following sections.

3.5.1 Linkage to care

Continuity of care after trial closure requires that participants are appropriately linked to alternative facilities, where their care needs can be met. In HIV and other chronic diseases' research, appropriate linkage to care is very important, since a lack of appropriate linkage could result in treatment interruptions, which is critical in the overall management of the disease condition. In HIV research, ensuring continuity of care, treatment, and support during and after research is especially important for those who are HIV positive (or who become HIV infected during trial participation).

Various stakeholders have highlighted the importance of supporting the linkage to care process following research closure, and many have considered this as a researchers' responsibility. The reasons include: ethical/moral reasons such as reciprocity, compensating of participants for their commitment in research, to avoid exploitation of research participants; the need for continuation of care for trial participants, a duty to care as a researchers' role, and to maintain trust and the relationships created during research (Clouse et al., 2010; Dainesi & Goldbaum, 2011; B. Haire & Jordens, 2015;

Merritt & Grady, 2006; Sofaer et al., 2009; UNAIDS, 2012a; Wang & Ferraz, 2012). In a study by Sofaer et al. (2009) which assessed the views of research participants on the obligations of researchers about post-trial obligations, participants expressed the need for researchers to ensure that participants are facilitated during the transition period from research to post-trial care, to ensure that continuity of care during this period is sustained.

However, despite the need and importance, linkage to care following trial closure has been reported to pose significant concerns. Some studies have reported a lack of adequate facilitation and support to link to alternative care facilities following trial closure, which resulted in considerable loss to continued care, with resultant negative effects on the participant's health and wellbeing. For example, in a study in Zambia by Stephenson et al. (2008) which assessed the impact of temporary closure of an HIV research clinic on the health of study participants, findings indicated that 84% of the respondents reported that the closure had a negative impact on them, and 87% of these rated loss of medical care as the main impact. The mortality rate among the HIV-positive participants was also reported to have doubled during this period. The loss of healthcare was perceived as the most negative impact on participants, reflected in increased mortality rates. The key recommendation from this study was that research projects should make transition plans and budget for mechanisms to reduce the negative impact the closure may have on participants.

Similarly, in an event organised by TED (Technology Entertainment Design) Talks conference in the UK in 2012, Boghuma, a medical doctor and researcher in HIV cure research reported about a lady from Cameroon, who, 18 months after completing participation in an HIV clinical trial had not accessed further HIV care and treatment (Boghuma, 2012). The lady was clinically very ill and the main reason for not linking to post trial care was lack of adequate knowledge of where to go since HIV services were freely available in her local setting. Boghuma recommended researchers to have clear plans for supporting trial participants to access post-trial care.

In another study conducted in Zimbabwe and South Africa by Clouse et al. (2010), to evaluate the uptake of additional counselling services and clinical care among women who acquired HIV during the trial, it was established that only 44% of the participants were provided with referrals to public healthcare facilities, 18% declined any further care after leaving the research, while 25% could not be traced for the post-trial evaluation. The limitation of this study was that the evaluation was done later after many participants had been exited from the trials. The authors challenged researchers to make

post-trial care plans early and recommended further research to investigate and understand the barriers to establishing a continuum of care between clinical trials and public sector health facilities.

In HIV research, special conditions have been identified to contribute to the challenges of linkage to post-trial care. Participants who acquire HIV during study conduct or those who enrol in research studies before accessing any HIV care⁴ are likely to still experience HIV stigma by the time of the closure, which can affect their access to care or disclosure of their HIV status to the family. These people may also lack awareness of the existing HIV care services/facilities, and thus may require more guidance. Additionally, socio-economic factors such as raising transport fares, finding time, and relocation to other settlements, have been established as important barriers to the continued access to/retention in post-trial care (Clouse et al., 2010). Researchers need to identify and adequately address these barriers during the transition process.

The above literature indicates that actually some HIV positive trial participants do not access further care following research participation. This is a worrying situation given the likely dangers associated to HIV drug interruptions and calls for a great need for supporting all HIV positive participants to link to alternative care after trial exit. UNAIDS (2012a) recommends that to avoid challenges associated to post-trial access to the required HIV services, HIV trials should only be conducted in communities where access to these facilities is assured. Nonetheless, existing literature does not offer adequate information on the influencing factors for the negative trends in the continuity of post-trial care, or how linkage to care can be improved. This calls for a systematic and context-based evaluation of the linkage to care process, focusing on the needs, expectations, and experiences of actual trial participants, and the practices of the researchers during the transition process. This will be helpful in suggesting ways of facilitating linkage to post-trial care in the various contexts.

The guidelines reviewed in chapter two above suggest the need for appropriate linkage to post-trial care, in order to facilitate continuity of care e.g. for HIV positive research participants. The majority of the authorities (Rennie & Sugarman, 2009; UNAIDS, 2012a; UNCST, 2014a) considered referral as an acceptable approach, where trial participants are provided with letters to deliver to post-trial care facilities. Empirical research conducted in this area also suggests that referral is acceptable among key stakeholders as an approach to facilitate linkage to post-trial care. For example, in a

⁴ common in PMTCT trial participants who enrol after detection of the HIV status during antenatal care

study by MacQueen et al. (2007), respondents accepted referral as a fair way to address trial participants' care and treatment needs, although they expressed doubts about the adequacy of local health-care options. Similarly, a study by Sofaer et al. (2009) which sought to establish the views of trial subjects about the post-trial obligations of researchers in Boston, identified facilitation of linkage to care through referral and provision of guidance on where they can seek proper care, as one of the main responsibilities of researchers.

Despite referral being a widely accepted approach, some commentators suggest that referral alone may not be enough in particular situations. For example, in some settings, the trial treatment may not be readily available in the public healthcare system, and referral alone may not guarantee adequate access to post-trial care. In such circumstances, some authorities have advocated for the provision of interim care and continued provision of treatments while trial participants try to identify suitable facilities and settle in care (Grady, 2005b). Clouse et al. (2010) demonstrated this recommendation by explaining how participants in the MIRA program (which aimed at establishing a continuum of care between HIV vaccine trials and the general care facilities) were linked to post-trial care. The authors explained that they did not only ensure that participants were linked to sustainable care, but also that they monitored them for some time to ensure they had settled well in care. These findings suggest that researchers may need to continue engaging with post-trial participants after the initial linkage, to ensure that continuity of care is sustained.

The sustainability of care and treatment also requires that participants continue accessing the right treatment for the disease condition involved. This may in most instances involve the trial medication. The following section presents literature regarding the need for, and obligations of researchers to provide the trial interventions.

3.5.2 Provision of trial medications

The need to continue to provide a trial intervention to research participants and the participating communities has been extensively debated in literature. Various studies have been conducted to specifically seek to establish the expectations of stakeholders regarding post-trial care. In these studies, access to the trial intervention has been considered one of the major post-trial care needs of trial participants especially in the low income settings.

In a study in Tanzania, Vallely et al. (2009), sought to establish what constitutes an appropriate standard of health care for participants in HIV prevention trials. Participants

in this study recommended that researchers should ensure effective access to antiretroviral drugs and should provide supportive community-based care for women identified as HIV positive during the trial. Participants also argued that this care should be sustained even after the trial. In another study in Kenya by Shaffer et al. (2006), which sought to describe the concerns and priorities of key stakeholders regarding ethical obligations held by researchers in an HIV/AIDS clinical drug trial, participants advocated for provision of lifelong continued drug therapy, ongoing adverse event monitoring, and primary care as the primary obligations for researchers. Although these two studies presented a variety of expectations, a common finding was the need for continued and sustained provision of HIV treatment even after trial closure. These data support the current debates in HIV post-trial care, which identify the need for access to HIV treatment and care, and its sustenance beyond trial closure. These issues have been emphasised by some authors as presented below.

Essack et al. (2010), conducted a study to assess stakeholder perspectives on ethical challenges in HIV vaccine trials in South Africa. Participants identified access to treatment for those who become infected with HIV as a major concern in the conduct of HIV research. Similarly, in a multinational study by MacQueen et al. (2007), which evaluated the perspectives of different stakeholders on care options for HIV prevention trials, respondents were concerned about the sustainability of care and treatment beyond the trial for participants who become infected during the trial. Grady (2005a) also recommended researchers and sponsors to provide intermediate treatments to trial participants while they await licensure of the trial medications, while for those treatments which may be expensive for the communities/countries to achieve, they can liaise with other stakeholders who can offer such support.

While the above literature provides useful information on the expectations and/or recommendations regarding the provision of the trial interventions, there remains a gap in our knowledge on how this obligation is met (or not) in real life settings. Some empirical literature has registered unsatisfactory stories in this area. For example, in a multinational study conducted by Ramjee et al. (2000), which explored the challenges in the conduct of vaginal microbicide effectiveness trials in low income settings, it was discovered that ethical issues arose in providing care and support to the subjects who became infected with HIV during the trial. In this study, it was reported that women could only be offered routine sexually transmitted disease treatment and counselling, while ARVs were not offered. Although conducted a number of years ago when access to ART was quite a challenge compared to today, given limited evidence in this area, these

findings draw our attention to the issues which might require focus while investigating post-trial practice.

Key questions related to the provision of the trial interventions include: who is the rightful person to provide the interventions, to what extent or for how long should these be provided, who should benefit, and whether providing ongoing care is an achievable expectation. Varying views have been presented on these issues. In a study by Barsdorf et al. (2010) which explored a South African community's perceptions of who should provide what to HIV trial participants, as well as how and why this should be done, participants expressed that researchers are obliged to provide care and treatment to post-trial participants until they are capable of getting alternative care.

Similarly, Dainesi and Goldbaum (2012), conducted a survey to analyse the perspectives of clinical research stakeholders in Brazil concerning post-trial access to study medications. Participants in this survey included Ethics Committee (EC) members, clinical investigators in HIV/AIDS and diabetes and their participants, and research sponsors. Findings from the survey indicated that although the majority of respondents answered that medications should be provided free by sponsors, the opinions varied in the different groups. For example, investigators and sponsors believed the medications should be provided only before available in the public health sector; EC members suggested that the participants should be maintained on the treatments, while patients expressed that the benefits should be assured for life. These findings seem to highlight that different stakeholders may have different expectations and opinions regarding the obligations to provide trial interventions and of post-trial care in general. However, having used a survey approach, studies which use more in-depth data collection techniques would be able to provide a deeper understanding of stakeholder perspectives on this issue.

Although the opinions on this subject vary, numerous authors have suggested that the biggest responsibility to provide post-trial medications/care falls on researchers and sponsors (Essack et al., 2010; Lo, Padian, & Barnes, 2007; MacQueen et al., 2007; Pace et al., 2006; Schuklenk, 2010). This is particularly relevant in low income settings where the governments may not be able to provide such treatments to the public. However, in the low income settings, putting the responsibility for providing post-trial interventions on researchers may be challenging and some fear that it may scare away research sponsors in these settings. Hence some authors (Merritt & Grady, 2006), have suggested that such responsibility cannot be shouldered alone by sponsors, and instead advocate

for a joint effort between different stakeholders such as the sponsors, host governments, NGOs and charities.

The subject of who is the rightful beneficiary of post-trial benefits has also been of concern in literature. The debate has based on whether those who take part in research should alone benefit from the trial interventions or the benefits should be extended to the entire participating community. In a study by Grady et al. (2008) which explored the views of community members in Uganda regarding research benefits for hypothetical HIV vaccine trials, the majority of participants were in favour of community benefits while very few (16%) preferred benefits for only the research participants. On the other hand, a multinational study by Pace et al. (2006), which sought to establish the views of Institutional Review Board/Research Ethics Committee (IRB/REC) chairs, investigators, and research participants, regarding post-trial access to tested interventions among HIV trial participants, yielded interesting but ambiguous findings. In this study, some respondents recommended that the trial drug should be provided free of charge worldwide, others said that it should be provided free to the participating community, while others suggested it should be provided free to only the research participants. Although the above two studies do not reflect opinions of those actually participating in the trials, they both seem to imply that participating community benefits are essential in HIV trials and may be preferred to the individual ones. Further research on actual trial participants will be required to provide more insights on this aspect.

3.5.3 Compensation in research

Compensation in research has been one of the major recommendations in policy guidelines (CAHR, 2008; UNAIDS, 2012a; UNCST, 2007, 2014a). The main areas of concern for compensation include: injuries/risks incurred during research, inconveniences encountered such as pain during phlebotomies, and loss of time/money during research participation. Although these issues are pertinent to all research studies, the complications related to HIV research participation makes the need for compensation of particular relevance. Moodley (2007), in a paper entitled "Microbicide research in developing countries: Have we given the ethical concerns due consideration?", underscores the need to consider both the physical (medical) and psycho-social risks⁵ associated to HIV research participation.

Other stakeholders have also regarded compensation as a crucial issue which deserves a front platform. In a study by Essack et al. (2010), to establish stakeholder perspectives

⁵ The different risks/harms related to HIV research participation have been discussed in the background section

on ethical challenges in HIV vaccine trials in South Africa, compensation for physical harms emerged as a key concern among the respondents. In another study by Sofaer et al. (2009) which assessed the views of participants about post-trial care, participants presented differing views regarding the need for compensation for injuries resulting from trial interventions. Some strongly suggested that researchers were fully responsible for the care/compensation for the adverse effects from trial interventions even though these occurred many years later, while the majority felt researchers are not obligated to do that. However, of those who felt researchers may not necessarily compensate the participants, the majority felt researchers had the obligation to at least inform participants of the adverse effects even if these occurred later in life. This recommendation points to the need to keep track of the former participants, to assess for the possible adverse effects and also to update them of these if they occurred. Nonetheless, there appears to be limited empirical research on actual trial participants' views on this aspect, and further research in this area is required.

In addition to the need for compensation for injuries and risks, various stakeholders have also been concerned about the time and commitment participants undertake while attending research studies (Kwagala, Wassenaar, & Ecuru, 2010). Various authors have expressed fears regarding possible negative effects of monetary research benefits/compensation. For example, fears that offers of financial benefits could be coercive have been widely documented (Grady, 2005b; Kwagala et al., 2010; Largent et al., 2012; Roche et al., 2013). However, evidence suggests that although financial benefits could be appreciated or could even influence research participation, these may not be necessarily coercive. For example, Byrne, Croft, French, Dugosh, and Festinger (2012), who evaluated perceptions of coercion among research participants using a Financial Incentive Coercion Assessment (FICA) questionnaire, reported that although some participants acknowledged participating in research due to financial reasons, they did not perceive the benefits to be coercive. Although this issue has been a subject of much debate in literature, there appears to be limited understanding of the concepts regarding financial issues in research (Grady, 2005b; Largent et al., 2012; McGregor, 2005; Wertheimer & Miller, 2008), and research to make these more understandable would be much needed. In addition, much of the research in this area tends to mainly base on the perceptions of individuals rather than on actual experiences. This area requires further inquiry.

3.5.4 Monitoring and follow up care

Various authors have presented concerns regarding a possibility of adverse effects emerging from trial interventions, which can have various impacts on the participants

(Emanuel et al., 2000; Haire, 2013; Nalubega & Evans, 2015; Sofaer et al., 2009). HIV in particular has been associated to a range of unwanted effects including the physiological, physical, psychological, social, and economic effects (Dhalla & Poole, 2011; UNAIDS, 2012a). The majority of the commentators have been mainly concerned about the physical effects such as those resulting from adverse reactions from the trial interventions. These call for proper follow up and monitoring of trial participants after trial closure.

Authors (Emanuel et al., 2000; UNAIDS, 2012a) argue that trial interventions especially in earlier phase research, may have a lot unknown about them, which exposes participants to long term risks, which will require long term monitoring. Similarly, Ho (2010) notes that participants who acquire HIV during trials can initiate HIV treatments which may require monitoring and follow-up following trial closure due to the likely unwanted effects, yet there appears to be no clear mechanisms on how/who will address these complications.

Authorities such as UNAIDS (2012a) and World Medical Association (2013) recommend the need for researchers to have prediction of all the likely adverse effects from the trial interventions, have advance plans of monitoring for these, and intervening when they do occur. However, although such authorities may also acknowledge that possible effects can occur long after trial conclusion, there are no clear guidelines/policies to address this issue, which leaves an evidence gap in this area.

Some empirical studies have evaluated the perspectives of stakeholders regarding the care of unwanted effects occurring long after trial closure. In a study by Sofaer et al. (2009), which assessed the views of participants regarding the obligations for providing post-trial care, the authors reported conflicting views of the respondents regarding the care for adverse effects which developed after trial closure. In this study, the majority suggested that researchers may not be responsible for such care while very few felt researchers were obligated to do so. Nevertheless, this area has been generally under researched increasing the need for empirical research to be undertaken in the area.

3.5.5 Provision of trial feedback

Trial feedback has been reported as an important aspect of post-trial care by various stakeholders and authorities (Cox, Moghaddam, Bird, & Elkan, 2011; Emanuel et al., 2000; Getz et al., 2012; MacNeil & Fernandez, 2007; UNAIDS, 2012a; World Medical Association, 2013). Providing trial feedback is thought to have positive effects for former

participants such as feeling appreciated and valued for their contribution to the research (Getz et al., 2012).

Empirical evidence has also indicated that trial-feedback is valued by stakeholders. For example, in a study by Gikonyo et al. (2013), which sought to explore the experiences of key stakeholders of two malaria vaccine trials involving healthy children on the Kenyan coast, findings indicated that feedback of findings was valued and accepted by both participants and researchers. According to the respondents, giving trial feedback was helpful to reassure participants of trial safety and also to clarify issues regarding blinding and control groups. Similarly, a survey by Cox et al. (2011) conducted to assess clinicians' and patients' attitudes and experiences towards feedback of trial results in cancer trials in the UK indicated that, the majority of respondents supported the idea of offering results to trial participants, but differed in the opinions regarding timing and the method of delivering the results.

In another study by Fernandez et al. (2009), which sought to establish the attitudes and needs of adolescents and caretakers of children with cancer regarding provision of trial results, the respondents indicated that they had high expectations of trial results and also felt this was their ethical right. This finding is also related to those of other authors (Partridge, Burstein, Gelman, Marcom, & Winer, 2003; Partridge et al., 2009; Schulz, Riddle, Valdimirsdottir, Abramson, & Sklar, 2003), in which study participants indicated a high need for receiving trial feedback.

The above studies shed some light in regard to the desire of participants to receive trial feedback. Interestingly, evidence suggests that some individuals may actually not be much interested in trial feedback or may have priorities in regard to the types of the feedback. In a study by Dixon-Woods, Jackson, Windridge, and Kenyon (2006), which sought to establish the views of pregnant trial participants regarding receiving trial results, less than a fifth of the participants showed interest in receiving the trial results.

On the other hand, individuals have shown special interests in particular types of trial feedback. These have majorly included the need to know individual trial outcomes such as treatment arms, or the general trial outcomes such as how the research main objective had been answered. Sofaer et al. (2009), in their study to establish the views of participants on post-trial obligations, reported that participants wanted to know their treatment allocation such as if they received placebo or an active drug. Similarly, in a study by Armstrong et al. (2013), regarding the views of research participants about unblinding following trial participation, participants expressed the need to know their

treatment arm. Other authors (Dixon-Woods et al., 2006) have reported similar findings where trial participants expressed the need to know their treatment arms, while in some studies (Moutel et al., 2005), participants have expressed the need to know the more general findings. These findings imply that individual participants may be interested in receiving different trial outcomes and that both the general and the more specific outcomes may be important to them.

Another important theme regarding provision of trial feedback concerns the timing of providing the feedback. While feedback has been mainly provided after all results of the trial have been confirmed and validated (a process which takes approximately one year for most research projects), various stakeholders express the need for researchers to disseminate trial outcomes as early as possible, to enable for example, initiation of effective trial interventions (Fernandez et al., 2007; Sofaer et al., 2009; UNAIDS, 2012a). In some studies where the views of participants regarding this subject have been assessed, some have indicated the need for participants to receive the feedback immediately following trial closure (Cox et al., 2011). Such views may however be based on the need for individuals to know more personal outcomes such as their improvement or not in health status during trial conduct, which may not necessarily require disclosure of the overall trial outcomes.

Despite evidence indicating the need for providing trial feedback, knowledge on the application of trial feedback in practice seems unclear, while the limited available literature suggests that trial feedback is rarely provided. Some studies which have investigated this area suggest that most study volunteers never receive trial feedback. For example, a postal survey conducted in the UK by Di Blasi, Kaptchuk, Weinman, and Kleijnen (2002), which assessed whether and how investigators of placebo controlled randomised trials inform participants of their treatment allocation at trial closure and the barriers to feedback, found out that less than 50% of investigators gave feedback to participants. Reasons for this included not considering it relevant, while a few (24%) thought that this could bias results. However, since this trial focused on disclosure of treatment allocation, the fear of the disclosure biasing results could have been a genuine concern. In another paper by Rigby and Fernandez (2005), which reported about the practice of reporting the plans for providing trial feedback among researchers in America, findings showed that although the majority supported the practice, only 30% had clear/formal plans of providing trial feedback. Nonetheless, the majority of the reviewed studies having been conducted more than a decade ago, it is possible that the discussed trends on trial feedback have changed, necessitating further research to generate more current evidence.

A number of barriers have been identified as potential hindrances to the dissemination of trial feedback. These have included: problems of preparing lay summaries, contacting participants, time constraints, financial constraints, the fear of results having negative emotional impacts, some researchers not taking it seriously (MacNeil & Fernandez, 2007; Partridge et al., 2003; Partridge et al., 2004; Rigby & Fernandez, 2005), and the fear of biasing results (Di Blasi et al., 2002). A lack of proper guidance on this area of practice has also been blamed for its lack of proper implementation Cox et al. (2011).

Nevertheless, the actual practical experiences of providing trial feedback is under researched and further research is required. Specifically, no empirical study has been identified in HIV research addressing this particular issue, indicating a huge evidence gap in this area.

3.6 Conclusions from the literature

The previous sections have highlighted the pertinent issues around post-trial care. Issues particular to HIV research have been particularly highlighted. The literature reviewed has indicated an important rationale for post-trial improvement in research practice, and more importantly in HIV research, as this presents peculiar concerns. Important gaps in evidence have been identified, which provide a basis for the rationale of the current study.

For example, there has been no empirical study which has assessed the perspectives of important stakeholders such as actual trial participants and research staff on post-trial care (Nalubega & Evans, 2015). Although some of the post-trial care aspects have been researched, this has been in other fields such as Cancer or Malaria, and not specifically in HIV. For research around HIV, the majority have based on hypothetical scenarios or on the views of other stakeholders, and not actual trial participants.

Some authors have also argued that the area of post-trial care is neglected by many researchers (Grady, 2005a; Pratt et al., 2012; Wilson et al., 2007), both in practice and in research. In research practice for example, post-trial care seems to be paid limited attention compared to other areas such as informed consent, standards of care during research, and monitoring and management of adverse effects during trial conduct. Such a practice gap was identified in a document review by Ciaranello et al. (2009), which aimed to establish the ways in which post-trial services were described in protocols and informed consent forms of ARV clinical trials. In their review, it was established that less than 50% of the documents included details or plans regarding post-trial care, compared to other aspects which received considerable attention. Similarly, in a systematic survey

to establish the reporting of informed consent, standard of care and post-trial obligations in global registers of randomized control trials in the fields of HIV, Malaria and Tuberculosis trials, Cohen, O'Neill, Joffres, Upshur, and Mills (2009), reported that a very small percentage of trials (1%) indicated provision of post-trial benefits. In another research by Shah, Elmer, and Grady (2009), which assessed 18 studies in order to examine whether the National Institutes of Health (NIH) guidance document was being implemented in NIH-funded ART trials conducted in developing countries, the findings indicated that none had a guarantee for long-term sponsor funding after the trials, which limited post-trial provisions.

These findings imply that post-trial care is not a priority for many researchers, even though it appears to be crucial for research participants and other non-researcher stakeholders, as some findings from the literature have indicated. These data also highlight a need to evaluate actual post-trial practice, based on the views of individuals close to the research process, to inform improvements in post-trial care delivery.

Authors have made various recommendations regarding how post-trial care can be improved. A review by Wilson et al. (2007), about closure for patients at the end of a cancer clinical trial concluded that post-trial care was being neglected by many health workers. The authors argued for researchers to devise mechanisms of ensuring the provision of post-trial care (such as discussions and feedback on the outcomes of the trial treatments) to promote participants' wellbeing and to enable them to cope with the termination. Pratt et al. (2012), observe that the current ethical guidelines on post-trial obligations (care) are largely uninformed by realities of research practice in low income settings. The authors have identified a need for developing research guidelines that are sensitive to local needs of participants, and which should be contributed to by different stakeholders such as the government, researchers, communities, and research sponsors. Sofaer et al. (2009), also recommend systematic and consistent discussions on post-trial obligations with potential participants during the informed consent process, since this is thought to increase recruitment rates, improve researcher-subject relationships, alleviate participants' post-trial anxieties, and increase trust in the research.

Despite the recommendations on this issue, how the termination process is handled in actual practice is an under-researched area. Various gaps have been identified in the literature and a number recommendations have been made. The following section identifies the key research gaps identified in the area of post-trial care.

3.6.1 Research gaps

The literature reviewed has established that current post-trial care practice is poorly implemented. This may be attributed to the lack of context specific guidelines on the issue, (as most guidelines tend to be generic) while other aspects of post-trial care may not be addressed. Authors have recommended the need to establish context based guidelines, which should put into consideration the research contexts and the needs and expectations of the particular participant groups. For example, research conducted in low income settings may necessitate more supportive approaches during trial closure, owing to their socio-economic standards of the people and the disparities in the care between research and the general healthcare facilities. In addition, research involving chronic conditions may carry added post-trial obligations for researchers, as participants may require further care/treatment following study termination (Sofaer et al., 2009; Unguru et al., 2013).

In relation to HIV post-trial care, specific evidence gaps have been identified as presented below.

First, most of the policies/recommendations made regarding post-trial care have taken place in the high income settings, and there is inadequate representation of the developing countries. This leaves a gap in the adequate representation of the issues that underpin research in developing countries, in spite of the fact that they are major geographical sites for clinical research. Research targeting stakeholders in the low income settings will be helpful to contribute to both local and international research guidelines and policies.

Second, current guidelines are generic as they apply to all types of research, without consideration of the contextual factors which can affect the way research is conducted. There is need to develop guidelines that are context specific, in order to meet the needs of the participants in particular contexts. This can only be achieved through conducting research within these particular contexts.

Third, most debates involving HIV have either focused on HIV research in general, or on aspects of the research process, other than post-trial care. HIV drug trials involving HIV positive people may pose particular post-trial concerns such as: the need for continued access to HIV care and treatment after research termination, monitoring for side effects of the trial drugs, and the effects of either complete stoppage from HIV drugs or change of therapy for the participant. Other issues that are found to be of interest in HIV trial closure relate to the psycho-social and financial implications of the closure, which may

be of particular significance in the low income settings. Research focusing on the post-trial perspectives of HIV positive individuals may provide a broader understanding of their specific needs and may be helpful in designing interventions to address them.

Fourth, many HIV trials have focused on hypothetical (rather than real life) scenarios, or on other stakeholders other than the actual research participants. This limits our understanding on actual expectations, needs, and experiences of the trial closure scenario. To bridge this evidence gap, we need to investigate people who have experienced the trial closure process. This can only be achieved through an in-depth understanding of what actual HIV research participants expect, need, and experience during the trial closure process, and how the process is currently managed.

The proposed research will seek to illuminate, explore and understand significant ethical issues which are specific to HIV drug trial closure, within a low income setting, and will provide novel contributions in this field. This will hopefully bridge the existing gap between ethical theory and ethical practice in the conduct of HIV drug trial closure. Findings from this research will be integrated into existing policies/guidelines to improve HIV drug trial closure practice in Uganda and other related settings.

3.6.2 Research aim and objectives

Research aim

To explore how care is perceived and enacted in HIV drug trial closure in a low income setting, from the perspective of participants and research staff.

Specific objectives

1. From the perspective of research participants and research staff, to establish the views, opinions and understandings of the ethical/legal/moral post-trial obligations in HIV drug trials.
2. From the perspective of research staff, to explore the experiences, practices and processes related to care for HIV drug post-trial participants in a low income setting.
3. From the perspective of research participants, to explore the experiences of care at trial closure.
4. From the perspective of research participants, to establish the experiences of transitioning from HIV research to care/community.

3.7 Conclusion

This chapter has reviewed relevant literature related to the proposed study and presented the identified gaps in research evidence in this area. The chapter has then set

out the aims and objectives of focus for the current study. The following chapter illuminates and discusses the methodological approach employed in this research.

CHAPTER 4: RESEARCH METHODOLOGY

4.1 Introduction

This chapter provides an overview of the methodological approach adopted in this research. First, the research strategy and its underpinning philosophy is discussed, followed by the research design, under which the study sample, data collection procedure and data analysis are presented. A discussion on how the rigour of the research was maintained is presented and reflexivity concerns are addressed, and the chapter concludes with a discussion of the ethical considerations for the research.

4.2 Research strategy

The current study sought to establish care perspectives during HIV drug trial closure in Uganda. This required an in-depth understanding of the issues which underpin HIV trial closure from those involved in the process. An approach allowing for in-depth investigation was required. This study therefore adopted an interpretive-constructivist approach, which drew on the interpretivist epistemological perspective, as well as the social constructivist ontological perspective. The study further drew on the philosophical understandings of symbolic interactionism. Since the interpretivist approach tends primarily to use methodologies that are qualitative (Mack, 2010), a qualitative approach was used in this study. This section describes the methodology applied in this research, discusses its underpinning philosophy, and provides a rationale for choosing the approach.

4.2.1 *The qualitative research paradigm*

Qualitative methodologies are research approaches that are mainly concerned with the meanings of phenomena in society. These approaches primarily focus on data in the form of words, which may include observations, interviews or documents (Creswell, 2009; Gribich, 1999). These approaches seek to uncover, understand and interpret attributes such as thoughts, perceptions, feelings, behaviours, interactions, and social contexts, to explain the perspectives of participants on a given phenomenon (Gribich, 1999). Unlike quantitative research which will be concerned about controlling phenomena, by establishing relationships between variables and testing these with statistics, qualitative research is instead focusing on description, understanding, and empowerment of research subjects (Joanna Briggs Institute (JBI), 2012). Qualitative approaches are particularly relevant where there is little information known in the field and where the issue of investigation is quite complex and may require a more detailed/in-depth exploration (Department of Health (DoH), 2010).

Because of its focus on the perspectives of research participants and their contexts, qualitative data collection normally occurs in real-life (naturalistic) contexts, usually through the collection and analysis of materials that are narrative, subjective and holistic (DoH, 2010; JBI, 2011; Polit & Beck, 2006). This implies that the researcher will be closer to the subjects and deeply engaged all through the entire research process (i.e. from question development to data analysis and reporting) (JBI, 2012). This therefore makes the researcher a key player in the research process (Strauss & Corbin, 1998). Since the researcher remains an insider, connected, and near to the research, qualitative research has been criticized as being highly subjective, which has sparked some concerns regarding the quality of qualitative findings.

According to the critics of the qualitative paradigm, the lack of objectivity and also the lack of control of external factors raises concerns of rigour within the approach. Strauss and Corbin (1998), stress the need for the researcher to be aware of this limitation, and thus pay attention to their own position in terms of their philosophical perspective and their professional background, while also exhibiting flexibility and openness in the research process, and being able to appraise what influence these can have on the research findings (i.e. being reflexive). Being reflexive is argued to improve the rigour of qualitative findings (JBI, 2012; May, 2002).

Furthermore, generalisability of qualitative findings has been a contested issue among commentators (Mack, 2010), owing to the small numbers of subjects normally required. However, some view the small numbers as a strength, as they argue that the detail and effort involved in interpretive inquiry (of smaller numbers) allows an in-depth acquisition of knowledge, which makes it possible to have a detailed understanding of a particular phenomenon, which otherwise would be difficult without an in-depth investigation (Mack, 2010; May, 2002; Silverman, 2004). Moreover, although the primary role of qualitative research is not to produce generalisable data (Charmaz, 2006), it is argued that the generalisability of qualitative research is possible and is founded on its potential to produce theory which has a wide application (Charmaz, 2006, 2014; Levy, 2006; May, 2002). Hence knowledge generated through qualitative inquiry may be reliably applied to similar contexts in society.

The current study aimed to explore subjective information regarding HIV drug trial closure. This required an in depth investigation of the different perspectives of the respondents. In addition, there was very little known about the subject of study, which necessitated an inductive and flexible approach. These factors influenced my choice of a qualitative methodology. In addition, meeting these requirements deserved a careful

consideration of appropriate qualitative design. A grounded theory methodology was adopted for this study and the rationale for the choice of this approach is explained in details below.

4.2.2 Rationale for choice of methodology

Qualitative approaches such as phenomenology, ethnography or narrative research could be applied for this study. Phenomenological studies focus on studying phenomena (experiences), their nature and meaning, while emphasizing an understanding of the world from the viewpoint of the individual viewing it (Maltby, Williams, McGarry, & Day, 2010). This approach is appropriate for studies exploring the lived experience of a person (Reiter, Stewart, & Bruce, 2011). Ethnography seeks to describe the behaviour of participants from a cultural perspective (Silverman, 2004), while narrative research involves participants telling stories about their lives in their own words, and often involves one or a few participants (Bowling, 2002). The aim of this study however, goes beyond a description of participants' lived experiences of research participation, an in-depth understanding of a participant's story of research participation, or an understanding of the cultural perspectives of HIV drug trial participants. The current study aimed to comprehend the interpretations participants make out of their experience of care during HIV drug trial closure, and also to elicit care practices in HIV drug trial closure.

Grounded theory aims to construct a theory about issues of importance in people's lives through an inductive approach (Cormack, 2000; Reiter et al., 2011), and is particularly suitable for investigating complex social phenomena, with little or no existing theory (Levy, 2006). Considering that very limited empirical evidence exists in the area of HIV drug trial closure, the choice of a grounded theory approach was appropriate. Furthermore, this study was looking for different perspectives of the phenomena (i.e. meanings, experiences, views, opinions and practices), which may not be adequately investigated using a phenomenological, ethnographic, or a narrative approach. The approach of grounded theory is explored in details in the following section.

4.2.3 Grounded theory

Grounded theory has its origins in the beliefs of positivism (Glaser) and pragmatism (Strauss) (Charmaz, 2006, 2014; Strauss & Corbin, 1998; Walker & Myrick, 2006). The approach was generated from research on the dying by Glaser and Strauss in the 1960s, having been developed as an alternative to the then dominant hypothesis testing research in sociology (Charmaz, 2006; Glaser & Strauss, 1967; Oktay, 2012; Strauss &

Corbin, 1998). This approach provides explicit, flexible, analytic guidelines that direct researchers in data collection, analysis, and eventual construction of a substantive theory (Charmaz, 2006, 2014). This helps researchers to control their research process and to increase the analytical power of their work, and may also provide a way of ensuring the rigour of a qualitative study (Charmaz, 2006; Levy, 2006; Reiter et al., 2011). These characteristics make the grounded theory approach particularly suitable for novice researchers, who may not be very familiar with qualitative designs.

In contrast to other approaches which set out to test a hypothesis or a theory, grounded theory researchers start with broad research questions and allow the emergence of relevant theory grounded in the data themselves (Charmaz, 2006, 2014; Oktay, 2012). This is done through undertaking data collection simultaneously with data analysis, constructing analytic codes and categories from the data, using the constant comparison approach, advancing theory development, memo writing to elaborate on the categories, theoretical sampling, saturation and sorting, and undertaking a detailed literature review after an independent analysis of the research findings (Charmaz, 2006, 2012, 2014).

Grounded theory as an approach has developed through stages, from the classic grounded theory by Glaser and Strauss (traditional), to Strauss and Corbin (evolved), and finally to a constructivist approach by Charmaz (Charmaz, 2006; Mills, Bonner, & Francis, 2006). These appear to have different perspectives on the overall theory development, although their differing views do not necessarily imply that one view is more superior to the other. Rather, these differences appear to be reflective of the epistemological and ontological positions that the theorists adopt (Higginbottom & Lauridsen, 2014; Mills et al., 2006). For example, Glaser had a positivist belief; Strauss had a qualitative research focus, while Charmaz prefers a constructivist approach (Charmaz, 2006). Table 7 below illustrates the different perspectives shared among the different generations of the grounded theory methodology.

Table 7: Comparison of grounded theory generations

Adapted from Borrelli (2015, p.85)

	GLASERIAN GT	STRAUSSIAN GT	CHARMAZIAN GT
Research aim	Emergent; no initial literature review	Identification of a pragmatic experienced-based issue; initial literature review	Making sense of a social situation (specific context)
Theory Development	Emergent	Interpretation	Co-construction
Relationship Researcher-participants	Independent	Active	Co-construction
Data analysis	Comparing incidents; integrating categories and properties; theory delimitation; theory writing	Open coding; axial coding; selective coding; theoretical coding	Line by line conceptual coding; focused coding; theoretical coding

The current study employed the social constructivist approach by Charmaz (2006, 2014). My choice of the approach was mainly influenced by my philosophical position. As table 7 above demonstrates, the constructivist approach values the co-construction of meanings between the researcher and the researched. My own belief agrees with the constructivist approach, where the conclusions made from studying a given society are believed to be co-constructed and cannot only depend on either the data collected from participants or on how the researcher interprets them. As Higginbottom & Lauridsen (2014) comment, in addition to other factors, the choice of a grounded theory approach may also depend on a personal viewpoint.

Although grounded theory suggests that researchers enter the field without prior knowledge of the research problem and therefore no prior literature review should be done (Glaser & Strauss, 1967), in order to meet the requirements of a PhD proposal, an initial literature review was undertaken. Moreover, it has been argued that in grounded theory an initial review of extant literature can be helpful in certain situations such as: for PhD students, for most research proposals requiring funding, to ensure that a similar study has not been done, and to indicate that there exists a problem worthy researching (Dunne, 2011; Hallberg, 2010).

4.2.4 Underpinning philosophy

The positivist and the interpretivist approaches are common epistemological stances discussed in healthcare research. Although healthcare research has tended to use the positivist approach (Mack, 2010), the interpretivist approach has recently been appreciated as well in healthcare research due to its contribution in informing practice and healthcare policies. Interpretivism seeks to understand social phenomena, by understanding and interpreting human interactions, social actions and their meanings, and how these can influence human behaviour (Armonk & Sharpe, 2006; Hudson & Ozanne, 1988; Porta & Keating, 2008). This can be achieved through seeking subjective attributes such as meanings, reasons, and motives; which are normally context and time specific (Armonk & Sharpe, 2006; Porta & Keating, 2008). Because of this, the constructivist beliefs become very relevant in the interpretivist approach.

A constructivist approach is particularly concerned with studying how and why participants construct meanings and actions in specific situations, with considerations of both the role of the researchers and that of the research participants in the resultant research outcomes (Andrews, 2012; Charmaz, 2006). Thus, social constructivism proposes the notion that social phenomena are not only produced through social interaction, but also go through a process of continuous revision by the actors. Hence the knowledge of society is concerned with the analysis of how society constructs reality (Andrews, 2012; Berger, 1991; Mills et al., 2006). This is opposed to the view of objectivism which views the social phenomena and their meaning as existing independent of social actors and thus having a reality of their own, a view inclined to a positivist philosophy (Andrews, 2012).

Since constructivism acknowledges the role of the individual in the construction of social reality, and also acknowledges that interpretation is integral to understanding social behaviour, it has been viewed as an approach that underscores the importance of reflexivity (Berger, 1991; Charmaz, 2006). However, it is also evident that language plays a key role in understanding social interactions and interpretations, which is why it is beneficial to have an understanding of the role of language in understanding society. This is explored through the viewpoint of symbolic interactionism.

Symbolic interactionism is a theoretical perspective that gives consideration to the role that language and symbols play in constructing meanings about a given society (Becker & McCall, 1990; Charmaz, 2014; Cohen, 1989). This perspective views people as active beings engaged in practical activities in their own worlds. This opens an opportunity for researchers to make meanings out of the actions, interactions, and events of the

population they study (Andrews, 2012; Charmaz, 2014). Knowing people's patterns of communication is thus relevant in learning about their views and the meanings they ascribe to the realities in their worlds.

This research sought to derive the understandings, meanings, experiences, interpretations, and practices of care in HIV drug trial closure. Thus the study drew from the above philosophical standpoints in order to elicit a deeper understanding of the phenomenon under study, and to understand how HIV drug trial participants and researchers construct their reality regarding transition from HIV research to usual care.

4.3 Data collection techniques

Grounded theorists seek to include all data sources that might contribute to theory development. Although the grounded theory approach commonly uses interviews for data collection, other methods such as observations, diaries, images, and past literature are acceptable and can be very essential in deriving rich data (Charmaz, 2006; Glaser & Strauss, 1967). The following section discusses the data collection techniques used for this study.

4.3.1 Individual (in-depth) interviews

Individual interviews are interviews where the researcher interviews only one individual participant. These are particularly the method of choice where the subject of interest is sensitive and participants are not likely to speak openly and frankly in front of others (Polit & Beck, 2006). Other advantages of individual in-depth interviewing include the encouragement of personal thoughts, respondent attentiveness to questions, and offering the opportunity for the interviewer to sense non-verbal feedback (Murphy, Dingwall, Greatbatch, Parker, & Watson, 1988; Reiter et al., 2011). This approach results in the collection of rich, in-depth and informative data. In-depth individual interviews were used to collect data from former HIV drug trial participants. This was to facilitate an open discussion of participants' post-trial experiences which may be sensitive, and also to collect rich and detailed data appropriate for the grounded theory approach.

4.3.2 Focus group discussions

Focus Group Discussions (FGDs), also known as group interviews are discussions that take place in small groups of between 6-8 individuals representing the group of interest, and are directed by a moderator who controls the flow of the discussion (Levy, 2006; Reiter et al., 2011). These are commonly a preferred approach when the researcher is interested in the outcomes of brainstorming sessions, is not concerned about the effect

of others in a small group influencing opinions, and participants are likely to speak openly and frankly in the presence of others (Polit & Beck, 2006; Reiter et al., 2011). This study employed FGDs to interview research staff regarding their views and practices of HIV drug trial closure. This approach promoted the sharing of ideas between research staff, which enriched the discussions.

4.3.3 Key informant interviews

Key informant interviews are in-depth individual interviews with individuals who have adequate knowledge about a given subject (Kumar, 1989; USAID, 1996). These can also be done face-to-face or on telephone. The main purpose of the KIIs is to gather as much information as possible in a particular subject, from those who are likely to have a deep understanding of the phenomenon. Hence, these individuals are usually purposefully selected to meet the requirements of the research (Kumar, 1989). Like in-depth IIs, KIIs tend to include a limited number of participants, usually from 15-35 (USAID, 1996). For this study, KIIs were used to elicit information about the practices of trial closure and post-trial care from key individuals. Initially, the KIIs were intended for trial coordinators, to be able to gather information on policies which were in place to guide trial closure. However, after failing to realise enough number of staff from some trials for FGDs, a number of research staff were interviewed as KIIs. Thus KIIs were used to gather data from all trial coordinators and some research staff.

4.3.4 Document review

The grounded theory approach allows for use of data from various sources, including documents. This can be helpful in situations where for example, one needs to review information about the existing policies on a particular practice, and to compare with the information from other informants (Murphy et al., 1988). In this research, ethical documents were reviewed to particularly identify the guidelines on post-trial care aspects in the included trials. This was a helpful strategy for triangulation of data, as it enabled the researcher to compare the views of the respondents with the information in the ethics documents.

4.4 Sample characteristics, size and sampling procedure

4.4.1 Target Population

Participants were female and male adults. In grounded theory, data can be collected from multiple relevant sources to provide different perspectives of the phenomenon (Charmaz, 2006; Reiter et al., 2011). This study involved two groups of participants. The first category included former HIV drug trial participants. These were individuals who had successfully participated in an HIV drug trial and were exited following a planned period

of trial participation. All the participants included in this group had been exited from the trials for at least three months, and had not spent more than 12 months.

The second category included research staff, who participated in the included trials. The categories of staff included were: nurses, clinicians (medical doctors), and those related to counselling such as counsellors, home visitors or community liaisons officers. In addition, the research specifically aimed to interview the trial coordinators of the included trials. All research staff should have been involved with HIV clinical research for a period of at least 12 months.

4.4.2 Inclusion criteria

Former HIV drug trial participants should have fulfilled the following criteria to have been included in the study.

- Be HIV positive
- Participated in an HIV drug trial (e.g. for HIV treatment or prevention)
- The trial should have lasted for a minimum of 6 months
- Should have participated for all the required trial period
- Must be interviewed within three to 12 months of study termination⁶
- An adult⁷
- Capable and willing to provide a written informed consent⁸ to participate in the study

Research staff should have fulfilled the following criteria to have been included in the study.

- Worked directly with research participants⁹
- Involved in trial closure processes
- At the time of the interview, should have been participating or recently worked on an HIV drug trial within one year
- The drug trial should have targeted adults
- Capable and willing to provide a written informed consent to participate in the study

⁶ This is to allow capturing of fresh post-trial experiences, since if delayed, there is a possibility of forgetfulness which may confound the data collected.

⁷ Adult was considered from 18 years and above

⁸ A signature/name for those capable of writing or a thumbprint with a signature of an impartial witness was considered.

⁹ Staff such as clinical research nurses, research clinicians, research doctors, research counsellors, and field officers tend to work more directly with research participants unlike laboratory or data staff.

For documents to be included, these should have consisted of information regarding research ethics and regulation of trial conduct.

3.4.3 Exclusion criteria

- All those who did not meet the above criteria were excluded.
- Participants not capable of speaking/writing English or Luganda, and where it was impossible to find a suitable translator were to be excluded. However, no potential participant was excluded basing on any of the above criteria.
- Documents concerning trials which were still ongoing by the time of the interviews were excluded.

4.4.4 Sample size and sampling techniques

The study aimed to recruit a maximum of 30 HIV post-trial participants for in-depth interviews. However, since the study adopted a grounded theory approach, the number of participants were less than the originally projected, as it depended on when theoretical saturation occurred. Therefore, the study included 21 former drug trial participants. Balance of gender and geographical setting were taken into consideration, to ensure perspectives of the various participants' contexts. The study included 3 trials from two research institutions. Each of these was located in a different geographical setting. Therefore, participants for individual interviews were purposefully and conveniently selected. The researcher purposefully sampled the respondents, by identifying only trials which met the inclusion criteria. This was done by gathering preliminary information of specific trials from the institutions, assessing to see if there those which met the criteria for inclusion. Many trials were excluded at this point for failing to meet the inclusion criteria. For example, a number of trials had been terminated more 12 months earlier, while others did not specifically deal with a drug trial. After establishing eligible trials, the selection of participants was done purposefully and conveniently. This was especially helpful since there were limited participants who met the inclusion criteria. For example, participants in two of the included trials were nearly completing 12 months, hence the section of participants depended on those who had not completed the 12 months. Another trial which was still ongoing had many potential participants who had not yet made three months after trial exit. Hence such participants could not be included. According to Murphy et al. (1988), sampling in qualitative research may be two dimensional, i.e. one targeting the sampling of groups or settings to be included, and another sampling for the specific cases to be studied or the cases to be studied. Hence, qualitative researchers tend to employ the opportunistic, non-random sampling techniques.

The study further targeted to include a maximum of five FGDs with up to eight research staff in each. However, due to practical difficulties, it was not possible to have all the five planned FGDs. The main reason was that some research sites did not have enough staff to make up for a FGD, especially since we wanted to have each focus group to consist of staff of the same profession. Hence, we managed to only conduct 2 FGDs, one with 10 research nurses from Trial 1, and one with three staff from the counselling department, who were also from Trial 1. The rest of the seven research staff, and the three trial coordinators were interviewed as key informants. Effort was made to have a representation from the different cadres of research staff. The sampling of research staff therefore was purposeful, to include staff from the different cadres, and also the coordinators of the included trials.

Furthermore, two ethical documents were included from two of the three included trials. These were purposefully sampled, in consideration of research regulatory issues, which resulted into the exclusion of the documents from one trial, which was still ongoing at the time of data collection for this research. Finally, theoretical sampling (Charmaz, 2014; Emerson, 1981; Hammersley, 1985) was used to ensure saturation of emerging categories, in keeping with the grounded theory approach. This mainly related to the post-trial participants, as other sources of data i.e. research staff and documents were limited to allow data saturation.

4.5 Research setting

Three trials (Trial 1, Trial 2 and Trial 3), were included from two research institutions. The institutions were Joint Clinical Research Centre (JCRC), where Trial 1 and Trial 3 were carried out and Medical Research Council (MRC) where Trial 2 was carried out. The three trials were conducted in different settings and different regions of the country. Details of the research context are discussed in the sections below. First, research institutions are described, followed by the clinical settings in which the interviews were conducted.

4.5.1 Research sites

Joint Clinical Research Centre (JCRC)

Joint Clinical Research Centre (JCRC) is an HIV/AIDS care and research institution located in Uganda, established in 1990 to respond to and provide a scientific approach to the national HIV/AIDS challenge. Since then, JCRC has become a centre of excellence that addresses the serious problem of HIV/AIDS. The institution is a not for profit, Non-Governmental Organisation (NGO), established by a collaboration between the Ministry

of Health, Ministry of Defence, and Makerere University Medical School (Joint Clinical Research Centre, 2015b).

Research is one of the core activities at JCRC. Through the years, JCRC has been on the forefront of global research on HIV/AIDS in Africa and has become an established clinical research site with extensive interaction and collaborations both locally and internationally. JCRC undertakes its research work in: HIV vaccines, antiretroviral therapy, opportunistic infections, public health and social behaviours (Joint Clinical Research Centre, 2015a). All studies are designed and conducted to international standards, so as to inform best practices and cost effective interventions that will shape national and international policies and guidelines.

Alongside research, JCRC also maintains a strong emphasis on patient care and public health. The institution offers advanced paediatric and adult HIV/AIDS care, with a comprehensive range of services, including tuberculosis management, nutrition support, special clinics for young people, adherence, psychosocial support and outreaches. The institution also operates a full-time TB clinic which provides specialized treatment and monitoring of TB cases among its clients. There is also a private clinic for clients who opt for specialised and private attention. JCRC pioneered the use of antiretroviral therapy in Uganda and the Sub Saharan African region in 1992, when it conducted the first antiretroviral therapy trial in Africa aimed at determining the safe and effective use of Zidovudine. Currently, JCRC is responsible for providing HIV care services to over 110,000 clients with over 45,000 patients on antiretroviral therapy (Joint Clinical Research Centre, 2015a). The two sites where two trials (Trials 1 and 3) from JCRC took place were Kampala (Mengo) and Mbale, and these are described in more detail below.

Trial 1 was carried out at JCRC in Kampala. Currently, the site is located on the outskirts of Kampala, the capital city of Uganda (about 10 km from Kampala, off Kampala-Entebbe highway). However, by the time Trial 1 was conducted, the clinic was located at Mengo, which is found within the centre of Kampala city. Kampala has a diverse ethnic population, although the Baganda, the local ethnic group, make up over 60 percent of the greater Kampala region. Although many Kampala residents have been born and brought up in the city, they still define themselves by their tribal roots and speak their ancestral languages. The majority of residents in Kampala are employed, with many surviving on small scale jobs (MoH Uganda, 2012b). The JCRC Kampala site recruits most of its trial participants from within Kampala and other neighboring districts, with the majority of participants coming from within a 20km distance from Kampala city. The majority of these comprise of the peri-urban populations who are low income earners.

Trial 3 was conducted at various sites of JCRC, however, this study drew on participants from the Mbale site, which was located in Mbale district. Mbale district is located in the Eastern part of Uganda, approximately 245 kilometres (by road), northeast of Kampala, the capital city of Uganda. The primary economic activity in the district is agriculture, and the majority of the population (92%) are rural, surviving on subsistence farming for income and food. The main ethnic group in the district are Bamasaba or Bagisu, and the commonly spoken language in the district is Lugisu (Lumasaba). However, the urban population is comprised of diverse tribes including the Gishu, Ganda, Iteso, Sabins, and many others. Hence in townships settings, the languages spoken differ with a majority using English for communication.

The Mbale research site is located in the heart of Mbale town, and is currently housed in the ministry of health hospital building along Pallisa road (Joint Clinical Research Centre, 2015c). The site was established in 2002, and started as a small JCRC outreach unit. The main reason for its establishment was to expand antiretroviral treatment to the rural communities of Uganda. Today the centre is a fully functioning health facility with a pharmacy, data unit, administrative wing and a modern laboratory serving the entire Eastern region of Uganda (Joint Clinical Research Centre, 2015c).

Medical Research Council/Uganda Virus Research Institute (MRC/UVRI)

Trial 2 was conducted at the Medical Research Council- Uganda Virus Research Institute (MRC-UVRI). The MRC-UVRI Uganda Research Unit on AIDS is an internationally recognized centre of excellence for research on HIV infection and related diseases. The unit was established in 1989 at Kyamulibwa, Kalungu district as a pioneer site, following a request from the Uganda Government to the UK Government to contribute to the understanding and control of the HIV pandemic in Uganda. The reason for choosing a rural site was to ensure that rural populations were included in HIV research since at that time, much of the research was being conducted in urban settings. Over the years, the research expanded and new centres were opened in Masaka (Central Western region), Entebbe and Kampala (Central region), and Jinja (Central Eastern region). In 2005, the program was upgraded to a Unit status to become one of the two MRC-UK Units in Africa (the other is in Gambia), thus a strong commitment with MRC UK and the UK Department for International Development (DFID) was created (Medical Research Council, 2015a).

Most of the studies within MRC require close collaboration with health service providers in the area. Participants in the majority of MRC trials continue accessing routine HIV care

(e.g. HIV counselling, and other routine medications unrelated to the trial) from their HIV care providers. Thus MRC collaborates with different service providers including government facilities such as hospitals and NGOs. At rural sites, MRC works with the public health services and other partners to upgrade and equip rural health centres.

Trial 2 was conducted at two MRC research sites, i.e. the Masaka and Entebbe sites. However, the current research drew on participants from the Masaka research unit which is described in more detail in this section. Masaka district is located in the central part of Uganda, approximately 140kms by road, southwest of Kampala along the Kampala-Mbarara highway. The district comprises of a diversity of ethnicities, although the majority of the people are Baganda, with the largest part of the population practicing the Baganda culture and using Luganda language for communication. Subsistence farming is the main economic activity of the district and the majority of the rural population are described as poor. However, food supply remains relatively good throughout the year due to fertile lands and a stable climate (Index Mundi, 2016).

The MRC Masaka Research Unit forms the base for various studies conducted in Masaka district. The studies conducted here require close collaboration with health service providers in the area. The unit is located within the premises of the Regional Referral Hospital and of the AIDS Support Organization (TASO). The unit was established to evaluate innovative interventions aiming at better care of HIV infected patients. In several rural communities, the research team works with the public health services and with the International AIDS Vaccine Initiative to upgrade and equip rural health centres (Medical Research Council, 2015b).

4.5.2 Interview contexts

Participants had a right to select a venue and time of their choice for the interview. All participants were interviewed at research premises, which was convenient for both the researcher and the respondents. Participants' choice for the venue was partly influenced by the preference to be interviewed on the same day when they came to access care (especially for Trial 1 where the research and care units are at the same facility), while for others, HIV stigma is likely to have influenced their preference. For example, one participants rejected to be interviewed from her home even around her home area, and preferred to travel to the former research site, despite this being more than 100 miles away. However, some participants could not fully differentiate between the current study and the former trial, hence the majority of the participants felt they were required to be interviewed from their former research sites.

The majority of the interviews took place in research rooms, which were private, with minimal interruptions and therefore convenient for interviewing. For Trial 2, only one participant (out of eight) was interviewed in a tent. For Trial 1, although all staff were interviewed in research rooms (except for nurses who were interviewed as focus group in an Out Patient Department (OPD) waiting area), six out of seven post-trial participants were interviewed in an outside shelter within the premises of the research facility. For those interviewed in an outside shelter, the shelter was in an isolated and quiet place, which made the venue convenient for interviewing. For Trial 3 however, apart from one participant interviewed in a side room (which was relatively noisy and not so private), the rest of the post-trial participants were interviewed from outside, under a tree. There was minimal privacy in this area and there were some interruptions during the interview sessions. Additionally, there were noises in the background which affected the quality of some recordings. For the same trial, one staff was interviewed in a side room which was exposed to noise and some interruptions. The remaining two staff were interviewed in research rooms which were private and convenient for interviewing. All in all, there were minimal interruptions during the interviews, and the overall quality of interview recordings is considered good.

All interviews (except for one staff) took place on working days, during day time, and within working hours (8:00am-5:00pm). The timings could be associated to a need to fit the interview time within other ongoing work schedules (for research staff), to fit within participants' clinic days, and for the convenience of the selected venue since most of these operate on an outpatient basis (on working days and within working hours).

4.6 Data collection process

Data was collected for a period of 10 months, from October 2014, up to August, 2015. This period took into consideration the time used for preliminary data analysis, as this was concurrently done with data collection. Access, recruitment, and data collection procedures for trial participants, research staff and documents differed significantly. These procedures are summarised in figure 3 below and explored in more details in the next sections.

4.6.1 Access and recruitment

Accessing former HIV trial participants necessitated breaking their confidentiality by disclosing their HIV positive status and thus presented ethical concerns. To preserve their confidentiality, participants were first contacted by their former research institutions, to ask for permission for me to approach them. There, former HIV drug trial participants were contacted by a member of the research institutions where they

previously participated. This was done using phone calls or a home visit by a staff from the participating institution. Although the researcher facilitated this process, the researcher did not have any contact with the trial participants until a member of the research institution had made an introduction to them. Participants from Trials 1 and 2 were contacted and met the researcher on a one to one basis, while the initial contact with Trial 2 participants was in a group gathering. The research staff responsible introduced the researcher to the participants, explained the purpose of the study, and asked for those who were willing to participate in my study. Participants were given a chance to ask questions, which the research staff responded to, and where required, I was also asked to clarify on a few issues.

For participants who agreed to participate in the current study, I was given access to their details and was free to contact them for a formal informed consent session, where the details of the research were explained, and consent was sought for the participants to take part in the study. Following oral consent of the participants, we arranged for a suitable time and venue for the interview. The participants were provided with the patient information sheets to take with them and get more clarifications about the nature of the research, providing detailed information on aspects contained in the informed consent form. These documents were in the language more preferred by the participant. These are provided in appendix 1. The participants were also encouraged to share with their relatives, in case this was important to them. Prior to the interview, the informed consent form (appendix 2) was read and explained in details to the participant. Consent to take part in the study was elicited by a written full name and signature or a thumbprint of the participant. There was no need for a witness/translator, since the researcher was conversant with the two languages (Luganda and English) used during the interviews.

The majority of the participants who were contacted accepted to participate in the research. All potential participants from Trial 1 consented to participate, two potential participants in Trial 2 refused to provide consent and they did not provide particular reasons for refusing to participate. One potential participant in Trial 3 failed to turn up on the date of the interview, and when contacted by a home visitor, she failed to leave home due to fear of her husband as she had not disclosed her HIV positive status to him. Our meeting failed for two days and although she wished a reschedule of the interview, this was not possible as my time to leave the field had reached. The approach to data collection from post-trial participants was purposeful, to enable emergent issues to be followed up from the research staff. Therefore, the researcher ensured that before

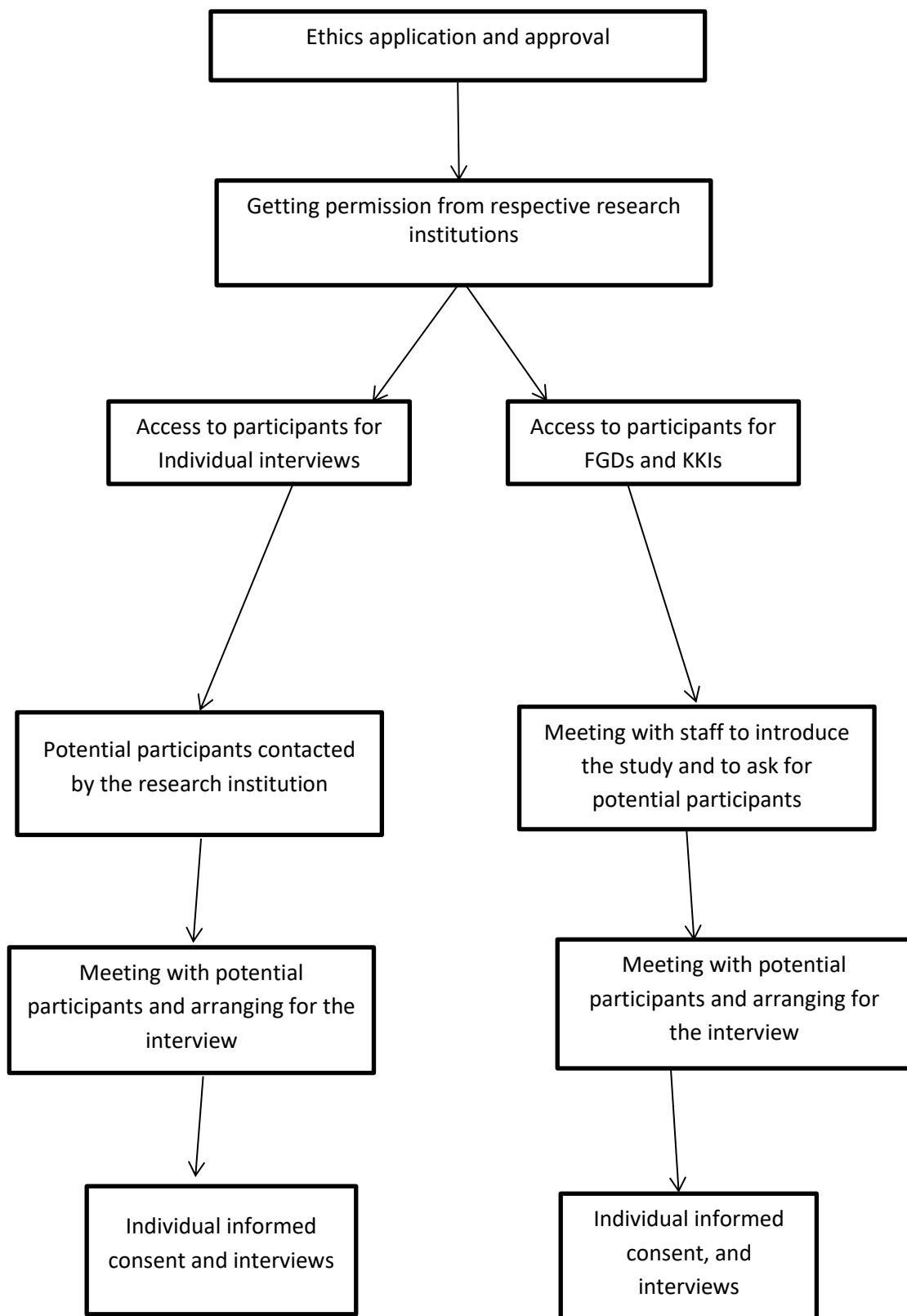
interviewing research staff in a given trial, a few interviews had to be collected first from post-trial participants.

Only two FGDs were held and were at the same research site. One was with research nurses and another with staff related to counselling/home visiting. Initially, a staff meeting was organised where I was invited to speak to them about my research and to ask for their participation. During the same meeting, those who showed interest to participate were offered with an information pack about the research. Later, I contacted the departmental heads, who helped me to mobilise the staff for the discussions. On the day of the FGDs, I further explained about my research and sought for individual written consent, which they provided using a signature. Following consent of the participants, I conducted the group discussion. All FGDs were conducted in the English language. Participants in the FGDs were encouraged to express freely their views about the topic and were all informed about their equal opportunity to participate in the interview. Prior to the interview, FGD members were briefed on how the interview was going to proceed. Participants were encouraged to speak one at a time, to respect one another's views and no to interrupt. They were put on nametags with pseudonyms which were used in identifying them during the group discussion and in reporting the research findings.

The current research also utilised key informant interviews. These included all three coordinators of the three trials, clinicians from Trial 1 and all research staff from Trial 2 and Trial 3. The initial access to participants for KIIs was similar to those for FGDs. These were initially approached through the research administration, e.g. the program coordinators. After being introduced to the potential participants, I explained the research to the potential participants. Those who showed willingness to participate were provided with information sheets to read more about the study. Appointments were made with individual participants for the interviews.

Lastly, access to documents preceded consent from the participating institution, which was provided during the overall permission to undertake research in the given institutions. Although three trials were involved in the current study, only two trials were involved. This was for ethical reasons, as one of the trials was still undergoing and using information from documents guiding the trial was considered inappropriate.

Figure 3: Access and recruitment process



All interviews (individual, FGDs and KIIs) were tape recorded, and where necessary, field notes were taken to summarise the key points and reflections. Data collection followed an iterative approach, consistent with the grounded theory approach, where initial data informed later data collection (Charmaz, 2006; Levy, 2006). All interviews were collected by myself and no case required a translator or the presence of a second party. No participant was excluded on the basis on language barrier.

4.6.2 Data collection instruments

Semi-structured interview guides were used for individual in-depth interviews, FGDs and KIIs. The tools consisted of broad open ended questions with prompts, to allow as much as possible, an open and detailed discussion to emerge from the participants. The content of the tools were driven by the research aim and objectives, the literature reviewed, and the inputs from my supervisors. The tool for individual interviews were originally in the English language, but was translated into various languages including Luganda, Ateso, Gishu, and Japadhola, which are the commonly used local languages in the catchment areas of this research. However, only the English and the Luganda versions were used since all participants were capable of communicating fluently in either of the two languages. Copies of the data collection tools are found in Appendix 3.

To ensure the appropriateness of the tools, these were reviewed by my supervisors and by the ethics committees which reviewed and approved this research. The tools were not piloted before actual data collection, and instead, all initial interviews conducted were considered as part of the formal interviews. However, basing on the flexibility allowed in the grounded theory approach (Charmaz, 2014), questions in the interview guides were constantly modified according to the emerging insights. The original interview tools nonetheless remained a useful guide throughout the data collection process.

4.7 Data analysis

Recorded interviews were carefully listened to and transcribed prior to data analysis. As previously stated, interviews were either in the English or Luganda languages. Interviews in Luganda were transcribed first before being translated. All transcription and translation were done by the investigator, who is fluent in both English and Luganda. Transcription was done promptly after the interview was conducted, and the analysis process commenced, prior to conducting further interviews. The length of the interviews varied and lasted between 25.5 to 66.2 minutes.

Data analysis followed the standard format of grounded theory. This was done through open coding (line by line coding), focused coding (coding larger sections of data),

developing categories and showing their relationships between them (axial coding), comparing and collapsing categories (theoretical coding), and finally building a theory (Charmaz, 2006, 2014). Although these steps were not necessarily undertaken in sequence, the researcher endeavoured to stick to them. Following the principles of grounded theory is helpful in exposing the thoughts, ideas, and meanings contained within the text of the interviews, which contributes to a credible process in theory construction (Charmaz, 2006; Oktay, 2012). In addition, techniques such as memo writing, theoretical sampling, and theoretical sensitivity, through constantly comparing data were undertaken during the analysis process. These techniques ground the researchers' interpretations and consequent theorizing in participants' experiences (Mills et al., 2006). Data collection and preliminary analysis occurred concurrently, with earlier data informing subsequent data collection.

The analysis of the data was facilitated by a Computer Assisted Qualitative Data Analysis (CAQDAS) software, NVivo 10. Use of CAQDAS have been cited by various authors (Hutchison, Johnston, & Breckon, 2010; Petra & Jaka, 2015; Saldana, 2009) to be useful, in not only providing an easier approach to managing massive qualitative data, but also for its possible contribution towards the credibility, validity, and the overall quality of qualitative research. Specifically, some authors (Hutchison et al., 2010) have credited the use of NVivo software in grounded theory studies, as this offers a framework which facilitates most of the key processes and characteristics of the grounded theory approach, thereby improving its quality. The data analysis process for the current study is explained in more details below.

4.7.1 The coding process

Coding in qualitative inquiry means grouping of segments of data and assigning meaningful labels to them (Charmaz, 2014; Saldana, 2009). The coding process is considered the initial analytic step towards generating theory (Charmaz, 2014; Strauss & Corbin, 1990). Codes represent the actions, or processes that are imminent in the data, and capture a conceptual interpretation of the data, by the researcher defining what they see, while trying as much as possible to stick to the data (Sbaraini, Carter, Evans, & Blinkhorn, 2011). Through coding, I was able to maintain an interactive engagement with the research participants, by constantly interacting with the data (Charmaz, 2006). This process enabled me to have an analytical understanding of the actions, processes, and meanings that trial participants assigned to the trial closure phenomenon.

Initial coding in the constructivist grounded theory approach involves identifying all possible meanings from the data, by trying to remain as open as possible to any

theoretical possibilities which may exist (Charmaz, 2006, 2014). Initial coding sticks closely to the data, and attempts as much as possible to use labels/words which reflect actions and processes (Charmaz, 2012; Saldana, 2009). Charmaz (2014) argues that coding for actions and processes (rather than topics and themes) carries the potential to define connections between data. As soon as the interviews were transcribed, initial coding commenced. This was done first outside the NVivo software, in a word template, which was designed to provide a space for the data on the right side and one for the codes on the left. This helped me to constantly look back at the data and reflect on the codes assigned. According to Saldana (2009), initial manual coding can be helpful in deriving concepts, which provide a framework that can then be fitted in a CAQDAS, to guide subsequent analysis. Although there are many approaches to initial coding e.g. word-by-word, line-by-line, paragraph-by-paragraph, or even coding a larger section of data specific to incidents (Charmaz, 2012, 2014), I preferred the line-by-line approach, which enabled me to tease out all possible concepts and to ensure that any important codes were not missed (Charmaz, 2006).

Because initial codes are provisional (Charmaz, 2014), I endeavored to remain open to any new possibilities of interpretations from the data, by trying to constantly review the codes to ensure they best fit the data. Initial coding also facilitated my analytical process by identifying codes which were more close to the data, and trying to pursue these in subsequent data collection. In addition, initial coding was helpful in enabling me to see gaps in the data, which required 'filling' as early as possible by the theoretical sampling technique. Throughout the initial coding process, I was sensitive to codes which appeared to be more theoretical. Some of the initial codes were found to be more conceptual and were used as theoretical categories in the final model, following minor modifications. For example, 'advocating for post-trial follow-up', 'feeling uncertain about post-trial care', and 'advocating for financial support' were initial codes which gave rise to more theoretical codes such as 'follow-up care and monitoring', 'worry about future care', and 'socio-economic support' respectively. Initial coding continued until I had coded three interviews, after which I initiated the focused coding process. Although no specific criteria exists on when focused coding can be initiated, Charmaz (Charmaz, 2006, 2014) recommends that this can occur as soon as the researcher has established a strong analytical direction.

Focused coding is a process where one attempts to group larger quantities of data, into meaningful, interpretive codes. Here, the researcher pursues the most significant or frequent earlier (initial) codes to group larger quantities of data (Charmaz, 2014; Sbaraini et al., 2011). During focused coding, the researcher tries to make decisions

about their data, by trying to identify those codes which carry the most analytical insights (Charmaz, 2014; Strauss & Corbin, 1998). In the current study, focused coding was undertaken, in order to elicit more conceptual codes which represented the data. The process of focused coding initially followed a manual approach. Initial codes were grouped and renamed according to how they best represented the data, while some initial codes automatically became focused codes, after realizing that these could adequately represent particular data. The process of focused coding eventually led to the identification of concepts, which were transformed into tentative categories. After identifying the tentative categories, further data analysis was transferred to the NVivo software, where focused coding, categorisation, and theory construction continued on all collected data.

Forming categories is another important analytic step towards theory construction. Categories can be understood as conceptual elements, which link codes and theory, and are essentially the building blocks of theory (Charmaz, 2014). During the analysis process, categories are used to further refine data conceptualization, by reassembling it into more coherent wholes (Strauss & Corbin, 1998). While forming categories, I endeavored as much as possible to retain the meanings of the original data, by constantly comparing the emerging categories with the data and the codes. As I kept listening to the interviews during transcriptions, some of the categories could be identified from the data. I kept track of these and constantly compared them with the already existing ones, their dimensions/properties, and the codes.

Naming of categories took into account logical relationships of the name given and the data it represented, ensuring that, as Strauss and Corbin (1998) denote, the category names are more abstract than the concepts they represent. In this case, I strived to uncover the abstract meanings inherent in the focused codes, and gave them labels which best represented more abstract conclusions. Some of the categories which emerged from the focused codes are summarized in table 8 below.

Table 8: Development of categories from focused codes

Focused codes	Tentative categories
Feeling hopeful about research Feeling sad for leaving research Feeling bad for leaving research Feeling uncertain about a post-trial care institution Worrying over transferring to new care facility Feeling unhappy about research closure Desiring to continue research participation	Emotional effects of research closure
Being burdened by OIs Feeling burdened by OIs Feeling desperate for failing to afford medications Receiving free medications Feeling a burden of treating OIs Anticipating complications due to untreated OIs Advocating for treatment of OIs Feeling uncertain about ability to treat OIs Worrying about health status	The burden of opportunistic infections
Peer networking and support Importance of peer networking Disadvantages of not networking with peers Maintaining peer networking and support Importance of post-trial follow-up Advocating for trainings in post-trial care institutions Importance of peer support and networking Becoming peer educators Fearing to separate with peers Desiring to network with peers Fearing to separate with peers Importance of peer support	Social support
Advocating for financial support Importance of financial empowerment Encountering transport difficulties Advocating for financial support	Economic implications

In addition, some categories emerged which suggested trial closure to be a process rather than a one off event. The tentative categories which initiated this insight were: 'pre-closure care', which categorized data relating to post-trial care perspectives occurring before the actual trial closure; 'care during transitioning', which captured data about post-trial concerns, needs, and practices during the period of actual trial closure and linkage to post-trial care facilities; and 'post-trial care', which categorized data on the post-trial perspectives of participants after linkage to post-trial facilities. These tentative categories later defined the three phases of the transition process, as shown in the transition model in chapter nine of this thesis. As a means of verifying my analytic steps and ensuring the analytic decisions were well grounded, copies of initial transcripts, codes, and categories were sent to my supervisors, who reviewed and commented on them.

Further analytic processes involved axial coding, where the properties of the developed categories were identified, defined, related with each other (Mills et al., 2006; Strauss &

Corbin, 1998), and refined further through the technique of theoretical sampling. The phase of axial coding sought to conceptualise the HIV trial closure phenomenon, and it was further guided by constant comparison and memoing techniques, which allowed linkages between categories and their properties to be refined and included in the iterative analytical process (Walker & Myrick, 2006). Strauss and Corbin (1998) express that axial coding enriches the data, by identifying the crucial properties, dimensions, and associated relationships of the categories.

While undertaking axial coding, questioning plays a key role in the expansion and interpretation of the data (Strauss & Corbin, 1998). These questions carry analytical power and fosters analytic interpretation rather than a description of the data (Charmaz, 2012). Throughout data collection and analysis, I endeavoured to dig out the answers to the 'what', 'why', 'when', 'where', 'how', and 'who' questions. For example, in relation to the studied phenomenon, I asked questions such as: how were participants linked to post-trial care, where did participants go for post-trial care, what type of care was provided during trial closure, why did respondents suggest that specific actions were relevant to post-trial care, who was responsible for providing particular care, etc. Asking these questions enabled me to acquire detailed information which was helpful in enriching the categories identified, and provided explanatory power to the developed theory (Charmaz, 2012). Figure 4 below provides an example of a memo in which questions were used to guide further data collection, analysis and conceptualisation.

During axial coding, diagrams were also used to link different categories and subcategories together, showing the relationships between them, and how they contributed to the subsequent theory. Grounded theorists consider diagramming as a central component of the analytic process (Mills et al., 2006). Making linkages between categories and sub-categories using diagrams enabled me to make more sense of the data, and significantly contributed to the analytic process. An example of a diagram which was drawn is presented in figure 5 below.

Figure 4: Using questions to guide further data collection

**Facilitating transitioning/process-action memo
/23/06/2015**

Who? Staff have a responsibility to link post-trial participants to care. Participants can be of two groups. The naïve and the experts. The experts are easier and may/are facilitated differently from the naïve. The experts may be easier to facilitate since they are familiar with the environment and may have overcome HIV stigma. The naïve may be more difficult because they are going to new environments all together and may also still suffer from stigma thus may require a different form of facilitation, involving different actions/actors. Collaboration among stakeholders appears vital in the transitioning process.

NB: While collaborating to ensure post-trial participants are linked to care, the roles of different stake holders may pose different responsibilities. Particularly for the public but also for the NGO sectors, how are the staff in these facilities enabled to do their work?

How? Referral so far has been the only way post-trial participants are linked to care. This is done through providing referral letters and other forms of facilitation e.g. transportation costs and directions to the place (for those who are not familiar). Well as this form of facilitation may/has worked for the experts, it may not be very effective for the naïve. Moreover, even the experts claim to experience some challenges while being reinstated back into care, hence advocating for a physical facilitation where they may/are escorted and assisted to register back into care.

Why? Explore the reasons as to why post-trial participants may require facilitation and which forms should be appropriate.

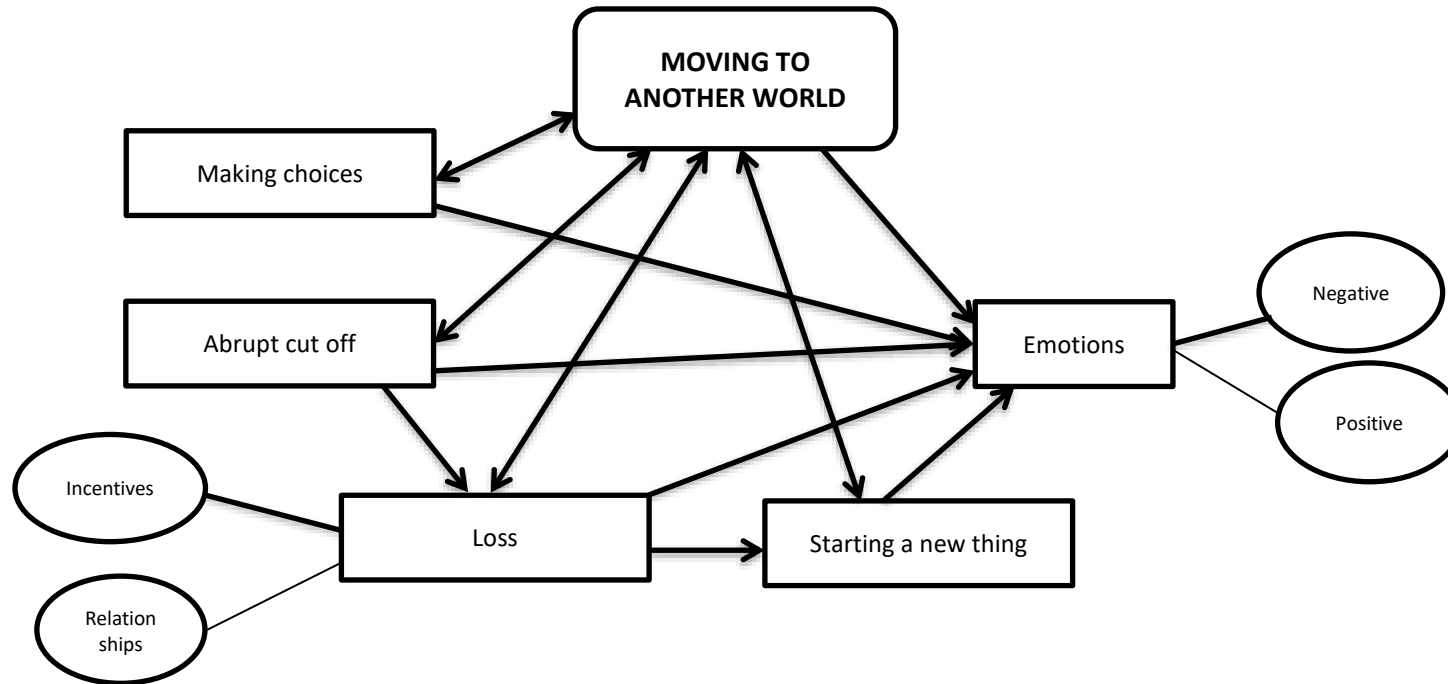
When? Most expert patients are referred before but towards the actual closure. Is it the same way naïve patients are referred and is it the best way it should anyway be or there is a need for adjusting. Explore these, in case one can get the naïve participants. If not possible to answer in the current study, this might require another research in future.

4.7.2 Theoretical coding and identification of the core category

Another important step towards construction of theory involves conceptualisation of the substantive categories through a process of theoretical coding, and relating them with possible predictions (hypothesis) (Charmaz, 2006; Strauss & Corbin, 1998; Walker & Myrick, 2006). According to Charmaz (Charmaz, 2006), theoretical codes are developed to make conceptual linkages to the focused codes and provide an analytical story about the analysis. The relationships and linkages between the different concepts during theoretical coding is assumed to empower the theory to be tested, modified or expanded by other researchers (Charmaz, 2012). In the current study, the process of theoretical coding was iterative, just like other analysis steps, and all theoretical codes emerged as close from the data as possible. This process translated the analytical material into a recognisable and understandable theoretical framework, the Facilitated Transition model.

Identifying a core category early in theory development provides researchers with an insight into the likely theory (Giske & Artinian, 2007). In the current study, I initially allowed as many categories to emerge as they appeared, without necessarily pinpointing out the core category. Through further refining of the categories, constant comparison, and theoretical sampling and coding, a core category was identified. A core category is defined as 'the central phenomenon around which all the other categories are integrated (Charmaz, 2014; Mills et al., 2006). Formation of a core category acknowledges that the researcher reconstructed the participants' stories, and acts as a representation of their 'voice' (Strauss & Corbin, 1990). The core category in this research was identified as the main process occurring throughout the data, and this emerged from linking the main processes of 'transitioning' and 'facilitating', which gave rise to the 'Facilitated Transition' concept. This concept appeared to represent the views of the respondents about post-trial care, by explaining how the trial closure process evolves, proceeds, and concludes. The views of the respondents appeared to suggest that transitioning of HIV positive participants in Uganda requires particular facilitative and care measures. The developed model is presented in chapter ten of this thesis.

Figure 5: A diagram representing the emerging theme of 'moving to another world'



4.7.3 Memo writing and sorting

Memo writing is a skill of noting down the ideas of the researcher as they emerge during the research process (Giske & Artinian, 2007). Memo writing is an important technique in constructing grounded theory. Charmaz underscores the importance of memoing in theory construction, as it provides an opportunity to start the analytical process early in the research, and also provides an intermediate step between data collection and writing the research draft (Charmaz, 2014). The process of memo writing helps the researcher to stay closely engaged with the research process, by constantly reflecting on the research progress and emerging insights (Strauss & Corbin, 1998).

Throughout data collection and analysis, various memos were written. These mainly fell under two categories: case memos and memos of themes. Case memos included summaries of the different data sources and interview proceedings. Immediately after conducting an interview, a summary of what transpired in the field and the key points about the interview were noted down. This was helpful to capture the initial ideas and fresh insights which emerged around the interview context before the full transcription and analysis of the interview occurred. Memos of themes were reflective accounts on the analytic processes. These ranged from early descriptive memos to more advanced (abstract) and analytical ones, as the analysis progressed. Memos varied in length and content, and progressively evolved in complexity, clarity, and accuracy as the research progressed. Memos were dated, given a label representing the main concept or code being referred to, and where applicable, quotes from raw data were used to emphasize on the memo content.

As Charmaz noted (Charmaz, 2014), early memos are usually done to provide a direction to the research, by observing and recording what is happening with the research, exploring and filling out the identified codes, and helping in focusing and directing further data collection. Initiating memo writing early enabled me to constantly reflect on the research progress and also supported my reflexive account. I constantly reflected on the data gaps I had identified, and specifically sampled data to fill them. An example of an early memo, written after analyzing the first six interviews is provided in figure 6 below.

Figure 6: An example of an early memo

Facilitating linkage to care/code/early memo/23/02/2015

Linkage to care may be taken as an easy process, but it may not be so. Linkage to care faces various challenges. Such challenges have been compared to what new participants attending a care facility for the first time face. For example, going through registrations (which is a lengthy process) which amounts to long waiting hours and, meeting new staff and clients.

Participants felt being facilitated during the time of linking to care is what would be appropriate in this situation. This would not only help to remove the hassles of getting into care again, but would also act as a way of updating the care staff about the people they took away and researched on: *"There are some people when you are given the medication after taking those referrals, when it will cause you major effects depending on your health. And yet if they could know that this is like this, and they explain to each other"* [Sumin, II5].

While participants reported to their former care institutions, they were likely to face challenges. Joseph thought those going to new institutions would even face worse challenges. For example, these are people going to a totally new environment i.e. new structures, new people, new staff, etc.. these would benefit a lot from a facilitated linkage: *"Now there are people who come from far and they are sent to a place they don't know, they find it challenging until they get familiar with the new place"* [Joseph, II2].

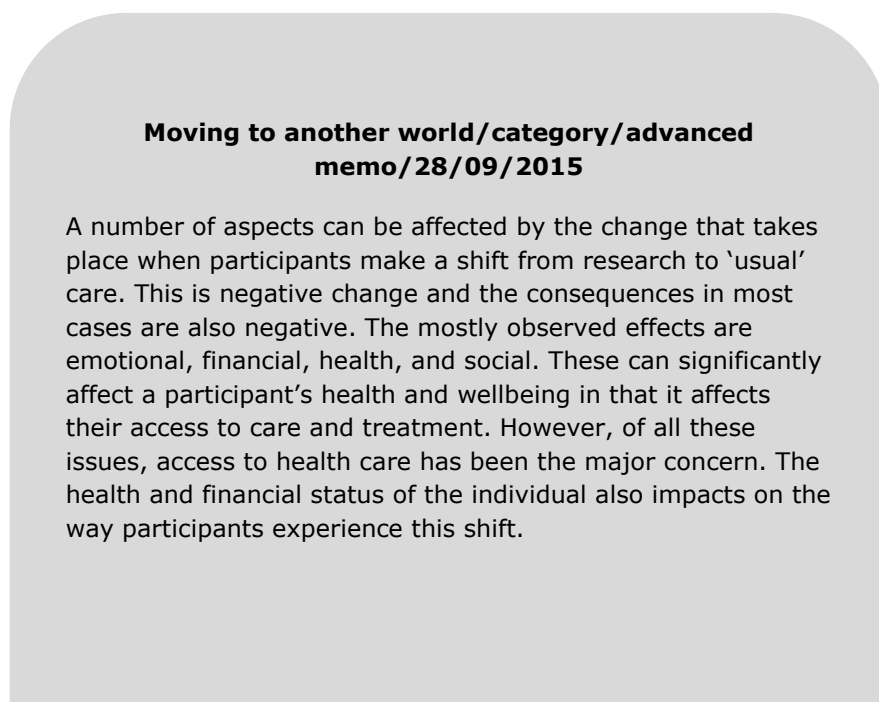
Being properly linked to care also may consist of follow-up to ensure participants have settled in care. **How long is the suggested period of follow up? (Explore in the code: follow up in post-trial care)**

NOTE: Linkage to care seems to cross cut throughout the transitioning process whereby there is a need to facilitate participants to get linked to care facilities. This process however could be broader than just the care facilitated, to the whole transitioning. **How can participants be facilitated during transitioning? Many factors come into play and these need to be explored.**

Advanced memos on the other hand tend to focus at the development of the categories, by elaborating how these emerge and change, and constantly making comparisons between emerging insights (Charmaz, 2014). Writing advanced memos in this research progressed as the analysis progressed. Analytical insights and their relationships were

constantly jotted down and these eventually led to the description of important processes about the studied phenomenon. An example of an advanced memo is presented in figure 7 below, describing one of the major categories in the research 'moving to another world' (which was further developed into a substantive category 'moving to a new care context'), and explaining the linkages between some concepts within the category, and also with another substantive category 'adapting to a new care context'.

Figure 7: An example of an advanced memo



Theoretical memos were subsequently sorted and arranged to provide a meaningful sequence, which contributed to the various sections of the thesis write up. Through the analytical processes described above, writing, sorting, and integration of the memos, I was able to identify the core category of this research. The analytic processes also facilitated the identification of theoretical relationships between the substantive categories, which contributed to the development of the conceptual model of Facilitated Transition.

4.8 Maintaining rigour and reflexivity

Maintaining rigour in qualitative research is paramount due to the quality concerns posed in qualitative approaches. One way of maintaining rigour is by researchers being aware of, and acknowledging their position and its possible influence on the research (Lambert, Jomeen, & McSherry, 2010; Sultana, 2007). Being a former research nurse in HIV drug trials, there is a possibility that my knowledge and previous experience in the research

area could influence my overall approach to the research. Having awareness of this possibility, I strived not to impose my previous theoretical knowledge and professional experience on the research. This was achieved through undertaking a rigorous approach to the research and by being reflexive. The following sections explain how the rigour of the research was maintained and how the major reflexivity concerns were addressed.

4.8.1 Maintaining rigour

Lincoln and Guba (1985) recommend a criterion for assessing the rigour of qualitative research on four constructs namely: credibility (how the representation of data fits the views of the participants), confirmability (ensuring that findings are confirmable and are grounded in the data), dependability (ensuring that the process of research is open, traceable and clearly documented) and transferability (ensuring that research findings are transferable to other specific related contexts).

In the current study, maintaining the credibility of the findings was very paramount. This was achieved by ensuring that the conclusions made during the analysis process fit within the views of the participants. The rigorous approach of grounded theory, where findings are initially derived inductively (Charmaz, 2012) was helpful to enable generation of findings which were grounded in the data. Undertaking a systematic approach to data collection, analysis, and interpretation, as guided by the grounded theory methodology allowed the emergence of themes/conclusions which principally relied on primary data from the respondents. This approach also did not give room for relying on pre-existing concepts, thereby limiting the possibility of 'forcing data' (Mills et al., 2006).

The rigour of the current research was further strengthened by the processes of theoretical saturation and constant comparison as provided for in the grounded theory approach. These techniques increased on the confirmability of the research findings. Theoretical saturation allows a researcher to gather data which adds to the knowledge of particular concepts which have been generated inductively from the research (Charmaz, 2012). In the current study, theoretical saturation was achieved through ensuring that, data collection after generating initial and important categories aimed to ensure that all relevant data about the important categories/concepts were gathered before leaving the field. By ensuring theoretical saturation, a (rich) more explanatory, and reliable theory can be generated (Strauss & Corbin, 1998). The constant comparative process was also helpful to ensure that that theory development was constantly assessed, by comparing the emerging data and categories. Furthermore, using verbatim quotes was important in ensuring the confirmability of the conclusions in the current study. In the current study,

all findings were supported by verbatim quotes from the respondents and/or from the reviewed documents.

To ensure the dependability of the research findings, a proper and clear record of the participant characteristics, inclusion and exclusion criteria, the study context, and participants' demographic data was taken during data collection. This was also a helpful approach in ensuring that the findings could be analysed/interpreted in context, which contributed to the overall rigour of the research, by enabling comparisons between contexts and also helping in the overall understanding of the studied phenomenon. In addition, rigour in the current research was strengthened by use of multiple data sources, a concept known as triangulation. The various data sources in the current study included the post-trial participants, research staff, and ethical documents. Triangulation can be helpful in enabling more dependable conclusions on a phenomenon (Levy, 2006; Zakiya, 2008), hence my understanding of the trial closure phenomenon was enhanced by the views from the various sources. Use of multiple data sources in the current research also allowed for comparison of the emerging insights, which contributed to the generation of more explanatory categories and to the overall construction of a more dependable theory.

Paying attention to negative cases has also been suggested to improve the rigour of qualitative research, as this can help to uncover the differing perspectives on the studied phenomenon and aid analytic generalisations (Gubrium, Buckholdt, & Lynott, 1982; Murphy et al., 1988). Although no apparent negative case emerged during the course of the current study, I kept open to identifying these throughout the research. However, there were aspects of the trial closure phenomenon where participants shared opposing views. For example, the aspect of financial benefits which has presented controversy in research, emerged as an area where opposing views were shared among respondents. Taking into account both the negative and positive views on some aspects helped to widen the overall understanding of post-trial concerns and contributed to the construction of the theoretical interpretation of the research findings.

Although contested by some authors (Murphy et al., 1988), the rigour of qualitative research can also be achieved through member checking, expert opinion, or receiving feedback from those who know about the research field (Levy, 2006). Due to resource constraints, no member checking was undertaken in this research. However, the supervision by my supervisors, who are experts in both the research area and the methodology was very helpful in ensuring that the research remained within acceptable standards. During the entire research process, I kept consulting with my supervisors,

who constantly checked and commented on the transcripts, emerging codes, categories, and the theory.

4.8.2 Addressing reflexivity concerns

In qualitative research, a researcher is assumed to be an important research instrument, which raises concerns of research trustworthiness due to the subjective nature of this type of research (Sullivan, 2002). Reflexivity is an aspect in qualitative research which is assumed to counteract the potential impact of subjectivity (Patnaik, 2013). Reflexivity can be understood as a subjective reflection on what a researcher is doing, and how and why they are doing it (Mason, 2002; McGannon & Metz, 2009). This reflection can then enable the researcher to confront and challenge their own assumptions about the research subject, while also recognising the degree to which their own thoughts, actions, and decisions during the research process may shape what they research and how they make conclusions on the research findings (Mason, 2002; Vanderback, 2005). Shaw (2010) notes that a central component in understanding reflexivity is the explicit evaluation of self, which involves reflecting one's thinking back to themselves, by examining their own role in the co-construction of meaning within a socially oriented research situation.

Although reflexivity can relate to reflection, these concepts are different. For example, while making a reflective account, one engages in more general thoughts about how participants' accounts have been adequately represented. Reflexivity on the other hand is thought to go beyond reflection, by endeavouring to evaluate the self, and acknowledging the role of the researcher as a participant in the production of knowledge construction, and not only an outsider and observer of a phenomenon (Patnaik, 2013).

Authors have established the importance of reflexivity in qualitative research, especially in terms of addressing methodological concerns in the qualitative paradigm, particularly the lack of objectivity. Some argue that reflexivity comes in to address this concern, by providing a framework in which a researcher may appraise and critique their role and contribution to the research process (i.e. their subjectivity) (Saks & Allsop, 2013; Wasserfall, 1993). Reflexivity can be applied throughout the research process, from the inception of a research idea and formulation of a research topic, through data collection and analysis. This can be done through an examination of how one's values and attitudes influence a research topic, the choice of a research methodology, designing of data collection tools, and conducting the interviews, to the final conceptualisation of the research findings (Patnaik, 2013).

Reflexivity and the researcher's theoretical and experiential perspectives

To be reflexive, requires consideration of one's theoretical, experiential, and socio-cultural perspectives, to evaluate how these might have impacted the research process. Aspects such as training and professional background, gender, social class, ethnicity, and culture should be evaluated as these may have a potential impact on how the research question might be formulated, the methodological approach selected, the data collection process managed, and overall data analysis undertaken (Patnaik, 2013; Sullivan, 2002). Patnaik (2013) explains this type of reflexivity as "introspective" reflexivity, where the researcher maintains an awareness that their experiences, attitudes, and emotions will have an impact on their engagement with research participants and the eventual data analysis. Being reflexive in this aspect enables the researcher to challenge their possible biases, prejudices and attitudes, which is important in minimising their influence on the research process, since they strive to retain their focus on the research and the research participants (Patnaik, 2013; Shaw, 2010).

My professional background as an HIV care and research nurse might have influenced how I approached the participants, how I collected and interpreted the data, and how I made the conclusions of the research findings. Having worked in HIV research for more than five years, I had experienced the transition process of HIV trial participants. I had personally participated in the closure processes and supported the participants during this process. I witnessed their frustrations about the closure and had seen some struggle to access healthcare after the closure of the trials. These background perspectives were important to recognise, and to appreciate their potential role in influencing the current research in relation to data collection, analysis and interpretation of the findings. For example, I acknowledge that my background as a research nurse influenced how I structured the questions in the interview guide, how I asked the questions and probed for more understanding of the emerging issues, and how I interpreted the data in terms of making meaning of the post-trial processes. Being aware of these possibilities throughout the research process was a helpful strategy to minimise their potential impact on the research process, and potentially increased the integrity and trustworthiness of the research findings (Finlay, 1998, 2005; Holloway & Freshwater, 2007; Mays & Pope, 2000).

Reflexivity and methodology development

It is argued that reflexivity should be applied while determining the research methodology. This is important to take care of the fact that in qualitative research, both the researcher and the researched, being in the same order, share related characteristics

which allows them to co-construct knowledge (Shaw, 2010). Patnaik (2013) explains the type of reflexivity regarding methodological considerations as “methodological reflexivity”. According to Patnaik (2013), methodological reflexivity strives to ensure that standardised methodological procedures such as the ethical, social and political considerations that govern the field of research have been followed during research conduct. This then contributes to the methodological rigour of the research.

Shaw (2010) elucidated on the importance of methodological reflexivity in contributing to the rigour of qualitative research findings. The author pointed to need to put into consideration the role that language may have on data gathering. For example, data gathering will involve engaging with the language, stories and experiences of other people, which requires a researcher to make a careful consideration while making meaning of these aspects (Sullivan, 2002). The constructivist grounded theory approach adopted in this research acknowledges the role of interacting with participants as co-constructors of knowledge. This approach greatly supported my reflexive undertaking, by observing its principles as closely as possible, which was able to minimise my own influence on the research processes.

Reflexivity during data gathering

The interconnectedness between the researcher and the researched remains fundamental in the qualitative research paradigm and requires to be acknowledged (Manderson, Bennett, & Andajani-Sutjahjo, 2006; Shaw, 2010). Shaw (2010) explains the importance of the interactions during a data collection scenario and how these interactions can shape our understanding of the data we collect. The research context, in terms of time and place in which the interview takes place, and the interviewer-interviewee relationships are important aspects in the research process, in shaping the resultant interpretation of the research findings (Shaw, 2010), and these should be acknowledged.

Reflexivity further entails the need to recognise the contributions different parties make in constructing the meaning on the studied phenomenon (McGannon & Metz, 2009). As a researcher, I strove to maintain a balance between answering the research questions while also being attentive to participants’ main concerns, and how these were communicated. By taking a reflexive stance, I ensured that I did not take literally the meanings derived from the participants’ narratives. Rather, I strove to stick to the inductive nature of the grounded theory process, and ensure that the interpretations made were congruent with the data. In addition, the constant comparison strategy in

grounded theory minimised the influence of subjectivity by constantly comparing the concepts in the emerging data.

Reflexivity during data analysis

It is important for the researcher to acknowledge their active role during data analysis, as this reflects a reflexive attitude. This is particularly important since interpretation is a key aspect of qualitative data analysis. Engaging in reflexivity during data analysis enables researchers to navigate through participants' accounts and how they respond to them, which helps the researcher to engage with their assumptions about the data and how they arrive at these assumptions (Shaw, 2010).

I kept a reflexive position during data analysis and interpretation, by acknowledging my role in these processes. I reflected on how my theoretical and professional background and experience might influence the meaning and interpretations I made out of the data. The more I interacted with the data, the more I made meaning out of it, and the less I felt my previous experience was exerted on them. The grounded theory approach was particularly helpful in shaping my reflexive potential during data analysis. For example, instead of using pre-conceived concepts to analyse the data, I derived concepts inductively. Although there was a review of related literature prior to data collection and analysis where several concepts regarding post-trial care were discovered, being a grounded study, these did not limit the inductive nature of the research. As McGhee, Marland, and Atkinson (2007) commented, the knowledge of the field and being familiar with some concepts should not limit the inductive nature of a grounded theory study. The initial phases of the grounded theory approach, which involves coding and identifying of emerging concepts was particularly helpful in making conclusions which are grounded in data, thereby limiting the potential impact of my pre-conceptions on the studied phenomenon. In addition, the overall analytical processes were supported by the grounded theory principles of constant comparison and memo writing, and constantly stepping back and reflecting on the data and the emergent theory. These processes promoted theoretical sensitivity which enhanced my reflexive experience.

Conclusively, although reflexivity can be a complex task, it is a very important aspect in qualitative research (Shaw, 2010). Engaging in this activity was helpful in improving the methodological rigour of the current study, as it enabled me to give consideration to my personal perspectives while undertaking the research.

4.9 Ethics

This research followed an ethical process which promoted its integrity. Ethical approval was sought from the University of Nottingham UK and The AIDS Support Organisation (TASO) Uganda, Research Ethics Committees (RECs) (Appendices 4 and 5 respectively). Following ethical approval, an application for the registration of the study was made to Uganda National Council for Science and Technology (UNCST), which is the national research regulatory authority in Uganda. Permission and registration for the study was granted and the current study was registered as SS 3608, on 10/11/2014. (Appendix 6). An introduction letter from The University of Nottingham UK (Appendix 7), and all ethical approvals were delivered to the management of the target research institutions (section 4.5.1 above). These institutions were informed formerly of the research details and permission to conduct the research was sought from these through the management. These institutions provided their permission before any access procedures could commence (appendices 8 and 9).

After being formerly introduced to potential participants (as explained in section 4.6.1 above), these were offered an information pack containing the study details. To facilitate understanding, the information pack was in a language most preferred by the potential participant. Participants were given a choice to go and consult with their family on their decision to take part in the current study if they wished. This was important to the context of study, as social relationships can be important in determining research participation even among adults in an African setting (Nalubega & Evans, 2015). Potential participants were allowed as much time as they wished to think about their decision on whether or not to participate in the research. The research objectives and methods were explained to the potential participants and a written informed consent was obtained from them before any data collection was commenced. The consent form contained information about the study purpose, the right to participate or to withdraw, assurance about confidentiality, potential benefits, potential risks, compensations, identifying and contact details of the investigator, identifying and contact details of the TASO ethics chairperson, a place for the name and signature for the participant, and a place for the name and signature for the investigator. Effort was made to ensure that the tools were in a simple language, with less use of technical terminology and vocabulary (section 4.6.2). Participants were further assured of their right to join or withdraw from the study at any time when they wished, without any negative consequences especially on their care. This was important since the majority of participants tended to consider the current study as part of the previous clinical trials and they could possibly feel obliged to provide information for the current study.

To ensure confidentiality of former research participants, the initial contact with them was made by their former research institutions (section 4.6.1 above). The investigator in the current study only contacted those individuals who gave their consent to be contacted by a non-research staff of the former trials. Participants were assured of total anonymity at all stages of data collection and handling. Individual participants were informed that the research findings were to be published, but their name or any other identifying information would not appear in the report. Use of pseudonyms for respondents and included trials provided a safe background of ensuring confidentiality in the current study. Although details of the participating institutions are reported in the methodology section (following their consent), reporting of the findings was anonymised to prevent linking them to specific institutions or trials.

Confidentiality of all information obtained from the participants was maintained by not allowing information on the respondents' identities to be accessible to non-members of the research team. Electronic data was stored on a device with a password that is only known by the investigator, while data in hard copies (e.g. from ethical documents) was securely kept under lock and key, and can only be accessed by the principle researcher. Furthermore, access to transcripts of the data was restricted to only the researcher and the supervisors. Finally, the data collected from this study will be kept at the University of Nottingham, School of Health Sciences for seven years following its collection, and will then be destroyed.

The current research had potential risks to the participants of which they needed to be protected from. For example, being identified as participating in HIV research carried a potential risk for social stigma. Effort was made to keep research participation as confidential as possible from the community and/or family, by allowing the participants to determine their favourable venue and time for the interview. In addition, due to the nature of psychological stress associated to HIV, it was anticipated that the in-depth interviews could evoke emotional distress among participants. Although this effect never occurred, measures had been put in place, e.g. of the researcher spending more time with the research participant and providing some counselling, and referring them for further counselling if deemed necessary.

The researcher had also anticipated cases of individuals who could have had health risks (e.g. those who failed to continue with HIV care following trial closure). If these occurred, the researcher had planned to provide necessary advice to these, by either guiding them on how/where they could access further care, or referring them for further support. Nonetheless, the health risk identified in the current study was mainly lack of

adequate resources to care for participants' healthcare needs, e.g. raising transport fares to healthcare facilities, purchasing treatments for opportunistic infections, and buying food. The researcher provided some advice especially on some of the existing NGOs in the community which could offer financial support and also encouraged the particular individuals to share their concerns with their current care providers. Overall, the financial concerns were generally difficult to address since they required more practical support.

Regarding risks associated to lone working, measures were in place to address this risk if it occurred, e.g. informing a colleague (from the respective research institution) of my whereabouts and keeping them updated before my arrival and while leaving the participant's home. However, as reported in section 4.5.2 above, all interviews were conducted at research premises, hence lone working did not emerge as a concern in this research. All the same, the research institution authorities were constantly updated about the times when, and venues where, I would be interacting with individual trial participants.

4.10 Dissemination of the research findings

A comprehensive report on this research in form of a PhD thesis will be submitted to the University of Nottingham, School of Health Sciences, and this will be archived in the school of Health Sciences Electronic Dissertations and Theses database. The findings of the current research have been disseminated in different forums, e.g. in local and international conferences as detailed in the preliminary section on page xiii above. The systematic review that informed the background and rationale for the current study was published in a peer review journal. Four papers from this research will be published in peer reviewed journals.

UNCST, TASO REC, participating institutions, and all respondents in the current study will receive a copy of the summary of the research findings. Effort will also be made to disseminate the findings of the current research to other RECs involved in reviewing and approving HIV research projects, other non-participating HIV research institutions in Uganda, NGO care facilities involved in HIV care, and some government facilities, especially in the catchment area of the current study.

4.11 Conclusion

The post-trial period is an important phase in the conduct of HIV research involving HIV positive participants due to the need to continue access to treatment, care and support. Post-trial care may be of particular importance in low income settings where research may provide better care compared to usual care. There is a need to develop ethical

guidelines that will address the specific care needs of participants in these settings. The contribution of relevant stakeholders in HIV drug trials is very important in the formulation of these guidelines. Using a constructivist grounded theory methodology, this research investigated the perspectives of HIV drug trial participants and research staff regarding care in HIV drug trial closure in Uganda. The current chapter has provided a detailed account of the methodological approaches and steps undertaken in this research. The next chapter presents an introduction to the findings of the research.

CHAPTER 5: INTRODUCTION TO THE RESEARCH FINDINGS

5.1 General introduction

This chapter presents an introduction to the findings of the study. The first part of the chapter presents the contextual and demographic characteristics of trial participants. The second part presents an introduction to the main findings of the research, by introducing the transition model in HIV drug trial closure developed in this research.

Throughout this document, pseudonyms for respondents, the included trials, research institutions, and other healthcare facilities will be used to maintain anonymity. In addition, when referring to participants who took part in this research, different labels will be used. For example, the term 'trial participant(s)' or 'participant(s)' will refer to HIV post-trial participant(s) who participated in this research, the term 'research staff' or 'staff' will refer to research/trial staff who were interviewed, while the term 'respondents' will be used when post-trial trial participants AND research staff are talked about together. On the other hand, the term 'healthcare staff' or 'facility staff' will be used when referring to healthcare workers from non-research institutions. Finally, the terms 'pre-trial care facility', 'previous care facility', 'primary care facility', or 'former care facility' will be used when referring to care facilities where trial participants attended care before joining the included trials, while 'post-trial care facility' will be used to refer to care facilities where trial participants attended their care after exiting from the included trials.

5.2 Contextual and demographic characteristics of respondents

This research included a total of 21 trial participants and 22 research staff from three HIV drug trials. In addition, two relevant sets of documentation were reviewed. The three trials are referred to as Trial 1, Trial 2 and Trial 3, and were conducted in two research institutions referred to as institutions A and B¹⁰. Trial 1 and Trial 3 were conducted from institution A, but at different sites, while Trial 2 was conducted from institution B. The three trials were conducted from relatively different social settings, as these were situated in different regions of the country, providing a wide range of social diversity. The specific contexts of the included trials and the sociodemographic characteristics of the participants proved highly relevant in the analysis and interpretation of the research findings. Details of the trial contexts and the demographic characteristics of respondents are presented in the sections below.

¹⁰ The two institutions have been described in details in the previous chapter.

5.2.1 Characteristics of included trials

The trial contexts are described mainly in relation to the general purpose of the trial, the study site, participant recruitment strategies, care and treatment during trial conduct and trial closure, and exit procedures. In addition, some relevant trial characteristic features are described, to assist with the interpretation of the research findings. These include; the immune/health status of trial participants at recruitment, experiences of HIV care/treatment before joining research, contact or not with pre-trial care facilities during research, access to HIV care and treatment during research, and the presence or not of a care facility attached to the research institution. These factors are provided in table 9 below.

Trial 1

Trial 1 at research site A aimed to test different second line therapies in patients failing on a first line regimen in Africa. This was a three arm parallel group, open-label, multi-centre, randomised controlled trial. Participants were included if they were HIV-infected adults who had taken a first-line NNRTI based regimen continuously for a total period of at least 12 months, and developed treatment failure defined by modified World Health Organisation (WHO) 2010 criteria¹¹. Patients who had poor adherence to therapy, who were known to be Hepatitis B co-infected, required concomitant medication which have known major interactions with study drugs, or women who were pregnant or breastfeeding were excluded. The trial had a 12 months' recruitment period and each patient was followed for 144 weeks. The trial was carried out at the urban site of institution A, located in Kampala, the capital city of Uganda. Although currently this site is relocated to the outskirts of Kampala, at the time of the trial, the clinic was located within the heart of Kampala city.

Potential participants were recruited from the national ART programs. These included any sites which provide HIV care and treatment such as; government institutions, NGO facilities and private institutions. Potential participants were sourced by collaboration between the research institutions and the care facilities where these participants received HIV care and treatment. During the trial, participants were seen every four weeks until week 24, then every six weeks until week 48, and then every eight weeks until the final trial visit. Some of these visits were nurse-led visits to check on adherence

¹¹ Modified World Health Organisation (WHO) 2010 criteria for treatment failure includes:

- New WHO Stage 4 event (with CD4 < 200 cells/mm³ and viral load (VL) > 400 copies/ml)
- CD4 < 100 cells/mm³, or CD4 fall to pre-treatment baseline or below, or CD4 < 200 cells/mm³ X 2 with previous CD4 > 400 cells/mm³ (with VL > 400 copies/ml)
- VL > 5,000 copies/ml x2

and physical well-being, to gather relevant health services utilisation data, and to identify any clinical events that might need further evaluation by a clinician. Participants received all their HIV and other healthcare, treatment and support from research, including treatment for any opportunistic infections. Incentives such as breakfast and transport refund were provided.

Trial closure followed a well laid out plan, using a Trial Closure out Manual. The manual detailed all the procedures required while exiting participants. From week 128 visit onwards, transition discussions were made with every participant and participants were asked to which institutions they preferred to exit. Participants were encouraged to ask any questions they had and their queries were answered. In general, linkage to care was managed through referral, by providing trial participants with written information, which consisted of a summary of their health situations and treatments during research. To maintain continuity of treatment, participants were provided with a buffer stock of trial medicines, usually for three months, to cover up for the time while they made arrangements to transfer to their post-trial care facilities. For participants whose trial regimens were not available on open market, these continued to access them from the research facility. By the time of the interviews for the current study, two post-trial participants were still accessing their HIV treatments from the research institutions, and they were not aware when this would stop. At trial closure, participants were informed that they will be invited for the trial results once these were ready for dissemination, and by the time of the interviews, these had not yet been provided.

Trial 2

Trial 2 was a three-year trial which evaluated the safety of discontinuing Cotrimoxazole prophylaxis among HIV infected adults on antiretroviral therapy in Uganda. This was a randomized double blind placebo controlled non-inferiority trial, to evaluate whether long-term primary and secondary prophylaxis with Cotrimoxazole can be safely discontinued among Ugandan adults on antiretroviral therapy, who have achieved sustained immune restoration (measured as a confirmed increase in CD4 count to 250 or more cells/mm³). Eligible patients were HIV positive adults aged 18 years and above, who were stable on ART and had confirmed sustained CD4 restoration to 250 cells/mm³ and above, who were able to attend designated study clinics.

Trial 2 was conducted at two sites of institution B, one in the Central region and one in the Southwest region of Uganda. However, this study drew only on participants from the Southwest region, located in Masaka district. Patients in long term ART care were referred to the study site from ART provision centres in and around Masaka. Patients had

been in ART care and on concurrent cotrimoxazole prophylaxis for at least 6 months. Recruitment into the trial took place over 24 months and participants were followed for a minimum of 12 months and a maximum of 36 months.

All participants were treated with concomitant anti-retroviral treatment in line with the national programme guidelines. These continued to be supplied by the pre-trial care providers. Participants were also encouraged to continue accessing counselling and support from their pre-trial facilities. Other medication(s) or treatments as necessary for the management of HIV related illnesses or other chronic disease conditions were provided in the study. Incentives such as breakfast and transport refund were provided. Trial exit procedures included documenting and availing each participant with a clinical summary and a referral back to their respective national ART provision centres, which were essentially their pre-trial care facilities. A buffer stock of the study drug, enough for three months was provided to each participant. At trial closure, participants were informed that they will be invited for the trial results once these were ready for dissemination, and by the time of the interviews, these had not yet been provided.

Trial 3

Trial 3 was a randomised controlled trial investigating three methods to reduce early mortality in adults, adolescents and children aged five years or older starting antiretroviral therapy (ART) with severe immuno-deficiency. This was an open label multi-centre trial, conducted in nine centres, in four African countries, with three centres located in Uganda. The current study only drew on adult participants from Uganda, at a site located in the Eastern region of the country. Three methods to reduce early mortality following ART initiation were evaluated, with each intervention being compared with the standard of care¹². The assumption was that each of the interventions would reduce early mortality in those starting ART with severe immuno-deficiency. Each intervention was administered in addition to standard of care for 12 weeks. Each participant was followed for 48 weeks in the trial and the overall trial duration was 3 years.

In addition to meeting other inclusion criteria, participants were included if they were ART naïve (including no single dose Nevirapine for Prevention of Mother to Child Transmission of HIV), and with CD4 count >100. Since patients with a CD4 count below 100 cells/mm³ should not have ART delayed, all patients eligible for Trial 3 were those

¹² The standard of care in previously untreated patients presenting late with very low CD4 counts is to initiate ART with 3 drugs from 2 classes, together with cotrimoxazole prophylaxis and macronutrient intervention only for those with low BMI (or low weight-for-height/mid-upper arm circumference in children).

testing HIV positive for the first time with a low CD4 count (i.e. those delaying presentation to care), or those who have defaulted before initiating ART and only return to care at an advanced stage of immuno-deficiency. For this research, all participants interviewed were HIV care naïve, meaning that they first received HIV specific care and treatment (including counselling) from research. This factor was particularly important in shaping the participants' understandings of what research means in comparison to usual care, and might have played a role in their responses to some aspects of post-trial care such as financial benefits, trial feedback and choice of post-trial care facilities.

The majority of participants were recruited from testing centers such as NGO based testing centres, government/public testing facilities, and private testing facilities. During the trial, participants received all their care in research and a transport refund was provided. Similar to other trials, linkage to care was mainly through provision of a referral letter. At trial exit, participants were informed that they will be invited for the trial results once these were ready for dissemination, and by the time of the interviews, these had not yet been provided as the main trial was still ongoing.

Table 9: Important characteristic features for included trials

	Trial 1	Trial 2	Trial 3
The immune/health status of trial participants at recruitment	Immune suppressed after first line regimen treatment failure	Had achieved sustained immune restoration	Severe immuno-deficiency
Specialised HIV care/treatment experience before trial participation	Had previous experience	Had previous experience	All included participants did not have specialised HIV care/treatment experiences prior to trial participation
Contact with pre-trial care facilities during research	No contact retained	Retained contact	No contact (there were no pre-trial HIV care providers)
Access to HIV care and treatment during research	Received all HIV related care and treatment from research	Received the trial regimen and all treatment related to opportunistic infections from research. Routine HIV care and ART medications were received from pre-trial care facilities	Received all HIV related care and treatment from research
Presence of a care facility attached to the research institution	Present	None	Present

5.2.2 Demographic characteristics of respondents

This study included a total of 43 respondents. Twenty-one of these were trial participants while 22 were research staff.

Of the included trial participants, seven were from Trial 1, eight were from Trial 2, while six were from Trial 3. The majority of trial participants (62%) were female. Trial participants were in the age range of 26-59 years, with the majority being above 40 years. Only one participant had attained a university degree, and the majority were below college level, having either stopped at ordinary or primary levels, or had no education at all. The education status trend was also reflected in participants' employment and socio-economic status, where very few were in official employment, and the majority depended on small scale jobs, subsistence farming, or other sources of income such as support from families or friends. Some participants reported not working due to ill health, while others had lost their formal employment due to illness. Most participants resided in rural or peri-urban settings. Participants' demographic characteristics are summarised in table 10 below.

Of the included research staff, three were trial coordinators, four were clinicians, five were related to counselling and home visiting, while 10 were nurses (one of the trial coordinators was also a nurse). Trial 1 included 15 research staff, Trial 2 included four research staff, and Trial 3 included three research staff. The difference in the representation of research staff numbers in the different trials was mainly determined by the availability of the staff in a given trial. In terms of gender, only 27.3% of research staff were male. This trend could be explained by the larger number of nurses represented in the sample compared to other cadres, since the majority of the nursing workforce are female. Table 11 below presents the characteristics of the included staff.

Table 10: Trial participant characteristics

Name (Pseudo)	Trial	Age	Sex	Education	Employment	Marital status	Residence	Pre-trial care facility	Post-trial care facility
Edwin	Trial 1	41	Male	Primary	Subsistence farming	Married	Rural	NGO research based	NGO research based
Janet	Trial 1	54	Female	College	Self-employed (runs a day care centre)	Single	Urban	NGO non research based	NGO research based
Joel	Trial 1	59	Male	O level	Subsistence farming	Cohabiting	Rural	NGO non research based	Research facility
Joseph	Trial 1	40	Male	Primary	Self-employed (taxi driver)	Married	Peri-urban	NGO non research based	NGO research based
Madina	Trial 1	50	Female	O level	None	Married	Urban	NGO non research based	NGO research based
Ruth	Trial 1	44	Female	College	None	Single	Rural	NGO research based	Research facility
Sumin	Trial 1	30	Female	O level	Salesperson in a milk outlet	Single	Peri-urban	NGO non research based	NGO non research based
Abdu	Trial 2	35	Male	O level	Religious teacher	Married	Peri-urban	NGO non research based	NGO non research based
Aidah	Trial 2	46	Female	Primary	Subsistence farming	Married	Rural	NGO non research based	NGO non research based
Baker	Trial 2	52	Male	Primary	Self-employed (Tailor/fisherman)	Married	Peri-urban	NGO non research based	NGO non research based
Bettinah	Trial 2	33	Female	O level	Restaurant attendant	Widowed	Peri-urban	NGO non research based	NGO non research based

Brenda	Trial 2	27	Female	Primary	School cook	Separated	Rural	NGO non research based	NGO non research based
Byekwaso	Trial 2	50	Male	None	Subsistence farming	Married	Rural	Government facility	Government facility
Nabakooza	Trial 2	54	Female	Primary	Subsistence farming	Widowed	Rural	NGO non research based	NGO non research based
Naluwugge	Trial 2	49	Female	None	Subsistence farming	Widowed	Rural	NGO non research based	NGO non research based
Dennison	Trial 3	46	Male	College	Self-employed (short term construction contracts)	Married	Peri-urban	None	NGO research based
Mariako	Trial 3	41	Female	College	Secondary school teacher	Separated	Peri-urban	None	NGO research based
Marion	Trial 3	34	Female	O level	Personal small scale business	Divorced	Peri-urban	None	NGO research based
Mukhwana	Trial 3	26	Female	College	Cashier in a computer café	Single	Peri-urban	None	NGO research based
Nandi	Trial 3	28	Female	College	Primary school teacher	Single	Peri-urban	None	NGO research based
Wilberforce	Trial 3	46	Male	University	None	Married	Peri-urban	None	NGO research based

Table 11: Research staff characteristics

Name (Pseudo)	Cadre	Sex
Anne	Nurse	Female
Destiny	Nurse	Female
Elhana	Nurse	Female
Mabel	Nurse	Female
Menke	Nurse	Female
Mubiru	Nurse	Male
Rose	Nurse	Female
Salif	Nurse	Female
Tina	Nurse	Female
Gloria	Nurse	Female
Prosy	Counsellor	Female
Joy	Counsellor	Female
Charlotte	Counsellor/Home visitor	Female
Favour	Counsellor/Home visitor	Female
Bernard	Community Liaisons Officer	Male
Lydia	Clinician	Female
Mark	Clinician	Male
Nsubuga	Clinician	Male
Wambo	Clinician	Female
Alloy	Trial coordinator/Nurse	Male
Ivan	Trial coordinator	Male
Jane	Trial coordinator	Female

5.3 Introduction to the study findings

The aim of this research was to establish how care is perceived, experienced and enacted in HIV drug trial closure in Uganda. Specifically, this research sought to understand how HIV positive trial participants expect, understand and experience care as they transition from HIV drug trials to the public healthcare system or community.

From the perspective of research staff, this research sought to establish how staff understand, perceive and practice post-trial care in HIV drug trials involving HIV positive participants.

Following data analysis, it became clear that transitioning of HIV positive participants from research to usual care is a process, involving distinct yet overlapping phases. These phases include: The pre-closure phase which represents events occurring before the actual trial closure but that underpin and influence post-trial care, the trial closure phase which is the active phase of the closure in which trial participants are prepared and exited from the trials, and the post-trial phase which represents the events occurring after trial participants have been linked to post-trial care facilities until 12 months later. These phases are demarcated by specific time points, which reflect how the transition process evolves, proceeds and concludes. However, these demarcations as reflected on Facilitated Transition model are somewhat arbitrary, as there is a tendency of overlaps, in terms of the events which occur within these phases.

The transition process encompasses the events which occur when an HIV positive trial participant, following planned completion of participation in an HIV drug trial, is exited from research and linked to the public healthcare system to continue with the recommended HIV services. The main events which occur along the process relate to trial participants' care expectations, needs, experiences, and decisions. Although the main events appear to occur during the trial closure and post-trial phases, the research found that they are strongly influenced by the events which occur before the actual trial closure, i.e. during the pre-closure phase. For example, prior experiences of care in the public healthcare facilities, care experiences during previous research, and care experiences during the conduct of current trials significantly shaped trial participants' post-trial care expectations, experiences and decisions. In addition, the main events which occur during the transition process are largely influenced by individual participant situations before, during, and after trial closure. For example, individual factors such as the health status and social-economic situation may influence the care needs and experiences during the transition process.

The care delivery gap between research and the Ugandan public healthcare system significantly influenced the events which occurred along the process. The research and the Ugandan public healthcare contexts were described as two 'different worlds' in terms of service care provision, with research usually offering exceptionally higher standards of care compared to the public healthcare facilities. The main care discrepancies between these two contexts were identified in: the quality of the general medical care such as the

ability to appropriately diagnose and treat HIV related problems, the availability of HIV treatments especially for opportunistic infections, staff attitudes and approaches towards HIV patients, time management, privacy, and provision of incentives such as food or transport facilitation. Hence for the majority of trial participants, leaving research means moving from a more to a less desirable position.

At the various phases of the process, specific concerns (care needs) arise, being influenced by the various factors explained above. Specific actions are required to facilitate trial participants during these phases. These actions are underpinned by the ethical and moral responsibilities of the researchers, and are principally aimed at establishing a continuum of HIV care and treatment after trial closure, promoting positive care experiences for trial participants during the transition, and enabling the settlement and adaptation of trial participants to the care in the public healthcare system.

A Facilitated Transition Model, which summarises the main events occurring at the various phases of the transition process was developed basing on the findings of this research. The model is presented in chapter 10 of the thesis. The findings of the current study are presented in three main chapters and are introduced in the following sections.

5.3.1 Contribution of included trials to specific research findings

Although broadly all main themes and most categories were contributed to by all included trials, there was a remarkable difference in regard to the contribution of specified trials to the particular findings of this research. The variations in the contribution to particular findings was likely related to the specific trial contexts (described in table 9 above) as explained in the findings chapter.

Generally, all trials acknowledged the loss of the quality care from the research and seeking future care as particular concerns during the trial closure period. In addition, clinic delays in post-trial facilities, dealing with difficult/unwelcoming staff, meeting transport and treatment costs, and other domestic needs following trial exit, and requiring the support of researchers and other stakeholders were crosscutting concerns among the included trials. The main concerns which presented variations among the included trials were: the need for recognition for trial participation, which was almost explicitly expressed by Trial 2 participants; the fear of side effects from trial interventions and thus the need for timely trial feedback, which was only a concern among Trials 1 and 2; practical challenges during establishment into post-trial care, which was a particular concern for Trials 1 and 3; concerns of being exposed while

attending post-trial care facilities, which was a major concern for Trials 1 and 2, and the need for and practice of peer support which was particularly reported by participants from Trials 1 and 2. A summary of how different trials contributed to the respective trial findings is presented in table 12 below.

Table 12: Summary of findings from trial participants and their association with the included trials

MAIN FINDING	SUBSTANTIVE CATEGORY	KEY FINDINGS	MAJOR CONTRIBUTING TRIALS
MOVING TO A NEW CARE CONTEXT	Going through an emotional turmoil	Losing quality care and supportive relationships	Trials 1, 2 and 3
		Needing recognition	Trial 2
		Uncertainty about future care and treatment	Trial 1, 2 and 3
		Fear of side effects from trial interventions	Trials 1 and 2
		Anxiety of not knowing trial outcomes	Trials 1 and 2
	Dealing with practical challenges	Deciding where to seek care	Trials 1 and 3
		Challenges during re-establishing into care	Trials 1 and 3
ADAPTING TO A NEW CARE CONTEXT	Adapting to the routines in public care facilities	Enduring clinic delays	Trials 1, 2 and 3
		Being in the open	Trials 1 and 3
		Dealing with different staff	Trials 1, 2 and 3
	Adjusting to the increased financial demands	Meeting transport costs	Trials 1, 2 and 3
		Meeting treatment costs	Trials 1, 2 and 3
		Attending to other domestic needs	Trials 1, 2 and 3
	Finding support	Support from researchers	Trials 1, 2 and 3
		Support from peers	Trials 1 and 2
		Support from the family and other stakeholders	Trials 1, 2 and 3

5.3.2 Introduction to chapter six

Chapter six presents findings related to how trial participants experienced trial closure and linkage to post-trial care processes. These findings mainly correspond to the trial-closure phase as presented on the Facilitated Transition Model in chapter nine. Trial closure was usually an emotional experience for most of the trial participants, and to the majority, it was non-desirable. A sense of loss of the quality care received in research, coupled with other underlying fears and concerns about access to alternative care in the Ugandan healthcare context contributed to trial participants' emotional reactions to the closure. Trial closure created significant health concerns among trial participants including uncertainty about future access to adequate and appropriate HIV care and treatments, fear of possible negative effects from trial interventions, leaving research without knowing trial outcomes, and fear of facing difficulties while getting established into post-trial care. The above concerns were particularly attributed to a feeling of being abruptly discontinued from the quality research care, which could not be matched with the available alternatives. Trial participants also became engaged in a decision making process of where to seek post-trial care. This process was quite stressful as it required carefully understanding and evaluating facilities which could provide care related to that in research, yet also putting into consideration other factors such socio-economic influences.

Although trial participants reported receiving some support during this process, it was not sufficient enough to address all their care needs. Participants suggested other facilitative measures from researchers and other stakeholders, which could be implemented in order to improve their transition. These included; facilitating linkage to post-trial care, providing appropriate and timely trial feedback, recognising their effort in research participation by providing some financial or material support, and monitoring for possible side effects from trial interventions.

5.3.3 Introduction to chapter seven

Chapter seven presents findings related to the post-trial phase of the transition process, and reports the experiences of trial participants of seeking and accessing HIV care following trial closure up to 12 months later. Accessing care in public healthcare facilities required the participants to adapt to the routines of service provision in the Uganda public health care system. Having been in research where they received high standards of care, made adjusting to post-trial services challenging for the majority of participants. For example, in research, there were usually adequate diagnostic and treatment facilities with adequate availability of drugs including those for treating opportunistic infections, trial participants usually spent fewer waiting hours since there were less numbers of

patients, research staff were perceived as very caring, there was privacy which was particularly important for those who still experienced HIV stigma, and there were incentives provided such as transport fees and sometimes food which was important for those with limited financial abilities.

The above aspects of care appeared to be the direct opposite to those in many of the post-trial public care facilities. For example, many trial participants reported severe clinic delays due to large numbers of patients at their facilities, many facilities lacked medications especially for treating opportunistic infections and participants required to buy these by themselves, a large number of participants described staff's attitudes as unwelcoming, there was no proper privacy as patients are usually attended to in an exposed environment, and trial participants had to pay their own transport fees and lunches. Most of the above factors eventually increased the financial demands on the participants. Those who were still experiencing ill health faced special care needs, as they usually failed to work, yet they required more finances to spend due to the need to frequently attend healthcare facilities, purchase medications, or food. Participants reported very minimal support during this phase and recommended various supportive approaches, including psychosocial, material, and financial support.

5.3.4 Introduction to chapter eight

Chapter eight presents findings derived from ethical documents and from the views of research staff. These findings relate to the ethical and moral responsibilities of researchers regarding HIV post-trial care, which emerged as the practical activities researchers engaged in or felt were necessary to facilitate the transition of trial participants from HIV research. The various care needs expressed by trial participants at the different points of the transition process called for facilitation and support. Information from a review of ethical documents such as the trial protocols and the trial closure standard operating procedure documents provided insights on how post-trial care was regulated in the included trials. On the other hand, researchers reported engaging in various activities to provide support to trial participants during the transition. The main activities included psychological preparation and support, addressing attachment and stigma concerns, and practical support activities. The psychological support offered aimed at: allaying trial participants' anxieties and fears related to trial closure, preparing them for trial exit, providing guidance on where and how to seek post-trial care, and providing financial advice. The practical support provided aimed at addressing the practical needs of the participants during the transition, and these mainly involved referral to support linkage to care, and provision of a buffer stock of trial medications to facilitate continuity of HIV treatment during the linkage to post-trial care facilities.

The current support however was viewed as insufficient to appropriately address the needs of trial participants during the transition and suggestions were made on how post-trial care for HIV people in Uganda could be improved. Some of the critical recommendations made included physical linkage to care of the participants, post-trial follow-up care and monitoring, and financial support. There was general recognition for the need to involve various stakeholders at different points of the transition process, and ethics authorities were viewed as important actors in the implementation of post-trial care, by their role in instituting and enforcing post-trial care policies.

5.4 Conclusion

This chapter has presented a general introduction to the research findings. First, the contextual and demographic characteristics of the respondents have been presented. Second, this chapter has provided an introduction to the main findings of the research, in which the transition process in HIV drug trial closure was introduced, and the content of the main study findings' chapters introduced. The next chapter presents findings related to the first substantive category, 'moving to a new care context'.

CHAPTER 6: MOVING TO A NEW CARE CONTEXT

6.1 Introduction

This study suggests that there is a 'care gap' that exists between research facilities and the Ugandan public care facilities. This gap shaped the reactions/actions of most of the trial participants when faced with the reality of trial closure. This gap exists primarily in terms of care provision, with the main aspects of concern being availability of treatments, especially for opportunistic infections, staff interactions with clients, provision or not of incentives, and clinic waiting times. The research and the public care contexts were perceived as significantly different, with research usually perceived to be offering exceptionally high quality care compared to the public care facilities. This chapter describes how HIV post-trial participants experienced care as they navigated through the psychosocial and practical complexities associated with trial closure and re-establishment into usual care facilities in Uganda.

Trial closure was usually an emotional and undesirable experience for most trial participants. A sense of loss of the quality care received in research, coupled with other underlying concerns such as ill health, low-social economic status, and the negative perceptions and experiences of care in the public healthcare system contributed to trial participants' emotional reactions to the closure. Trial closure created significant health related concerns among trial participants, including uncertainty about future access to HIV care and treatment, fear of possible negative effects from trial interventions, and leaving research without knowing the impact and outcomes of trial participation. In addition, trial participants expressed fear of facing difficulties while getting established into post-trial care. The above concerns were particularly associated with a feeling of being abruptly discontinued from the quality research care, which could not be matched with the available alternatives in the public health care system.

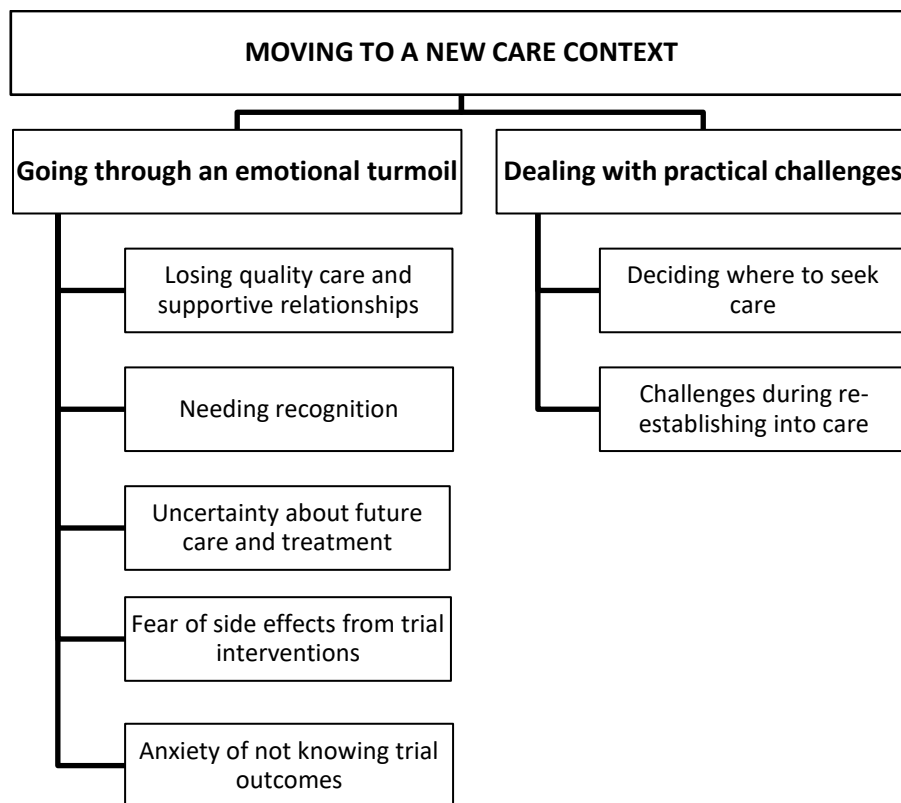
During trial closure, participants also engaged in a decision making process of where to seek post-trial care. This process was quite stressful as it required a careful understanding and evaluation of available care facilities which were likely to provide quality care to match that of research, yet also putting into consideration other factors such as the psychosocial and financial implications of their choices. These concerns called for various supportive measures.

Although participants reported receiving some support during the transition process, this was not sufficient to address their complex needs described above. Participants suggested other measures which could be implemented to improve their experiences during this process. The main ones included provision of appropriate and timely trial

feedback, a more facilitated 'linkage to care process', for example by using physical handover of participants to their post-trial care providers, financial support and empowerment, follow-up care and support after trial exit, and monitoring for possible side effects from trial interventions.

Findings in this chapter are presented under two main sections. The first section describes the emotional impacts and needs of trial participants during the trial closure period, and the second section describes the practical experiences and needs of the participants during linkage to post-trial care facilities. The findings of this chapter are summarized in figure 8 below.

Figure 8: A summary of chapter six findings



6.2 Going through an emotional turmoil

Trial closure often resulted into a complex emotional reaction among the HIV positive participants. Some of the emotions expressed included sadness, fear, worry, uncertainty, hopelessness, and despair. These emotions were attributed to a number of factors including, loss of the quality care and treatment and of supportive relationships, the need of finding alternative care, the possibility of experiencing side effects related to trial interventions, leaving research without knowing trial outcomes, and feeling not recognised for their contribution to research. In addition, trial participants reporting undergoing difficulties of deciding where to seek care while some reported practical difficulties while re-establishing into new care facilities. The negative emotions and impacts were also highly associated with participants' perceptions and experiences of the low standards of care in the Ugandan public healthcare system. The feeling of being cut off from research care abruptly also increased participants' negative reactions to the closure. Many expressed the negative emotions and impacts while explaining their reactions and feelings, and care expectations, needs and experiences of trial closure. These issues are explored in more details in the following sections.

6.2.1 Losing quality care and supportive relationships

Participants expressed how trial closure exposed them to loss of the quality care and treatment in research and other research related benefits. To many, loss of research care meant loss of the best or only available and trusted means of access to quality care. The aspects of care most participants were concerned about included: the ability to adequately assess and manage their health conditions, provision of treatments for opportunistic infections, the general approach of the staff, privacy, clinic waiting times, and provision of incentives. Many participants expressed negative emotions attributed to being stopped from research care. For example, some expressed feelings of sadness as shown in the quotes below.

...and in leaving here, I am one who felt most sad I think, because of leaving here, because the service was good, (Joseph, Trial 1)

So when they informed us that the research was coming to an end, we said 'let them extend the study a bit,' but they said 'no, they only gave us three years and we are going to close.' So we had to accept it because their time had ended, but we felt bad, because of the way we used to be, because we were happy in research and then they told us they were closing. (Brenda, Trial 2)

(I felt) Bad (about the closure) because I used to come here without, here there was no jam, everything was prepared for us, I wished to continue with them but the time caught up with me. (Mukhwana, Trial 3)

Although the above concerns explicitly relate to the loss of quality care, these feelings were largely influenced by trial participants' pre-closure care experiences, such as their experiences before joining research and also during research conduct. These concerns were highly attributed to the fear of returning to the undesirable care conditions often experienced in previous care facilities or the public healthcare system in general. The public healthcare facilities were portrayed as offering 'poor' quality care, characterised by clinic delays, a lack of medications especially for treatment of opportunistic infections, lacking privacy, and having unwelcoming staff. In contrast, while in research, trial participants reported accessing timely and quality care, in privacy and from staff who were very friendly. This contrast in care between the two contexts appeared to be the major basis for the feelings of loss as represented in the quote below.

I felt sad, I felt sad, we felt sad (about the closure), because the first reason nurse, whenever you would become sick (during research), even if you came without a 100USHS which is required for private facilities, because the problem up there (at former care facility), when you come on a date other than your return date, and you haven't been brought on a wheel chair, they mistreat us. You have to first sit and wait, you feel very bad and nobody cares, and they are telling you that you didn't come on appointment, because they informed us that we should go to private facilities (whenever we are sick). Nurse time comes, for me I am a widow when I don't have even 100USHS¹³. [...] But here (in research) whenever you would come sick, the truth is that they would attend to you immediately and give you treatment which the others did not have. For them you have to suffer a lot for them to attend to you. They want to send you away, 'go away, you have come on a date which is not on your appointment,' so, you feel that if you had the money, you would have gone to a private facility and they would have attended to you already. But here whenever you would come, even if you have TB, whatever the problem, they would care for you. [...] It (the closure) was very painful, because they loved us; they never felt inconvenienced by us. (Naluwugge, Trial 2)

In addition, there were other factors which appeared to shape the feelings of loss of the quality care among trial participants. These included being ill at the time of closure, which increased the need for care and treatment especially for opportunistic infections, and having a poor social-economic status, which rendered participants incapable of affording treatments when in need. Although these factors were implicitly expressed in

¹³ Analogy to being with an 'empty pocket' or having no money at all

most of the narratives, it is clear that they contributed to the emotional reactions to the closure.

They prepared us, but we were not very pleased because they informed us that we were closing yet we were used to always having treatment, and whenever one would be sick you would only raise transport and come here and you are given treatment. So that (the closure) took us backwards, in that you can go to a hospital while sick and you explain to them and they inform you that 'no...we don't have this medication,' and they write it for you as it is supposed to be. So most of us were not aware that the medication is very costly, so you would reach and realise that you need medications of about 50,000USHS or 70,000USHS. So you find that it was hard for some of us, depending on one's situation. (Byekwaso, Trial 2)

Some participants felt a sense of abandonment when research care was discontinued, and more so when they perceived this to have been done abruptly. Participants felt they still needed and also deserved the attention and care of researchers even after trial closure. The main reason for this was the fear that specific concerns could arise after trial exit, which could only be explained or managed by researchers. Although this concern was related to fear of possible side effects of trial interventions (as will be shown in a later section), it was also related to the loss of the quality research related health services as one participant expressed.

But these ones, they just close and we go and hassle on our own, you go to a doctor and he charges you what he can and he even never explains to you properly, that this is like this and this. He just informs you that 'you are going to be on treatment for such and such a period, you will give us 200,000USHS or 150,000USHS.' So for you, you hassle with the money and completing the treatment. But he can't tell you that this is caused by this yet the people we moved with (while in research) they have to know and investigate the cause of the problem. Because many of us get problems, for us on the new medications (ARVs), we usually get similar problems. So it becomes easier for this doctor (in research) to know about the program. (Byekwaso, Trial 2)

The above concern suggested a need for post-trial follow-up care and support for participants after trial exit. On the other hand, the above data points out how quality care was attributed to the nature of the participants' relationships with researchers. The caring attitude of research staff was highly regarded by the participants. For example, simple actions such as explanations and reassurance were important to them when they faced challenges at research facilities such as delays. Trial closure meant loss of these valued relationships. Participants from all trials expressed this kind of loss and similar to

other aspects of care, it was expressed in relation to their previous knowledge/experiences of care within the public care facilities.

I missed them (research staff), because we used to come here few of us so they would care a lot for us. So they would discharge you early, and you would go home early, so you wouldn't delay as they would ensure that they attend to you. So that affected me so much, removing me from here and sending me the other side after my time had ended. I wished if they could extend at least for a year. (Nabakooza, Trial 2)

I was worried about how those people are going to care for me (after leaving research). They may not care for me the same way site A was caring for me. Because they were caring for me so much, about the treatment and their care, their encouragement, their support, they could give me also moral support. So that is why I liked them so much. (Dennison, Trial 3)

Similarly, some participants reported missing their peers when research closed. Participants valued peer relationships as these offered them moral and psychological support. Some participants reported displeasure for leaving research without having a chance to say a 'proper goodbye' to peers and the staff. Many said they were taken unawares by the closure and only realized when some of their peers had already been exited from research. This made many participants to part without taking any contacts of those they wished, which was stressful. This concern raised a need for addressing attachment concerns. Some suggested the need for researchers to support future networking among trial participants and researchers. One of the strategies participants recommended for addressing attachment concerns and also to facilitate peer interaction is having formal gatherings between participants and research staff during the trial closure phase.

For me I had expected that we were going to have a party, and we dance a bit, we have completed the three years and nobody has died in it, we have all completed them very well. I was expecting the party or at least some music, and we would all be happy as we have completed the three years, and everyone would go back to their former institutions where they get their medications from. (Bettinah, Trial 2)

Yes, because it would be right nurse, they would make for us a party while exiting us, which can bring us together, and that would help us to come together and to connect. (Abdu, Trial 2)

The above data suggests a need for a formal, symbolic closure strategy. Although Trial 1 participants reported having had such a gathering during trial closure, this was a one off

event. Most of the participants felt they needed to have ongoing interaction with peers and research staff, since this was likely to be a good strategy not only for weaning them off from research care, but also for monitoring, care, and support after trial closure.

In addition to the loss of the quality care and of the valued relationships, some participants expressed feelings of loss of material benefits when trials closed. Benefits such as transport facilitation and refreshments were considered important to some participants as the quotes below indicate.

I felt bad because whenever I would come here I would be given some money. They would give transport, so I felt bad and I said I am going to suffer because every time I would collect medications, I would also receive some money. That was the main thing that pained me. (Nabakooza, Trial 2)

Yes, I missed the food assistance, (Mariako, Trial 3)

Loss of material benefits had financial implications on trial participants. For example, participants now had to plan to meet their transport costs which were usually provided during research. In addition, other losses as explained above also increased the financial needs of participants. For example, loss of the quality care and treatment meant trial participants may need to purchase some medications on their own, especially for the treatment of opportunistic infections. Because the majority of trial participants were of a low social economic status, many felt they needed financial facilitation to meet their increased financial demands as Nabakooza commented.

Like most of my colleagues I was with in the research, the majority of them don't have..., and that is what I brought up, the issue of money. Sometimes, people cannot even afford what to eat, they don't have..., they cannot afford to buy for themselves sugar because of poverty. But now if people are exited and they are given some money, you may find that one can at least afford to buy sugar and the situation improves, but I tell you the situation in our villages is so bad. (Nabakooza, Trial 2)

However, the need for financial support seemed to strongly emerge from an ethical or a moral perspective, such as the need for recognition for trial participants' contribution to research. This issue is explored in more details below.

6.2.2 Needing recognition

While trial participants acknowledged the voluntary nature of their participation in research, many felt their commitment and the time spent during research deserved to be recognised, and thus compensated. Aidah expressed this concern.

It (the care at closure) was not enough. Ask me why. Comparing, they would have thanked us, for volunteering, it is not easy. Not everyone can volunteer, may be they needed to send us with some appreciation, may be, I even don't know how to tell this to you. I think they would have sent us with an appreciation. Yes, because it is not easy, you come under rain, you come under sunshine, you endure and continue, we spend a full day here, you abandon other responsibilities and you still prefer to come. They ask you this and the other and you endure, they prick you, and you endure, blood gets lost and they call you back. [...] It is not easy, at least you need to give a person an appreciation. (Aidah, Trial 2)

Although the majority of trial participants did not have formal employments, they still valued their subsistence work such as cultivation or tending to their animals. Many felt the loss of time during research was equated to loss of money, which was a particular concern for those who felt they spent long hours during trial visits. Though delays at the research facilities were generally minimal especially in comparison to usual care, there were instances when this was a concern to participants as Baker explains below.

The issue of time, yes you know time is an issue that a person has to..., like a white man said that time is money, so even when we were being trained, they trained us about time management. So we came to realise that any time that you waste, you will have lost something. Every time you waste, you will have lost something, because even now, I will tell you that I left home early to go and do such and such a job, because I already had an agenda for my work. But now I have lost them, not in a bad way, not in a bad way, no, don't take it badly, but I have cancelled them because of this. So now, the issue of time was significant because it was a lot of time. We would spend a full day. There is a time that some of us almost left, when the last person would leave at about 7:00pm. Especially on a day when there would be many sick people, doctors would work hard but could not handle us fast. So you would find that all that day was for here. (Baker, Trial 2)

Some participants such as Bettinah felt they needed to be compensated for the risks undertaken to participate in research, even though these did not actually occur.

Sincerely we take medications but these medications we were taking were for trying (experimentation). You see it? What if you die, your children, you see? It would be good that at the end, there would be some appreciation, the one they are talking about. So even

though it is our lives, but they were also looking for the truth. We also cared and we said let us give it (life) in to establish what works. (Bettinah, Trial 2)

Participants acknowledged the need to have prior agreement on financial benefits. Byekwaso stated that after receiving no compensation at trial closure, he and others would have considered making a complaint on the issue, but acknowledged that since there was no binding agreement this could not be made.

Ok for me and my colleagues, we had expected to get some token. Considering the time we moved with our colleagues (the researchers) while they were being paid, although they did a bigger work than us, but also for us whom they worked on, the time we spent coming, there was work left unattended to as you also know that you woke up to come here, what remains behind has remained. That did not happen, and colleagues tried so much to inquire about it and we told them that 'let us leave it like that as it is supposed to be because we never had any agreement about it from the beginning. We never inquired about it, we never talked about it,' and we accepted and said that 'if it is available..., if it is not available..., ' (Byekwaso, Trial 2)

The above view seems to highlight the need for discussion of financial benefits during the informed consent process. Nevertheless, disclosure of financial benefits was strongly contested by some research staff, who felt such disclosure could lead to coercion of the participants as will be presented later in chapter eight of this thesis. As the above data suggest, the need for compensation/appreciation was an almost exclusive concern for Trial 2 participants. This could be related to their characteristics, whereby the majority were well and thus were capable of doing productive work, hence their concerns about time loss. In addition, previous research knowledge and experience appeared to have impacted on trial participants' perceptions and expectations of financial benefits. Trial 2 participants, of which many had previous research experience, had higher expectations of financial benefits compared to other trials. In fact, all participants in Trial 2 expressed this concern. Their perceptions and expectations appeared to be shaped by how this aspect of care had been handled in previous trials as expressed below.

... because I will refer so much to the other one (research) of FX, that while exiting us, they also gave us some money. Yes and now this one, they just exited us, and only gave us transport. So now that is why I have told you that I will insist on that, to show you that we didn't receive any money as such yet in the other one people were many in the FX study because there was good money. But this one had no money as such. (Baker, Trial 2)

By contrast, participants with no previous research experience expressed fewer expectations on financial benefits, and where this happened, it was after probing by the

researcher. Their expressions also appeared to indicate a need for financial support rather than for compensation or appreciation for their contribution to research as the quote below suggests.

When research participants are leaving research, I would like them (researchers) to visit our home areas, to know whether this person can be able to be visiting each of her return dates or what, because at times, people have no money and they need medication, many of them, they need it, and they can take that medication with a lot of food. So I would like may be on the side of the government to give a hand to such people, because these drugs are strong, without like drinks or food it can cause problems. So I would like may be the government or the research companies to help these people with giving like food stuffs, like that. (Mukhwana, Trial 3)

The above perspective occurred particularly among Trial 1 and Trial 3 participants. This group had experienced prolonged ill health and some had expressed inability to work due to ill health. Moreover, the loss of the quality care after trial exit meant that these had increased financial needs such as of purchasing medications for opportunistic infections or of facilitating frequent travels to care facilities, hence the need for financial support. Their health situations could also have influenced them to perceive research as care or a favour, thereby failing them to realise their own contribution to research. Indeed, some participants expressed no need for compensation, as they perceived that the quality services received in research were sufficient. This was a typical situation for Trial 3 participants who were severely immunosuppressed at trial enrolment and the majority greatly improved during research as expressed in the quotes below.

For me I wouldn't mind about the token, I wouldn't mind so much so long as I am now feeling better. But it is those people who are making their researches, it is themselves to think that may be look at the situation and say 'let us..., because we are doing our research on this person, let us give may be something for may be just for interaction, for giving us information, or making our research to work well.' It is themselves to decide what they can, may be like just an offer or what. But according to me, I wouldn't say it is important. Like me who is feeling better through that research. (Dennison, Trial 3)

Actually, it (compensation) is not (important) at all so long as I know my life is moving on well, me I don't have any problem. So long as I know my life moves on, it is moving on the line, and you have put me on the line, me I don't have any problem. (Nandi, Trial 3)

The above data suggests that many participants valued the care in research rather than separate material/financial benefits. However, it also appears there were misconceptions held among some participants as some appeared to have failed to differentiate between

HIV research from care. This could expose participants to exploitation in research. These findings may have an implication in determining the financial benefits of HIV trial participants, since different individuals may have different needs/or reasons for financial benefits. This will require the involvement of potential participants and assessing individual trial/participant characteristics before determining the financial benefits.

Generally, the findings from the above sections demonstrate that the need for quality care was fundamental to how trial closure was received by the participants. Central to this was the role previous care experiences played in shaping the expectations, needs, and experiences of post-trial care among participants. As the data shows, trial closure exposed participants to the loss of the valued care in research. This care was particularly important for participants who were experiencing ill health and in need of continued treatment for HIV related illnesses. To many therefore, in addition to the need for continuity of access to routine HIV care/treatment, trial closure also meant seeking treatments for opportunistic infections. Participants expressed fears related to seeking/accessing post-trial care and felt they required guidance on the next steps. The following section explores this issue in details.

6.2.3 Uncertainty about future care and treatment

Trial closure exposed participants to concerns about future access to HIV care and treatment. The thought of receiving lower standards of care within the public health care facilities instilled fear among trial participants. Some were worried when they could not ascertain the nature of care they would receive after leaving research, which created a sense of uncertainty. For example, Dennison who had no specific HIV care experience before joining research appeared uncertain about his future care upon leaving research.

I was a bit scared (about the closure) because I knew that may be where they are taking me they will not care for me may be the same way they have been caring for me here. So, I said may be they could keep me around, they keep me around within their services so that I could be getting the treatment the same way they have been doing. Because I knew may be when I go there, may be they will change that style of the treatment, the way they have been, may not be the same. So I was not happy. (Dennison, Trial 3)

Such uncertainty resulted in participants desiring to remain in research related care and this influenced their post-trial care decisions as will be shown later in this chapter. As the above quote suggests, the possibility of not finding alternative quality care was central to causing the negative emotions among participants. These emotions were largely attributed to participants' perceptions of 'poor' service delivery in Ugandan public health

care facilities and were informed by their past care experiences within these facilities. Some participants expressed a lack of confidence in their previous facilities. For example, Trial 1 participants who had previous treatment failure seemed to attribute this to the 'poor' care in these facilities and at closure, they wished they could continue in research or remain with some form of contact with researchers even after trial closure as Joel expressed.

When we were brought from there (the former care sites), my understanding was that they have removed me from that place because it was no longer capable. So when you get me from there and you bring me here and you send me back after giving me some treatment, and you send me back there, I think I cannot be contented. Why, because you got me from there and brought me, now again you have completed the research and you are taking me back, it means that I may go back to the same situation as I was. So that's why we needed to remain with their contacts. (Joel, Trial 1)

Like the above data suggests, many participants felt researchers were in a better position to manage their health. During the transition, participants were usually provided with some information about their health to deliver to the next healthcare providers, to enable them learn more about each individual participant and be able to offer appropriate care to them. However, such an approach was criticised by some participants who argued that the information provided in referral forms was very limited to adequately provide a clear picture of their health situations. This was especially important if complications arose. Although this concern could be important for complications arising from trial interventions, participants expressed a fear for their general care as Byekwaso explained.

When you are leaving, they don't give you the file. If they could leave you with the file and you move with it when you go to hospital, the health worker I find there like you now, you look at it and tell that 'the research was like this and this. He used such a medication while in research, and used this one, and also used this one. Now this disease may require such a medication, it should be treated with such a medication.' That didn't happen, we went alone and left our files behind and yet we didn't remain with any staff we can report to (our concerns), who can cross check behind. Consider follow-up an important issue. (Byekwaso, Trial 2)

Particular concerns were raised regarding access to treatments for opportunistic infections. By the time of trial closure, some participants still experienced ill health and such participants were worried about their continued access to treatment. Participants' fears about their care was partly attributed to the lack of availability of most treatments for opportunistic infections in the Ugandan public healthcare facilities. In addition, even

where treatments could be available, for example, in some NGO based facilities, the organisation of the services was not very favorable for the participants. For example, for most of the NGO based facilities, participants could only be attended to on their scheduled visits and if they required care on other days, they had to find alternative facilities for their care. e.g. going to the government facilities or private facilities which required payment. However, the poor socio-economic status of most participants made it difficult for them to afford such treatments, hence the worries.

What I felt as for me was that we were going to miss the treatment we were receiving from here. Because at health facility Y, sometimes there is no medications for treating other illnesses you may suffer from and so you have to buy that medication, yet here we would get it. (Abdu, Trial 2)

May be what worried me are the medications, because then (in research) I used to get the medications; even these medications for cough ... (Madina, Trial 1)

Some participants were also concerned about the long waiting hours at the public healthcare facilities. Although this was important to participants across all trials, those who were having jobs appeared to express this as a special concern, with those employed by others more likely to be more concerned as Sumin explained.

The most painful thing for me (about the closure) is that of time. Here you would come and get medication and you go back on time, and if you have anything to do, you can do it, which was not at health facility J. Because for me the major problem I have is work. You have to leave when your boss has arrived. Even today I had to wake up early and I did some work, I washed dishes, I mopped, I washed clothes. So he has to arrive first and you hand over the books, and you balance, then you can leave when he has also left. So here was nearby, and you would know it will take a short time, it becomes easy for you. That's why for me it (the closure) pained me. (Sumin, Trial 1)

In other instances, participants were worried about the exposure and lack of privacy in the public healthcare facilities, since patients are often attended to in general and exposed environments. This was different from the research settings where participants are usually attended to in private rooms. This concern appeared to be largely associated with HIV stigma and was particularly common to Trial 3 participants possibly due to their lack of previous HIV related care. Dennison expressed this fear.

And the second worry I told you about the congestion of the area because I have been seeing them, there is too much congestion and exposed. So I also wanted some confidentiality, (Dennison, Trial 3)

Although most of the concerns expressed related to the general care, some participants were specifically worried about access to the trial regimen following trial exit. This concern appeared to be particular to Trial 1 participants and could be attributed to being tried on second line HIV regimens, which are less likely to be available in the public healthcare settings compared to the first line. Two participants expressed this concern.

...for me what I was fearing or worried about was, because they informed us that we have been taking Alluvia, but what if I go to facility D and Alluvia is not there, it means I am going to receive a different medication. (Sumin, Trial 1)

So we were wondering that 'when the study ends, shall we be able to get the real type of drugs we are on or?' Because when I was starting at facility D, the drug I was on when I reached facility D, they never had it, so they had again to change and put me on the drug they had which was not working for me. So we were worried that 'really when the study ends, shall we really be getting the real drugs we've been getting while in the study?' (Janet, Trial 1)

Notwithstanding, some participants appeared to be less worried about their future care and treatment. Although few expressed such a view, their comfort was related to the trust they had in their pre-trial care facilities. Indeed, one trial participant rated the care in his pre-trial facility above that received in research while another reported feeling comfortable with the closure since she was assured of receiving all required care from her pre-trial care facility as stated below.

I was not affected badly (by the closure) because I was healthy, I did not have any health problem, and even where I came from they were still going to give me assistance. It is not like they said they have stopped providing ARVs,... (Aidah, Trial 2)

However, the above perspective seemed to be among those with a stable health status, who would therefore not require treatment for opportunistic infections. In general, the above findings suggest that trial closure left participants with significant fears regarding post-trial care. These fears were largely associated to a lack of confidence in the public healthcare facilities, in identifying and adequately managing HIV related illnesses. In addition, trial participants were worried about access to treatments, which were not usually readily available in the public healthcare facilities. These concerns suggest a need for guidance and support on identifying suitable post-trial care facilities, and for post-trial follow-up to ensure participants have been appropriately linked to care and are receiving the required care and treatment. Some of the concerns raised also related to a

possibility of participants developing problems which could be associated to trial interventions, and especially when these could possibly not be adequately recognised and/or managed within the public healthcare system. The next section explores this concern in more details.

6.2.4 Fear of side effects from trial interventions

Stopping trial related care created significant fears among participants which were related to a possibility of developing side effects from trial interventions. These fears were particularly important to intervention research and more especially for blinded trials, where people could not easily associate the side effects to a particular intervention or drug. For example, Trial 2 was double blinded, and involved the intervention arm being stopped from taking an HIV treatment. Many Trial 2 participants were concerned about the possible negative effects of stopping such a treatment, especially if these occurred after trial closure. These fears became more important when participants felt there was no opportunity to be in contact with researchers after the closure. Many challenged the aspect of 'fairness' on the side of researchers, for not having mechanisms of identifying and managing effects occurring after trial closure. This concern was a strong indication for post-trial follow-up care and monitoring as expressed in the quote below.

You have discontinued the person from the usual type of medication he was taking, and now you prepare him and exit him and inform him that 'go the research has ended.' When he reaches there, you would have restarted the medications he had stopped, you have not continued with him to know that after he has restarted it, what problems has he encountered. And even if he encounters a problem and returns here, the program would have closed, he will not find any one to explain it to. [...] For me I would expect that, that would be the correct research that you are aware of what is happening until you finally close. And you come to know that after the closure up to six months, what problems have been encountered by those who have participated in the program. (Byekwaso, Trial 2)

In addition to the need to protect trial participants from harm, some felt that monitoring for potential side effects from trial interventions would be important to researchers, for contributing to the overall trial outcomes. In fact, some participants argued that 'actual research' has not ended until researchers are sure that no effects can occur to trial participants arising from trial interventions. Participants recommended researchers to follow-up the participants to monitor for possible side effects, and also to establish how their overall care and wellbeing is, following trial exit as Baker explained.

... what they would have done is to continue moving, to continue inquiring to know after they have gone back to where they were (before joining research), how have they experienced life where they are; to know that what they were researching has had positive results or not. Because you may say that death, ok supposing there are those who died, and someone dies and you say that 'why has this person died?' But death is inevitable, it is for every person, but they may say that 'we had many people (in research), so and so used to be very ill while still with us, while taking such and such a medication, but he would keep falling sick but after going back he has not been falling sick again, or when he was here he used not to fall sick but after returning he falls sick often. I would say that this is the real summing up (concluding) of the research. (Baker, Trial 2)

Similar to other concerns which emerged during trial closure, fears of possible side effects were significantly related to the differences in care between research and the Ugandan public healthcare facilities. Participants commented how researchers were in a better position to adequately identify and manage possible side effects if these occurred, since they were equipped with the necessary resources and knowledge to do so. Public facilities on the other hand had limited resources and also their knowledge on research related issues could be limited. This concern strongly suggested a need for the involvement of researchers in the care of the participants after trial closure as indicated in the following quote.

I know that they are the ones who know that question better than where they have transferred them because the time they take with them. Because the other side (post-trial care facility), it is just a matter of presenting your..., may be your book and they write down and they send you to the pharmacy and they pick up your medication, but they cannot know the changes which is taking place within you. So the first people (researchers) they are the ones who are good whereby if you have any problem you can call them and you can go and they try to examine you again and see what is going on. (Wilberforce, Trial 3)

Many research staff were in agreement with the views of trial participants on this issue as presented in chapter eight of this thesis. In addition to the mistrust of the care in the public healthcare facilities intensifying participants' fears of possible side effects, some participants' fears were also increased when they were exited without awareness of the general impact of the research. As shown in the above quotes, some participants were worried about being restarted on a trial medication without first knowing the outcomes of the research. Others, particularly those who joined research while very ill were more concerned about knowing how their health was affected by research participation. These concerns related to the need for information on trial outcomes and are explored in more details in the next section.

6.2.5 Anxiety of not knowing trial outcomes

The need to know trial outcomes was expressed by participants across all trials, although some trials (Trial 1 and Trial 2) appeared to be particularly more concerned. By the time of the interviews for this research, participants appeared to be quite eager and anxious to receive the trial outcomes as the quotes below indicate.

I am very expectant to know what came out of the research, I am very expectant, to know what happened and what came out, what problems they found and what was good. (Bettinah, Trial 2)

That is what we were waiting for, even in calling us (for this study), we thought they were the ones calling us. For me I wanted, I had anticipated that they were going to tell me that 'Naluwugge, you have remained taking only ARVs.' That is what we came anticipating nurse, that is what everyone is expecting, that is what we are waiting for. (Naluwugge, Trial 2)

Although participants from all the three trials expressed a need to know trial outcomes, the eagerness to know varied among the trials. In addition, there was variation regarding the timing and types of outcomes preferred across the different trials. Trial 1 participants for example were particularly concerned about knowing their own personal health outcomes as a result of participating in the trial, instead of the general trial outcomes. This could be attributed to the context of Trial 1, where the majority joined the trial while ill and after failing on first line HIV regimens. These participants' priority therefore appeared to be focused on recovery. Joel illustrated this while explaining about the need for trial outcomes.

Outcomes about medications and also on our health, but mostly about our health; you have sent us off, but how have I gone? Have I met your expectations? When you look at where you found me, have I improved? But they have not informed us. We would like to know that "comparing to how we got you, up to now when we are sending you off, for us we have seen this and this difference." But we didn't get that. So now, for me I went when I wasn't contented. (Joel, Trial 1)

By contrast, Trial 2 participants seemed to be more concerned about the general trial outcomes. Their need could also be attributed to the context of the trial, where participants were relatively healthy and the trial purpose was to evaluate whether a certain treatment could be safely discontinued without causing them further complications regarding HIV management. Many Trial 2 participants appeared anxious to

know whether it was safe to discontinue this treatment as this would reduce on their pill burden. In addition, being a randomised controlled trial, some participants remained taking the trial medication while others stopped. However, since the trial was also double blinded, one could not tell which arm they were on. Those who experienced ill health during research or shortly after closure expressed concerns of not being able to relate their health situations to either taking or withdrawing the treatment under investigation. This was quite a stressful experience and some specifically desired to know the treatment arms.

...so the answer we are looking for is that if a person stopped taking TX and only takes ARVs, can they live? I don't know because we didn't come to know the types, that may be one was taking this and the other without (ingredients), yes that is the challenge we have, we don't know. (Aidah, Trial 2)

...and also for us to know that this one was on the real TX, this one was on one without ingredients (placebo). (Abdu, Trial 2)

Interestingly, the majority of Trial 3 participants were less interested about knowing the trial outcomes. Some felt their improvement in health confirmed that the trial medications worked while others just felt it was not necessary. Dennison expressed in the quote below why Trial 3 participants seemed reluctant about knowing the trial outcomes.

Interviewer: *Have you found out any information regarding the outcomes of the research you participated in?*

Respondent: *According to what I would say, because they were trying on the drugs they were using on us, so what I have seen what I conclude, I conclude that the drug they are using on us works. Those drugs work. Let them continue manufacturing us more drugs so that we survive. (Dennison, Trial 3)*

Interviewer: *How did you come to conclude that it works?*

Respondent: *Because it has worked on me, through the experience on my body, on myself that the drugs work. It has helped me through my life, from the time when I joined them, I was very weak, totally, I was physically weak, I could not handle any work, but now I have used that drug for one year and two months, now I am OK, I am OK. (Dennison, Trial 3)*

Related to Trial 1, Trial 3 participants were severely immunosuppressed and all interviewed participants had not accessed specific HIV treatment before they joined research. These participants appeared to associate research with standard care hence might have not had expectations of receiving trial outcomes or even to have considered

it important. For the few who showed interest in the issue (following probing), similar to Trial 1, they were more concerned about their own health outcomes rather than the general trial outcomes as the quotes below suggest.

I am interested, I am interested to know (about the outcomes) because I want to know where I am standing. Yea, I am interested. (Nandi, Trial 3)

Yes, because I want to know where my life has reached. (Marion, Trial 3)

I need to know of course, I have to know I am doing well, how my CD4 are, are they counting down or they are increasing, or maybe I have any side effects, so it is right to know. (Mukhwana, Trial 3)

The above findings suggest that individual participant or trial characteristics are important in determining the need for, and type of the trial outcomes. Surprisingly, participants' views on the timing of providing trial feedback appeared to differ from that which is currently implemented. For example, while in the current practice trial feedback is usually provided after the final trial outcomes have been confirmed, which usually occurs approximately one year after trial closure, participants expected to be informed about the outcomes before or shortly after leaving the trials as Joel's quote below suggests.

But this issue of sending us before they have informed us of what they did with us, for me I remained not contented. (Joel, Trial 1)

Joel's case however may have applied to his own individual outcomes rather than to the general study outcomes. Similar to Joel, some participants were particularly disappointed for not receiving the trial outcomes after a long (and promised) time. Some reported having patiently waited for trial outcomes in vain which was quite demoralising as Aidah expressed.

We are still waiting, because they had informed us that they will call us, I think in August. Now August passed, we are in April (of the following year). So now I don't know, it is up to our superiors (researchers). (Aidah, Trial 2)

A lack of awareness of the trial outcomes left many with a sense of being in suspense, especially when researchers kept 'silent' on them regarding what was going on. This feeling was expressed by some as 'being left hanging', or being 'left blind', as many remained with unanswered questions. This also created fear among some participants.

For example, Trial 2 participants who were investigated specifically to assess the safety of withdrawing a certain medication were concerned for leaving the trial without knowing the answer, yet some of them had stopped taking this treatment (as explained above). Moreover, these medications were restarted at the closure without any explanations (in regard to the trial outcomes), which left many concerned.

Except what my worry a bit is about medications, because for us we had expected that they will tell us that we have completed researching on TX, stop taking it completely, but when we were completing, they added us (TX) for three good months. (Aidah, Trial 2)

But the unfortunate thing is that we have not yet known whether it was true that even if you stopped taking TX, you can remain without experiencing any other complications. We have never received that answer in its fullness. We would want to get it because you have to know that 'what I participated in resulted into such an issue. (Baker, Trial 2)

In addition, some participants felt that a lack of awareness of trial outcomes could result into misconceptions and mismanagement of their health. For example, Trial 2 participants explained that since some of them never became ill at all during the trial, they could assume that withdrawing the trial drug (after leaving research) was safe, and since stopping it could reduce the pill burden, there was potential for some to become reluctant on using it. But some questioned that what if it was actually not safe to stop the drug?

They were researching about TX but we didn't come to know that when a person stops taking TX, how does it treat him/her, so we didn't come to know about that. So for me I can say that let me stop it (TX) and I become sick, and when I start it again I become fine, but they (researchers) didn't inform us about that. (Brenda, Trial 2)

Due to the (perceived) delay in receiving trial outcomes, some participants lost hope of ever receiving them. This concern was expressed by one participant, an issue attributed to a previous experience. This again showed the influence of previous research experiences on the post-trial care perceptions and expectations among participants as shown in the following quote.

I would argue researchers that when you bring your research, find some time, may be at closure, find some time and come back and say 'friends, what we were researching about went like this and this.' Because we didn't come to know the first one (trial results) yet we participated, the next one, they informed us that they (outcomes) would come, but they will come and it is you (researchers) still to know but for us who participated we will still not know (Brenda, Trial 2).

Trial participants recommended provision of trial feedback as apart of good trial closure practice as the data above suggests. In addition to informing them about the trial outcomes, this would be helpful in dispelling some misconceptions among them. Furthermore, this would create a sense of increased awareness about their health and could be empowering in regard to managing their own health as Joel expressed below.

Like for us who have been in the research, they need to teach us how to take our medications, what have they found, what themselves have found in us the patients. Now when they have finished explaining to us that 'this and this is what we have found, and you need to do this and this to ensure that the problem we have found is rectified'. But if we have not got such training and we leave this place and go, it means we have just gone. [...] That's why it's necessary for us to have their contacts. Like for me when I encounter a problem, I have to inform them and they devise other ways for me. But remaining like that is like remaining hanging in the air. So for me I will continue to insist, so that they can tell me the truth. (Joel, Trial 1)

The above concerns indicated a critical need for the provision of trial outcomes to participants in HIV trials in Uganda. While current practice tends to concentrate on providing the general trial outcomes, this research suggests that trial participants may expect different outcomes, including the more general and also those relating directly to their personal health. In addition, the timing of providing the outcomes seems to be an important issue among participants, with participants preferring to receive trial outcomes during or at least soon after trial closure. This seemingly contradictory situation may be emerging from the need for specific trial outcomes especially those relating to individual health, but also to fears related to the trial interventions. This situation might present significant challenges in trial closure practice, especially when ethical issues such as blinding or the need to first confirm the findings by different regulatory authorities have to be put into consideration as will be shown later from the perspectives of research staff. Approaching this issue might require consideration of the specific trial contexts on a case by case basis. Providing timely and appropriate explanations to participants may be helpful in many of these situations.

6.3 Dealing with practical challenges

The need for continuity of care required trial participants (who were HIV positive) to become linked to non-research care facilities after trial closure. For participants who were in HIV care prior to research, they could return to the same facilities or go to new ones following trial exit. For those who were not in HIV care prior to research (such as Trial 3 participants), they also had to find a facility to go to. Choosing a care facility was

an autonomous decision of the participants, however this required careful consideration as certain factors such as one's healthcare needs and the psychosocial and economic wellbeing of the participants were important in decision making. Trial participants required guidance from research staff as they made their choices and also practical support to overcome the practical barriers associated to being re-established into new care contexts. This section describes how participants made decisions of where to seek post-trial care, and describes their experiences/concerns of the linkage to post-trial care process.

6.3.1 Deciding where to seek care

The majority of trial participants acknowledged having had the right to make their own choices regarding a post-trial care facility. Having this right was considered good post-trial care practice by some participants as it showed respect from researchers as Madina expressed.

Ok, the way they talked to us was not bad because you were the one to decide for yourself. Now supposing they had told us that you go here, you go there, it would have been bad, but they left you to decide for yourself. (Madina, Trial 1).

However, a few trial participants implied not having made independent choices. For example, some reported relying on the 'instruction' of research staff in determining a care facility or just felt they had no choice at all and instead had to follow what the researchers suggested. This phenomenon was particular for Trial 3 where participants had not accessed specialised HIV care prior to research participation. The majority of these also appeared to assume that they had to automatically be linked to the care facility attached to research. These issues were reflected in how these participants expressed their voices, which implied limited choices. The element of trust for research staff, the power-relation differences, and a lack of adequate understanding might have contributed to their actions as represented in the following quotes.

No, they said that now you have been on test research, now since your time has already expired, now we are going to transfer you to another section. That is where you will be getting the treatment. That is what they told me. (Dennison, Trial 3)

Interviewer: How did you come to get care from here after you left research?

Respondent: The doctors..., because they just told me 'you will be going to the other side next time.' (Mukhwana, Trial 3)

As I reached here, they told me..., they gave me the day for joining that group, that 'now here you have left, you have to join that group.' They told me that 'now you are remaining with next week or next month, you will start joining your friends there,' they told me before (Marion, Trial 3)

On the other hand, Trial 2 participants appeared to have no or limited choices regarding their post-trial care facilities. This could have been related to the fact that their research facility did not have a care clinic attached to it and so, it was assumed that trial participants would automatically return to their pre-trial care facilities. This was also reflected in Trial 2 MOP document. If there were better options, it is possible that some Trial 2 participants could opt for these, considering that some expressed discontent with their pre-trial facilities. The lack of better facility options, coupled with the desire for quality care might explain why some Trial 2 participants wished for more research opportunities, which could be a potential influence for future research participation.

In addition, there are other factors which appeared to compromise the autonomous position of trial participants. For example, two trial participants reported continuing receiving their care in places they had not decided. Ruth, who travelled a very long distance (about 120km away from her home) and had chosen a facility close to her home still accessed care at the research site close to one year following trial exit. Moreover, although there was a reason for this as later established from research staff, Ruth seemed unaware as to why this was happening which indicated a communication gap between researchers and the participants.

I don't know (why I am still receiving care from the research clinic), it seems they will reach a time and they send me somewhere else, I also don't know. May be the viruses are still there, because the doctor told me that now the virus has reduced, and they are now few. May be they will first get finished completely, I also cannot tell. (Ruth, Trial 1)

To make their choices, trial participants required adequate information regarding the available care facilities. For example, they needed to know details about the service delivery in a given facility, such as the availability of drugs (especially the trial regimen). Such information was important since some public healthcare facilities may not have all the required HIV services. Research staff supported/guided trial participants to make their choices, while putting into consideration factors such as the distance one has to travel, and the quality of care in a given facility. The views of research staff on this issue are presented in chapter eight of this thesis.

These findings appear to show that although the decisions for post-trial care facilities were autonomous for most trial participants, some factors tended to compromise this position. These factors could be considered system factors and in most cases were beyond the control of researchers and/or the participants themselves. At an individual level however, a number of other factors were considered while participants made choices of where to go for post-trial care. These factors tended to revolve around the care differences between research and the public healthcare facilities in Uganda. Although other factors were relevant as will be shown later, many participants' expressions indicated that the need for quality care was the major motivation for selecting a given care facility. The quality of care mainly related to how trial participants accessed the general medical care such as medications and medical investigations, time management, and the relationships with the care providers as the quotes below suggest.

The care I got there (in research), it was just enough. I thought I am not going back to that place (pre-trial care facility), I have to go back to site A. Yes, the care and ok the distance also, but the care most. (Janet, Trial 1)

I chose to remain here (institution A) because their care was..., first of all I was used to them and I know them physically, their services, I could come, there is no congestion. Because the other places where they were trying to put me, I could see there is a lot of congestion there and a lot of time wastage there. (Dennison, Trial 3)

Trial participants often made reference to their experiences (or perceptions) of care in the research and non-research contexts as they articulated their decision making processes. Those who attended HIV care facilities before research usually compared these to the research care, while those with no specific HIV care experiences (mainly Trial 3) compared research care to the one in the general public healthcare system in Uganda. Thus pre-closure care experiences emerged as the major factor in the decision making process for post-trial care facilities. Joel demonstrated this issue.

Because I had observed the large number of people the other side, I knew it is still there. Then I thought when I remain here, it will be easy for me. Because sometimes, I have my work here in the city, so by the time you reach there and come back, you find many problems. But here once they finish working on me, I just go to town and do my work. That also motivated me to remain here, it will help me. (Joel, Trial 1)

The desire for quality care compelled some to go beyond other boundaries, such as transport difficulties so as to remain close to facilities which they expected to offer them quality care. Nandi had to travel about 45 km to reach her current care facility yet there were other facilities nearby her home. Similarly, Mariako also had to leave her own

district of residence (about 50km from the current care facility) in order to access care in a facility related to the research institution. Although Mariako seemed to be worried of possible side effects of trial drugs, her concern was mainly about the trust she had gained in researchers regarding her care as opposed to the mistrust she had in the public healthcare facilities. These two participants are quoted below.

The thing which made me to select this place (JCRC), they handled me 99, let me say 100%. The way they handled me is not like other hospitals, that is why I selected to stay here. And they told me 'can we change,' I told them 'no,' 'will you be providing transport,' I said at least I will be having, that date reaches when I have at least something little. I told them no, you leave me where I am. (Nandi, Trial 3)

I chose here, I chose to stay here, for at least sometime as I monitor whether the drug will not be bad on me, that's why I chose here. I have not even tampered to ask the other end, no. I just want to complete a year with them then I proceed if it does not affect me anymore. (Mariako, Trial 3)

However, other than the quality care, participants also put other factors into consideration while deciding where to go for care. These were mainly socio-economic and included the need for networking and social/family support, financial considerations, and HIV stigma. For example, in regard to the need to maintain social/peer networking, Edwin felt he had lost his peer networks from his pre-trial care facility and formed others within research. Remaining in a research related facility would therefore help him to maintain the network with his research peers, something he felt was important in his post-trial care.

What made me to refuse (returning to pre-trial care facility) is what I explained to you, when I told you the problems there. I am not used to the people there, yet at facility L (facility attached to research), we may reach and sit as the people who started from there and we chat, and one tells you this and another tells you this, and you find others who have moved around, and one person comes and tells you this is what I have encountered, so that also makes you to be strong. When you spend some time say one year, and you see your colleague alive whom they brought (in research) when he/she was going (to die), when he/she is finished, but when you see him/her and you chat, even that strengthens you. Yet there (in the pre-trial care facility) where you are going you don't know them. (Edwin, Trial 1)

On the other hand, Nandi who travelled a long distance as explained above also considered her family residence while making a choice of a post-trial facility. Nandi felt

she could receive family support if she stayed near her family especially in case she became ill.

I decided because this is home, because if I get sick I must come back home. This is home, that way is just a working place. My mum, my dad, what everybody stays this way. (Nandi, Trial 3)

For some participants, financial implications were a significant consideration for their decisions. This was mainly linked to the distance travelled and thus the costs incurred while travelling to the facilities. In other instances, HIV stigma was a major factor in influencing trial participants' choices of a post-trial care facility. For example, Ruth rejected a nearer facility in an attempt to hide her HIV positive status.

I want hospital K because at hospital K there might be fewer people I know, and also because some people are not aware that I am taking medication (for HIV). As we were asked to keep our secrets, so some people do not know that I am on medications (for HIV treatment). Because I thought that I may find others when I go, because the majority go to hospital S, so I thought I would change and at least go to hospital K, because it seems they also give people (HIV) medications from there. (Ruth, Trial 1)

Although not explicitly expressed, the issue of stigma seemed to be a bigger problem to trial participants who were newly diagnosed for HIV and therefore were likely to have little HIV care experience. This could be related to the lack of adequate psychological support usually provided to HIV positive people to help them cope with their diagnosis and to aid disclosure. Indeed, this point could be supported by the fact that HIV stigma issues never came up among Trial 2 participants who had a longer HIV care experience compared to other trials. This finding suggests a need for including HIV stigma related support during trial conduct and closure.

Other reasons mentioned for the choice of a care facility included being the only place a participant had received care from, which was mentioned by a Trial 3 participant, and a facility being their pre-trial care facility as mentioned by a Trial 1 participant. These reasons however could not be clearly evaluated as only a few participants mentioned them. Moreover, the only participant who selected a facility on the basis of it being her former facility was in the process of changing it for some reasons as shown below.

Interviewer: *What made you to decide the place to be getting your medications from?*

Respondent: *Because I used to get from there, and I said let me go back. But again I have realised that I may change and go to facility J. (Sumin, Trial 1)*

Interviewer: *What makes you want to change?*

Respondent: *What is going to make me change is transport and time. I will first go there and find out what happens there. (Sumin, Trial 1)*

The above finding suggests that trial participants were more likely to be influenced by other factors while choosing a post-trial care facility other than it being their former facility. This finding could also imply that some Trial 2 participants¹⁴, given other options could have changed their facilities. Conclusively, these findings indicate that although a number of factors played a role in trial participants' choices of a post-trial care facility, the need for quality care was most central. This was reflected in how, for trials with a research related care facility, almost all trial participants remained accessing post-trial care in these, as they associated them to research. Considerably, trial participants' choices of post-trial care facilities varied across trials, but were closely similar within trials. For example, all participants in Trial 2 returned to their former care institutions, all participants in Trial 3 joined the care facility attached to research, while most Trial 2 participants (over 70%) joined the facility attached to research, yet more than 70% of these had come from other institutions¹⁵. The reasons for these differences were highly associated to the characteristics of the individual trials such as the healthcare needs of the participants and the availability or not of a care facility attached to research as explained earlier.

6.3.2 Challenges during re-establishing into care

Some participants expressed concerns regarding getting re-established in post-trial care facilities. For some, this required going through a fresh and usually difficult registration process, which involved taking one's particulars, medical history, and other details required for registration of a new client in HIV care. While the registration process could be assumed to be a major concern for those reporting to facilities different from their pre-trial facilities, findings suggest that even those returning to their former facilities were worried about the process. Sumin, who chose to return to her pre-trial care facility and who had not yet reported there by the time of the interview anticipated such challenges and dreaded the day she would report to post-trial care.

...because now I think that the time I will go there, because on Friday I will be going there, because I know this is Christmas season, so next week they may not work until next year. So it seems I will go and spend the whole day there just because you have no file there, 'yet if they had taken you by themselves as they got you from there and brought you here,

¹⁴ Who all returned to their pre-trial closure facilities

¹⁵ Details of trial participants' pre and post-trial care facilities are presented in chapter 5.

and they take you with your papers. Because themselves would reach there and see the doctor by themselves and himself would give them all the papers concerning facility D and your results and they come with them, so also here they would have done the same thing. For it to be easy for us, because even here it was so easy, because we did not come that may be we lined up. But now it will take me time, because I will reach there and I start to explain about myself as a new person. That's why for me, I felt somehow bad about it (the care at trial closure). (Sumin, Trial 1)

As the above data suggests Sumin only expressed anticipated challenges of the re-registration process and not actual experiences, as she had not yet reported to the post-trial facility. Regarding actual experiences, quite few participants reported to have experienced difficulties during linkage to post-trial care. This situation could be partly attributed to the fact that some of the participants had not yet reported to their post-trial care facilities by the time of the interviews as in Sumin's case above, or because their experiences did not actually turn out to be as bad as they had anticipated, as in Wilberforce's case below.

What I remember may be is the friendship I had the other side, it was now as if I am going to another..., as if I am transferring to another generation whereby I had to begin afresh learning them slowly by slowly. That was my expectation and when I moved to the other side, really for the first time I was not that feeling ok, but otherwise, they also keep on trying to come up with the same care. (Wilberforce, Trial 3)

Similar Wilberforce above, other participants reported good experiences during linkage to post-trial care.

There was no problem because here they had asked me to wait for my return date. They asked me for my return date and I told them, and they told me that when I return, I should take the envelope. I did not encounter any problem. (Bettinah, Trial 2)

Trials 2 and 3 participants tended to report less negative experiences during the linkage process compared to Trial 1. For Trial 2, this trend could be attributed to their continued contact with their pre-trial facilities during research participation, which might have eased the re-establishment process since their client files remained active in these facilities. For Trial 3, their positive care experiences could be related to the proximity of their post-trial care facility to the research clinic, which was situated within the research premises, which enabled some form of additional facilitation from researchers.

Nevertheless, some participants reported experiencing actual challenges during the linkage to care process. These challenges appeared to be mainly attributed to facility

work routines and procedures, and also to facility staff approaches. Janet reported a bad experience during re-establishment into post-trial care.

Yes they gave me a date, and that date was a Wednesday, and when I came to this place, it was a tag of war. They told me 'you should go back, for us we don't treat patients on a Wednesday.' And I said 'this is what they told me; you see my form.' 'No, Wednesday is for pregnant women' and is it students, or youth? I still don't know I am still new in this place, but it was a tag of war. In fact, they didn't refuse, but they kept on saying, 'today you are not supposed to be here, no we are not ...' So first day, then after they considered me and they asked me to give them the papers. I told them that 'I am not here by mistake, those people referred me here, may be they chose a wrong date, a Wednesday, I don't know whether they know that, ...' you see it disturbed me so much as if I was rejected. (Janet, Trial 1)

Janet's dilemma however did not stop on the first day, as she reports continuing with similar experiences for the next two visits which followed, until she finally learnt the working routines of the new facility.

Then again, that was the first visit. Second visit, again when I went to the doctors' room, again he put me on a Wednesday, so when I came back on the third visit, I said doctor 'I don't want to come back on a Wednesday because things are not good for me. Whenever I come, those people are telling me 'why are you here now, are you pregnant?' Then I saw the scenario, today is my third time to come, so I told the doctor, 'I don't want to come back on a Wednesday, because things are not good for me.' So they changed to a Thursday. (Janet, Trial 1)

Similarly, Nandi reported experiencing delays during her registration after her documents went missing. Unlike Janet though, Nandi reports receiving good support from the research staff, since these were nearby.

Now my file first got lost, immediately I crossed (from the research clinic to the general care clinic), my file got lost. I sat almost for..., by 7:00 I was already here. I sat almost for five hours, I was not seeing anything. Then I had to look for (the research) doctors, I told them 'my file..., I am not seeing them reading me yet you told me you have taken me that way, but where is my file.' They had to renew, to make a new file. They were complaining that these students are the ones who go on mixing. So they had to make for me faster. So they convinced me and they told me..., they gave me medicine, they did for me what I wanted actually, they gave me medicine. (Nandi, Trial 3)

Although the above two participants were in care facilities attached to research and both faced difficulties, they experienced their care differently. Receiving researchers' support

or not appeared to have made the difference. In addition, although real negative experiences were reportedly few in this research, this data points to a possibility that some trial participants' fears could turn into a reality during reporting to new care facilities. Moreover, as in Janet's scenario, it is possible that resolving linkage to care problems may require multiple clinic visits, implying that even participants who may not experience any challenges on the first day of reporting could experience them during subsequent visits as they settle in.

Janet's narrative above also indicates that negative experiences during linkage to care could be damaging. For example, Janet reported feeling rejected by the way she was treated. To avoid such negative occurrences and to promote positive care experiences during linkage to post-trial care, trial participants made suggestions on how this process could be facilitated. For example, participants suggested a need for physical facilitation¹⁶, where they would be physically escorted to their post-trial care facilities, or where the post-trial facility staff would pick them up from the research facilities and take them for (re)registration. This concern also pointed to the need for stakeholder involvement¹⁷ in the transition process. Trial participants felt this approach would greatly ease the registration process and would save them from delays and other inconveniences. While arguing for this type of support, trial participants felt it was an act of fairness since in the first place, they were physically brought from their facilities prior to joining research. Leaving them to return on their own would show a lack of concern and care. Two participants were quoted on this issue.

For me what I see to make our life easy, where we are going to get medications from, as they brought us themselves from there, because you would go and they give you an appointment and you would go to facility D and they would pick you and bring you here. So in order to make it easy for us, they would do the same thing. They would get a person with their referrals and take him/her back to facility D and they open for you another file. So you are not disturbed... (Sumin, Trial 1)

I thought that they would do one thing, when a person is transferring from here, they themselves would take that person. Or the others would come for him/her. For example, when we were coming from facility D, these people came for us themselves. You don't encounter problems. (Joseph, Trial 1)

¹⁶ Physical facilitation also emerged as a strong recommendation among research staff on how to improve linkage to post-trial care

¹⁷ Stakeholder involvement was another important recommendation from research staff regarding facilitation of linkage to post-trial care as will be shown in another chapter

As explained earlier, concerns of linkage to care appeared to be related to the particular trial contexts. Unlike Trial 1, Trial 2 and 3 appeared to have favorable conditions to ease linkage to care. For example, while the location of the care facility for Trial 3 participants appeared to favour linkage, Trial 2 participants' linkage appeared to be eased since they retained contact with their facilities during trial conduct. These findings suggest that while physical facilitation and involvement of stakeholders may be important strategies for facilitating linkage to post trial care, retention of contact with pre-trial care facilities could also be a feasible means to eliminating some of the difficulties to linkage to post-trial care.

6.4 Conclusion

This chapter has presented findings related to the perspectives of trial participants during the trial closure phase, by describing how participants perceived and reacted to the closure, how they made decisions of where to go for post-trial care, and how they perceived and experienced the care during transition from trial to non-trial facilities.

The findings have indicated that trial closure was an emotional experience for participants, associated with: the loss of the quality research related care and valued relationships, health related concerns, and the process of identifying where and how to seek post-trial care. Although some participants reported less negative impacts, the data strongly suggests that the majority require support to address the complex issues surrounding trial closure and establishment into post-trial care.

Trial participants indicated how support was offered to meet some of their care needs during the transition process. However, the support offered appeared to be insufficient in meeting all their needs. For example, while some support was offered which appeared to address some psychological and practical needs during closure and linkage to care, the social-economic needs, concerns about trial outcomes, possible side effects, and practical challenges during linkage to post-trial were not appropriately addressed. These findings propose that, to meet the complex care needs of trial participants during the closure, efforts should be targeted at meeting the emotional, practical, and social-economic needs of the participants. Doing this will require a collective effort of the research team, but might also require involvement of other stakeholders. These issues are explored in details in chapter eight of this thesis, which presents the perspectives of research staff on trial closure. These findings also suggest that despite the difficulties participants may encounter at trial closure, early preparation, being healthy, and assurance of quality care from other facilities can minimise the negative reactions and improve participants' experiences during the closure.

Having looked at how trial participants experienced the closure and the linkage to post-trial care process, and basing on their concerns and fears about care in the Ugandan public health care system, it is important to know what happened to the participants after living the trials. The following chapter presents findings related to the post-trial phase of the transition process, and describes the experiences of trial participants after exiting from the trials.

CHAPTER 7: ADAPTING TO A NEW CARE CONTEXT

7.1 Introduction

Establishing in post-trial care was a difficult process for the majority of trial participants. Participants reported experiencing different challenges associated to accessing HIV care and treatment, and also attending to their day to day needs. These difficulties emerged out of the change from the high quality care in research to the lower standards of care within the Ugandan public healthcare system. This chapter presents findings related to the post-trial phase of the transition process, and describes how trial participants experienced and adapted to the post-trial contexts following trial exit. The chapter describes trial participants' accounts of how they negotiated through the complexities associated with accessing routine HIV care and treatment in the Ugandan public healthcare system, within a context of constrained financial abilities, ill health, and other domestic needs and responsibilities.

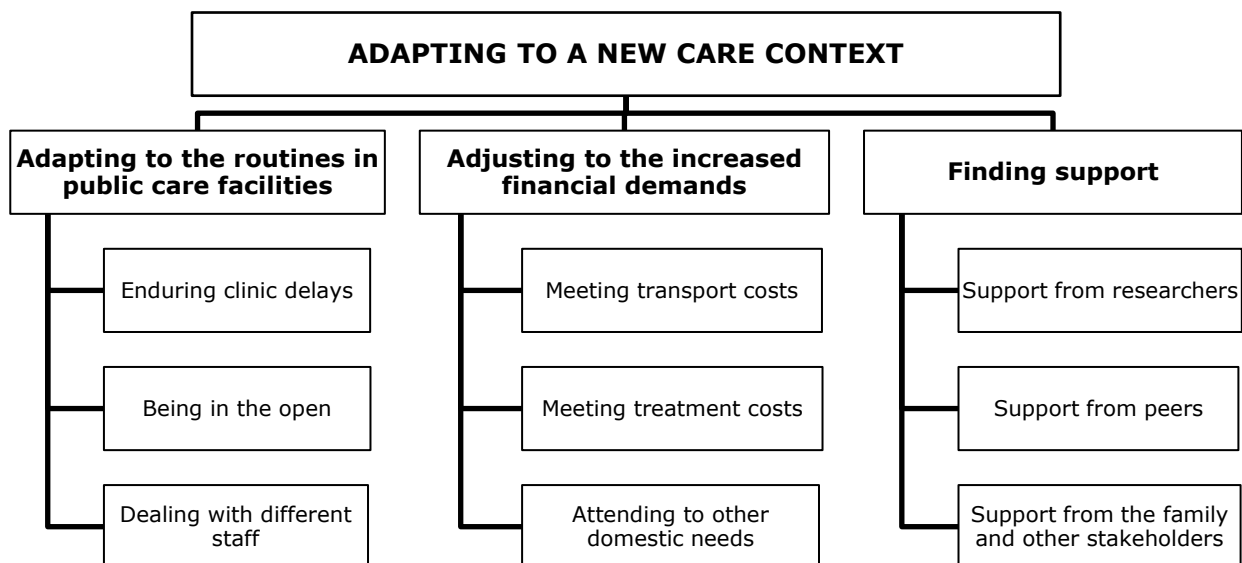
Joining post-trial care facilities meant accessing HIV care and treatment like the rest of the population. This meant having to re-adjust to the nature of the routine service provision in the Uganda public health care facilities. Adjusting to the routines of the public healthcare system proved very challenging for trial participants, who were used to high standards of care in research. For example, in research, there were usually adequate diagnostic and treatment facilities, treatments including those for opportunistic infections were usually free and timely, participants usually spent fewer waiting hours since there were less numbers of clients, research staff were perceived as very caring, there was privacy at the facilities which was particularly important to those who still experienced HIV stigma, and participants were usually provided with incentives such as transport fees and sometimes food, which was significant to those with limited financial abilities.

The above aspects of care appeared to be the direct opposite to those in many of the post-trial care facilities. For example, many participants reported severe clinic delays due to large numbers of patients at their facilities, many facilities lacked medications especially for treating opportunistic infections, participants described staff's attitudes as unwelcoming, there was no proper privacy as patients were usually attended to in an exposed environment, and trial participants had to pay their own transport fees and lunch. Most of the above factors eventually increased the financial needs of the participants. Those who were still experiencing ill health faced special care needs, as they usually failed to work, yet in most cases required more finances to spend due to the increased need to attend healthcare facilities, purchase medications, or specific food. Although very minimal support was reported, participants did seek support from peers,

researchers and the family. To improve their care within the post-trial phase, participants recommended various supportive approaches, including follow-up care and financial support, which may require the involvement of other stakeholders such as government institutions, research funders and sponsors, NGOs, and the general community.

The findings of this chapter are presented under three main sections. The first section describes trial participants' experiences of seeking and accessing HIV care and treatment within the routines of the Ugandan public healthcare system. The second section reports how participants navigated through the challenges of increased financial demands as a result of stopping research care. The third section describes how participants were supported during the post-trial period, and also reports some recommendations on how their care could be improved. These findings are summarized in figure 9 below.

Figure 9: A summary of chapter seven findings



7.2 Adapting to the routines in public care facilities

Trial participants required continuity of HIV care once they left research, which they sought within the public healthcare facilities, including the government and non-government institutions. Adjusting to the routines of the public healthcare system proved very challenging for participants, who were used to high standards of care in research. For example, participants had to get used to: the large numbers of patients

which often resulted into clinic delays, being seen in an exposed environment which could expose them to those they never wanted to see them, and meeting staff who are often perceived as uncaring. These situations were significantly different in research as earlier explained. While contrasting the care between the two contexts¹⁸, Nandi likened research care to 'caring for a baby' as shown below.

You find people leaving research, they have been handled as babies, so going that way, they will be handled as if..., (Nandi, Trial 3).

Although poor standards of care are often associated to the government facilities, this research revealed that the majority of participants, irrespective of their post-trial care facility encountered some challenges while seeking post-trial care. However, the above challenges could differ among individual participants, depending on their circumstances. For example, those who were new in care appeared to be more concerned about the exposed environments, while those who were employed appeared more bothered about the delays. These issues are elaborated on in the following sections.

7.2.1 Enduring clinic delays

Clinic delays at post-trial facilities were a common problem to trial participants. These delays were quite inconveniencing to participants who were used to spending relatively shorter times within research. Some reported losses to valued resources such as time and sometimes money as a result of the delays. While expressing their concerns on this issue, participants often compared it with their experiences in research, illustrating the care gap between the two contexts. Nandi reflected this concern in the following quote.

So I must come putting on..., I must take breakfast now, I must have lunch in the pocket, because there, there are very many people. You make a line, you do this, so there we take long, that is the thing. But this way (in research) I could just reach and they care for me, I just go. I could find myself eating lunch home. So that is the problem I have. (Nandi, Trial 3)

Although clinic delays were directly associated with the large numbers of patients at the public facilities, the delays were also attributed to how health care staff approached their duties, in terms of time management. Byekwaso elaborated on how healthcare staff contributed to clinic delays, and consequently to the overall negative care experiences of the participants.

¹⁸ Research staff also used related terms to explain the differences in the care provided in research and the public healthcare facilities. For example, research care was described as VIP care, very high standard of care, and high quality care.

A health worker reports at the time he wishes, he starts working at midday. But imagine a person who came early from home, you leave at 7:00am until midday before they have attended to you. You have not eaten anything, you didn't take tea, you have not received any treatment, that means that the illness will worsen from both sides; the hunger is illness, and the illness you came with is also painning you. When they start working, the longest they work is about one hour. Because they may begin at 10:00am, at midday the person says he is going for lunch, but when he has only treated 4 people, when they are about 100. That needs to be attended to. (Byekwaso, Trial 2)

As the above narratives indicate, clinic delays sometimes resulted into negative effects such as suffering and losses for participants. Those who were employed reported more concerns as the delays sometimes interfered with their time management, to meet their job demands and other domestic needs. Such participants needed to carefully devise ways of dealing with the now increased time demands. For example, Mukhana, who was entitled to only one day off duty in the week often found it difficult to access her HIV services amidst her work schedules and having to attend to other domestic demands. Mukhwana reported an incident when she missed a routine clinic appointment and explained how she managed this problem in the days which followed.

On every visit, I ask the doctor to give me a return date of my off, because at times she can give me a visiting date on the day I am supposed to be at work so I request her to give me the visit on my off. Because where I work, they can't allow us to just be off work anyhow. (Mukhwana, Trial 3)

Experiencing clinic delays while in post-trial care confirmed the fears participants expressed during trial closure. Although these appeared to be system factors, facility staff may play a role in how participants experience and adapt to these changes as explained later. In addition to clinic delays, some participants raised concerns related to receiving care in an exposed environment. This concern related much to those with HIV stigma tendencies and is described in more details in the next section.

7.2.2 Being in the open

The exposed environment within the public health facilities was perceived as unfavorable and sometimes inconveniencing to some participants. In most public healthcare facilities, the clinic set up makes it difficult for participants to maintain their privacy which is much valued in the context of an HIV positive status. The research setting was different since participants were usually attended to in private in order to maintain confidentiality. In addition, since the public facilities are often crowded, there is a likeliness that a person

can be exposed to more people compared to research where there are comparably fewer numbers. Trial participants expressed this concern while reporting their experiences of care in the public healthcare facilities.

*Actually the time of research, you don't fear anybody because you are one or two or three. But in the time of crossing the other way, you can find there a friend whom you don't want to know about you. So you keep on hiding, doing what, [...] of course there we are in a hall, this way you are one or two, you are an individual, so you are in a secret room.
(Nandi, Trial 3)*

The concern for privacy appeared to directly relate to the HIV stigma tendencies, which was a concern for some participants. Although HIV stigma could have existed even while in research, it appeared not to be a concern since the environment then was more private as explained above. As explained in the previous chapter, HIV stigma was more likely to exist among those recently diagnosed with less previous HIV care experiences compared to those with more. Although actual manifestations of HIV stigma were not evident in the post-trial phase, given the fears expressed in the previous chapter, continued psychological support for participants during and after trial exit, is necessary to facilitate coping and to encourage disclosure of the HIV positive status where necessary. This is especially important to those with little or no HIV care experiences prior to trial participation.

7.2.3 Dealing with different staff

A number of participants reported having experienced negative encounters with facility staff while seeking care from their post-trial facilities. The negative staff attitudes affected the confidence of the participants in the care provided at these facilities. Mukhwana, who reportedly witnessed a non-compassionate staff felt disappointed by the attitude the staff displayed to a fellow HIV infected patient and that had a negative emotional impact on her.

Ok, the only thing I can say is like on the side of these clients, at times they are segregated. Because there is a time I watched one doctor, she was eating she was a lady and a kid came across, that kid is on (HIV) treatment, that doctor didn't get a particle of food to give that baby. There are some words she talked about, then it affected me as a person; I said 'do they think that kid wanted to be like that?' Just giving out that food, it couldn't affect, or the kid couldn't have transferred the disease to her, because I felt bad as a person, I just looked at her and I kept quiet.... (Mukhwana, Trial 3)

Some participants associated the negative staff attitudes more to the government

facilities compared to NGO based facilities. This assertion however was not supported in other situations. For example, many participants who accessed care from NGO based facilities also reported negative experiences with facility staff. Brenda, who accessed care from an NGO based facility supported this argument, when she expressed strong emotions related to feeling 'uncared' for by facility staff.

And I went and informed them 'I am having headache,' but it was not a clinic day, and I informed them I was having headache but they never gave me any medications, not even Panadol, in fact I went away crying. (Brenda, Trial 2)

As Brenda reports, she went to her facility on a non-scheduled date and was not attended to. Unlike in research where participants are attended to whenever need arises, there is a tendency for the NGO facilities to not attend to their patients on non-routine appointments, except in extreme situations as Naluwugge explains.

...because the problem up there (at facility T), when you come on a date other than your return date, and you haven't been brought on a wheel chair, they mistreat us. You have to first sit and wait, you feel very bad and nobody cares, and they are telling you that you didn't come on appointment, (Naluwugge, Trial 2)

This finding illustrates that although participants reported negative care experiences with facility staff, system related factors could have contributed to these. For example, the organisation of services as shown above was a very important factor in how participants were cared for. In addition, a lack of availability of medications in the post-trial care facilities was largely related to poor care and blamed on staff rather than the system in general. This was in particular for medications for the treatment of opportunistic infections, as these were often unavailable in most of the facilities as will be elaborated later. These issues were quite important to the participants since they used to be significantly different within research. For example, in addition to research facilities being accessible most of the time, all required treatments used to be provided freely and timely to the participants.

However, irrespective of the cause, the negative care experiences could be damaging if not addressed. For example, as seen in Brenda's case above, she left emotionally broken. Brenda later expressed how she shunned going to this facility again even though she felt ill. Instead, she resorted to self-management through purchasing over the counter treatments. Byekwaso also expressed a concern of how some patients could decide to abandon care in facilities where they feel mishandled and instead choose to remain untreated, which could be detrimental to their lives and sometimes to the entire

community.

Because if we are mistreated, one can decide to remain in the village, maybe he is a TB patient and will say that 'leave me alone, I will not go to that place.' By the time he dies, he has infected about 30 people. He never took treatment. (Byekwaso, Trial 2)

These findings seem to suggest a need for proper communication and good attitudes from the facility staff, to make participants feel cared for even amidst other challenges. For example, there are simple actions by research staff which participants referred to as good care and were much appreciated. Some participants reported how research staff offered explanations in times when they could not be attended to on time, and that was considered as a caring approach. Such explanations could be reassuring to the trial participants and could improve their overall care experiences¹⁹. Brenda also stressed this point by arguing healthcare staff to make explanations to the patients, for example where some services were not available.

My appeal to health workers, those who interact with patients, let them try to ensure that when a patient comes, even though something is not available, console him and inform him that 'you will return on such a date, your medications will be..., but now it is over.' But informing him to go and buy, yet they had run to you for help, it means they don't have (money). So my appeal to them, let them care a lot for patients. If there is no medication, inform them... (Brenda, Trial 2)

The problem of a lack of availability of adequate treatments from the public facilities appeared to be much related to the perceived negative staff attitudes. Although the government facilities were always open to patients, these appeared to even be in a worse state regarding the availability of medications, especially for treating opportunistic infections. This issue was also closely related to the poor socio-economic status of the participants as they could not even afford to buy these medications from the private facilities. Accessing treatments for opportunistic infections and other financial needs became an important factor for post-trial participants since these were feely available in research. The following section describes how participants addressed the now increased financial demands after leaving the trials.

7.3 Adjusting to the increased financial demands

The majority of trial participants were of a low socio-economic status and reported financial difficulties during the post-trial phase. Many of the participants were

¹⁹ This same issue was highlighted by research staff when making suggestions on how to improve post-care for trial participants as will be shown in the next chapter

subsistence earners, surviving on small scale agriculture or businesses. For those formerly employed, they also had low income jobs such as working as hotel attendants, nursery school teachers, or school cooks. Many participants were not working at all, either due to lack of employment or due to ill health. Ruth, a qualified primary teacher was not working at the time of the interview due to ill health. Similarly, Wilberforce, the only graduate among those interviewed and worked with an international organisation abroad had to leave his job due to ill health and was jobless for more than a year. Such participants relied on the financial facilitation in research for travel and even to cater for some of their domestic needs. Trial closure thus had a negative financial impact on such participants as Wilberforce explains.

It (trial closure) has affected me because as I said I am in Uganda now and I am now not working anywhere, and the first one they could give you some transport and you could be able to transport yourself to your home and may be to have even a cup of milk, but on the other side now is where the problem is, you have to struggle for yourself and moreover somebody who is not working then, so it is a bit hard. (Wilberforce Trial 3)

In addition, since research related care was completely free, trial closure meant participants had to meet some of the new care costs on their own, especially since the public facilities often did not have these services. This meant an increased financial burden on trial participants. The main financial implications related to trial closure included the need to raise transport costs to healthcare facilities, meeting investigation and treatment costs especially for HIV related infections, and meeting other social and domestic responsibilities such as buying food. These issues are explored in more details in the following sections.

7.3.1 Meeting transport costs

Many trial participants expressed difficulties in meeting their transport costs to care facilities. This was in the context of other challenges such as having limited/no income and having other important demands. Nandi recounts her challenge of having to raise her own transport after she left research.

Actually when I left the research, I had to begin collecting my transport, that's the only problem I had. I had to begin collecting my transport. I must know this date, I must have such and such money. (Nandi, Trial 3)

Difficulties in raising transport costs still revealed the gap between research and non-research care contexts in low income settings, where access to even free care would be challenging because some people find it difficult to afford transport costs to the facilities.

Although none reported having missed their routine appointments due to transport difficulties, this was a potential problem especially to those with no income, who had multiple responsibilities, and/or travelled long distances. For example, Ruth who travelled for about 120km for her routine care by the time of the interview needed to use approximately £10 for her full journey. Ruth however had left her job due to ill health and was now depending on the help of her relatives. In addition, Ruth who was a single mother had other domestic responsibilities such as taking care of her children. Ruth seemed to be struggling to raise her transport fares and in some cases had to seek for help from different sources.

...we have to look for money for transport to fetch medication. And when I fail to get it, I call them (research staff) and I request them to help me with money to go and I collect the medication. They help me because there are times when it is very difficult, and may be you have children, and you realise time is nearing (to go for your medications), and children also, and we stay in such a situation. But as you are there, you find that God has enabled you to come back to hospital and get your medication. (Ruth, Trial 1)

The above data indicates that raising transport costs was difficult for some participants in the post-trial phase and appeared to affect those with multiple financial demands more negatively compared to others as in Ruth's case above. Although a professional teacher, Ruth had left her job due to ill health. Worse still, those who were ill in most cases required more finances to purchase medications especially for treating opportunistic infections, which increased their financial burden. The following section explains how trial participants struggled to meet their treatment costs after trial closure.

7.3.2 Meeting treatment costs

The post-trial treatment needs for participants included the need for routine HIV medications such as ARVs and for many treatments for opportunistic infections. Many participants appeared satisfied with the availability of routine HIV medications at their post-trial facilities as reflected below.

As for medication (for HIV treatment), we get it adequately and when they test your blood for CD4, they can give you a refill for three months. After three months you return and get more medications. (Abdu, Trial 2)

I have not encountered any problems, I get my medication on time, and I take it. When I come back, I am informed of what came out from the blood testing. (Joel, Trial 1)

Access to treatments for opportunistic infections emerged as a particular concern among participants. Although this concern was common across all trials, those with active infections, those with limited financial abilities, and those with other domestic needs appeared to be more affected. Participants were generally concerned when they could not afford the necessary treatments and feared this could result into complications to their health as Madina recounted.

...but the important thing is cough, it has been disturbing me, the chest, I start coughing, and yet the issue, even I have failed to raise the money to buy the medication, yet the doctor wrote it for me, but I have failed to raise the money, but again the truth is that nowadays I don't sleep. (Madina, Trial 1)

Despite the availability of other routine services as shown above, many participants expressed a lack of satisfaction with their care in the post-trial facilities, resulting from failure for them to provide treatments for opportunistic infections. Although such a problem affects the general population, trial participants appeared to feel these effects as they were still coming to terms with being cut off from the high quality research care. Often, participants expressed their concerns with reference to research care, revealing the care gap that exists between the research and the non-research contexts in Uganda. Brenda illustrated this issue.

Their treatment is not enough yet you often go there when you are not well, but their treatment is not enough. For them they only care about one thing, giving you ARVs, walk and go away, but if you tell them that you are sick, they can reach an extent of writing for you a note (to go and buy the medication). Because for me I expect that by the time you decide to leave your home and come to the health unit where you get treatment, it means you don't have enough money to take you to a pharmacy or to another hospital. So you also say, 'let me go for treatment,' and when you reach there they inform you that 'there is no medication, go and buy it'. That saddens a lot. Yet then when I was still here (in research), I don't have..., they never told me that 'go and buy medications.' I first suffered from skin rashes but whenever I would reach there, they would give me a tube and I apply it and the rash would reduce. (Brenda, Trial 2)

The organisation of services in most of the NGO based HIV care facilities also affected access to treatment for opportunistic infections. For example, as explained in chapter six above, the majority of them attended to patients only (or mainly) on their routine appointments. For those who became ill on other days, they were required to access treatment from government facilities. This situation was even more complicated as routine appointments were on a three-six monthly basis, which would affect those who were still vulnerable to opportunistic infections. Such arrangements appeared to

significantly limit trial participants' access to treatment for opportunistic infections as Bettinah expressed.

During research, the care was different from the one at the other side (in care). The other side, they give us non clinic days (days only to refill routine drugs), because they work from Monday to Friday. So if they give you a date may be Tuesday, Thursday, Friday, even if you come when you are sick, you cannot see the doctor, they send you to another hospital/facility to be attended to, which was not here, because here whatever problem you had, you would be given treatment, but now the other side, things have changed. (Bettinah, Trial 2)

Specific concerns often arose for those with complicated illnesses, who would thus require undergoing/ receiving complex investigations or interventions. For example, procedures such as x-rays and scans, some treatments, and some blood tests were more likely to be difficult to afford for the majority of trial participants, given their financial limitations. Participants felt researchers needed to take on such complex issues, as these were unlikely to be provided in the government facilities, yet participants could not afford them as well.

You see you may have serious problems, there is a situation which exceeds others; you reach the hospital, may be you are at facility Y and you are told that go and buy medications or go you need this..., go and have an x-ray, go and have a scan, such things, yet sometimes there is no money. Yet the other time the (research) institution would take care of them, especially such things, because even you, you cannot allow to be ill and the medication costs 10,000USHS and you know that 10,000USHS cannot take you to and fro, you just have to buy the medication and you return home early. But there are things that are heavier, going for the scan, going for x-ray, such things become heavy on our side since you see we come from deep in the villages. (Byekwaso, Trial 2)

Such concerns may indicate a need for researchers to engage in the post-trial care of trial participants. Researchers could be helpful in providing emotional support, and also for financial guidance and support where possible. This might also require involvement of other stakeholders who could be able to provide some support as researchers suggested in the next chapter. As mentioned previously, trial participants in some NGO facilities were required to seek care from the government facilities outside their routine facility appointment dates whenever they became ill. Despite being always accessible, participants reported how it was difficult to access treatments in the public facilities, as these did not often have treatments for many of the diseases. Similar to the impact of negative relationships with facility staff presented above, inadequate access to treatments for opportunistic infections resulted into some participants adopting risky

health management practices. For example, some resorted to self/symptom management by buying over-the-counter drugs, while others used local herbs as an alternative treatment as demonstrated below.

On the side of money, because when you go to the health units, they are for money, and because nowadays if they have not given you an appointment to come on a certain day, you cannot come here, you have to attend the health units in our villages which are for paying. So now if you don't have it (the money), that becomes the problem. They write for you the medication and ask you to bring such and such an amount of money, yet sometimes you don't have the money. So you can say 'let me go and be using local herbs,' yes, when you see you can't afford the money. (Nabakooza, Trial 2)

Difficulty in accessing treatments for opportunistic infections was worrisome, causing anxiety among those affected. Even with adequate routine medications, some participants felt the inability to adequately manage opportunistic infections could result into complications to their health. Madina, who had no obvious source of income and still experienced chest complications by the time of the interview expressed this concern.

...you are taking the other one (ARVs) properly, but now this cough which has come, for it, it causes problems, and now you happen to have no medications to treat it, you will keep coughing, coughing, the other one you are taking it very well, but again you are not sure what it (the cough) can cause you. (Madina, Trial 1)

The issues raised above present concerns of responsibility for the care of trial participants after trial exit, with a particular focus on managing opportunistic infections. Although some participants suggested the need for researchers to play a role in this, the majority felt post-trial facilities were responsible for ensuring their care and treatment. On the other hand, some felt this responsibility rested mainly on the government, while others felt a collaborative effort between different institutions was required²⁰. These opinions are reflected in the following accounts.

... the person heading that facility should put enough medication at the facility, because we are many patients. Because it is not only me, there is another person who has come when suffering from an illness different from mine, when it is even more severe, because for the headache, I will go back and buy headex, but now the other one, you are going to admit him and leave him there. You will not go there that 'may be let us go and take medications for him/her,' but you will leave him for the government to treat him, yet he came to you

²⁰ Research staff shared broadly regarding the need for collaboration in post-trial care as will be presented in the next chapter

for treatment because you are his health workers. So they have to ensure that they put enough medication in their facilities. (Brenda, Trial 2)

The government should at least put those other drugs apart from the retrovirals, also to assist those people, if somebody goes for drugs (ARVs), he can access even others. (Mariako, Trial 3)

Interestingly, although Trial 2 participants were recruited with a relatively healthier status than the other two trials, they seemed to report the concerns of access to treatments for opportunistic infections more than the rest. However, some of their views were not necessarily related to their current care experiences, but related to their experiences in the public facilities in general including those before trial participation. As previously mentioned, some participants relied on the support from research to meet some of their domestic needs and after trial closure, this became an important concern for them. This issue is explored in more detail in the following section.

7.3.3 Attending to other domestic needs

The majority of participants resided in urban and peri-urban settings where cultivation was not obviously possible, hence rendering them dependent on purchased food. For those who resided in the rural settings, some were unable to work due to ill health. This made access to food and other domestic necessities difficult to afford given that the majority of trial participants were of a poor socio-economic status. Due to their ill health and being on strong medications, some participants were required to eat a balanced or special diet and to have adequate rest. With no support provided to them, some seemed to be in a dilemma and sometimes experienced fear and confusion. This scenario is well expressed by Dennison.

Another thing which I want to talk is when somebody has become weak, he cannot do any work; now you advise a person not to do other work or hard work yet they need also to survive. Now how does that person..., those people who are sick and they cannot do any work, now you are giving treatment, treatment also needs some food, you eat and you take food, you eat and you take food. Now what about us, other people who do not have ways of survival and they may not have ways of getting food when they are on treatment, what help can you or can they give? Because like for us we are staying in town, not even town, even in villages, you find a person is sick and you have given him treatment, and he cannot use treatment without food. Now how will these people keep using treatment without food? Don't you see these medicines will weaken them more and even they can die because of (lack of) food, they have not eaten food, they don't have ways of getting food. (Dennison, Trial 3)

In relation to the above concern, some participants expressed fears of taking medications without proper feeding and felt this could be harmful to their health.

*... because these drugs are strong, without like drinks or food it can cause problems.
(Mukhwana, Trial 3)*

Trial 3 participants expressed these concerns more than other trials. This could be associated to their context as the majority joined research while very ill and thus required specific treatments including dietary requirements which were a part of their trial. Some participants specifically reported missing the food supplements provided in research. Those suffering from active illness seemed to have increased domestic needs and challenges as they were often unable to work due to ill health, yet required good nutrition as explained above. Such multiple burdens often led to ongoing stress. Some felt going through such stress could be further damaging to their health despite adhering to HIV medications. Wilberforce, who had no income and yet was required to pay school fees for a number of children expressed this concern.

...and when you look, you have the children and they have to go to school, and he is not strong enough to work, and then you know those things they just push that somebody to go very fast (to die) though he is on treatment. (Wilberforce, Trial 3)

The above data has shown that although participants freely accessed routine HIV medications, being cut off from research care resulted in some facing particular financial needs. To a large extent, the data show that many participants were still struggling and not settled in post-trial care. These issues suggest a need for supporting participants beyond trial closure. Although there was some support received during the post-trial phase, this appeared very limited and also informal. The next section presents the views of trial participants on this issue.

7.4 Finding support

By the time of the interviews for this research, many participants still experienced significant challenges. The main challenges included the psychosocial and financial concerns, and were closely associated to the discontinuation of research care. Participants required support to enable them to cope and adapt to their post-trial lives. Although participants reported receiving some support, this appeared very limited to address their needs. However, the little support provided was reportedly helpful in providing them with psychological and sometimes practical support during the post-trial period. The reported support was provided by researchers, peers and the family, while

many participants also appealed for more support from other stakeholders. The following section explores this issue in more detail.

7.4.1 Support from researchers

Trial participants reported receiving some support from research staff after trial closure. In addition to the emotional support, researchers played a role in monitoring and providing guidance to participants, to enhance compliance to treatment and clinic visits. Much of the support received was psychological and was offered through telephone communication. As a way of planning for follow-up care, participants reported being offered telephone contacts by researchers, to use in case they encountered any challenges during the post-trial period. Some participants reported engaging in telephone communication with research staff when they felt it was necessary as Mariako reports.

Interviewer: *After you left research, have you been in contact with the research staff?*

Respondent: *Yes, I call them when I have a problem and they give me advice.*

Interviewer: *Is it your initiative to call them?*

Respondent: *They said we can call them any time, of course their numbers were given to us, though we are getting drugs from the other end, but still they are still monitoring on us. (Mariako, Trial 3)*

Others reported being asked to report to the research facilities whenever they experienced any problems as the quotes below suggest.

...also because even them they give you their contacts, they say 'in case you have a problem, you just call us so that we can know what to do,' when you have problems, maybe the situation has worsened or what, you can call us. (Dennison, Trial 3)

They told me 'even if you felt something, just come to us we shall connect you.' They told me if there is anything I can't do I just come to them, they could help me through the other clinic. (Nandi, Trial 3)

The above data seem to indicate that trial participants were mainly responsible for initiating their own follow-up, and this approach appeared to be the standard. This data also implies that the follow-up did not depend on a structured and systematic approach. This finding is consistent with the findings from research staff as shown in the next chapter. However, relying on this approach raises concerns of reliability, considering that participants may not adequately identify the needs for follow-up. Moreover, such an approach also required finances, for example for making phone calls or traveling to the health units, which could prove challenging for participants who were already financially

constrained. In addition, for many of those who reported being in contact with research staff, this appeared to be on a casual basis and appeared to portray more of a friendly relationship rather than a health worker-patient relationship as expressed in the following quotes.

Actually me I just ring them and I just greet them 'hi, how are you?' Sometimes they ring me 'how are you, are you fine?' Like that. (Nandi, Trial 3)

Yea, because whenever I could come, we talk, we chat as friends, even may be when I have not seen them they call me, 'where are you going?' Like that. (Mukhana, Trial 3)

I had the best doctor and we had..., they cared for me in a good way because they are good, friendly, in fact even up to now where we are now we are good friends, they keep on calling me, 'how are you going on?' Then I could also tell them that I am going on well (Wilberforce, Trial 3)

Well as the above approach still discloses the informal nature of post-trial follow care, it also reveals the strong connections created between the research staff and trial participants. Such contacts appeared to be important in offering psychological support and also as a weaning strategy from research care. These findings seem to suggest a need for a more formal weaning and follow-up strategy as suggested in chapter six above and also supported by research staff in the next chapter.

However, due to their informal nature and largely relying on individual initiatives, it is difficult to ascertain the quality of support trial participants received, and its effectiveness in addressing their post-trial care needs. Nonetheless, such support appeared to be relevant for specific groups of participants, for example, those likely to experience HIV stigma and/or ill health, which was the case for many Trial 3 participants. Indeed, the above data is almost exclusively supported by Trial 3 participants. Apart from their ill health and the likelihood of HIV stigma which appears to have portrayed them as vulnerable people²¹, the reported engagement of Trial 3 participants with researchers could be attributed to the proximity of their post-trial care facility to the research clinic which was in the same location with the research facility. This could have made it easier for participants to interact with the staff compared to other trials. In addition, there appeared to be a misconception among Trial 3 participants, where research and non-research services and staff were regarded as being

²¹ Research staff reported making individual follow up on trial participants whom they considered vulnerable; for example, those still experiencing ill health at trial exit, those with social problems, and those with adherence or stigma problems, as will be presented in the next chapter

the same. This could mean that the care reported to be from researchers could actually have been that provided by the post-trial facility staff.

Trial 1 and 2 participants hardly reported any post-trial engagement with researchers and where this happened, the reasons were likely to be different from Trial 3. For example, some reported only being called back for trial related reasons, or when they were invited to participate in the current research as shown in the following quotes.

No, since we left here, for me I have never heard from them (the researchers).

(Nabakooza, Trial 2)

No, except when you receive a phone call that you are needed like the other time, but I have never heard from them again. (Byekwaso, Trial 2)

No, I got a phone call in May, when I was returning to collect medications and I was asked to first return the medications. I received a call again today. (Joseph, Trial 1)

Although there is a possibility that some of the participants were followed up for monitoring purposes as in Joseph's care above, it is clear that this was not uniform to all participants. This data suggests that current HIV trial closure practice does not specifically focus on the need for post-trial follow-up care and monitoring, yet this is a major concern for HIV positive trial participants as shown in chapter six. This reveals yet a major gap in the current implementation of post-trial care in HIV drug trials in Uganda. This gap was also significantly recognized by research staff as shown in chapter eight below.

Overall, this data indicates a limited engagement of researchers in post-trial care, and exposes gaps in identifying the needs and priorities for post-trial care and planning for these. Although some follow-up care activities were implemented, these appeared unplanned and unsystematic. Moreover, these largely depended on individual initiatives of trial participants, which questions the reliability and effectiveness of the approach in meeting the post-trial care needs of the participants. This approach also raises ethical concerns of safety of trial participants, considering that harmful effects from trial interventions are possible even after trial closure.

7.4.2 Support from peers

Peer support emerged as a key theme in this research, with trial participants reporting either seeking or offering support from/to peers. The support among peers was reported to be helpful for psychological and social support to the HIV positive participants, who

still required ongoing care and also appeared to be experiencing a range of challenges following exit from the trials. Trial participants reported keeping in contact with peers during the post-trial period as explained below.

Now days, most people meet each other here in Kampala. You come to town and you call your friend that "hullo, how are you", that "I am fine", that "come like this and meet me here". And you converse a bit, and when you meet over a cup of tea and you meet again, it is still good. (Joseph, Trial 1)

We keep reminding ourselves, and every situation one may be facing, how one left here, like now how we came and met, every one informs the other that 'for me I am like this, I am like this,' and everyone took each other's telephone contact and calls them once in a while. So, we keep communicating. (Naluwugge, Trial 2)

Although most of the connections seemed to be intended for networking as the above quotes suggest, some felt connecting with peers was supportive. In some instances, this acted as a counselling strategy, which helped in allaying anxieties among participants who still experienced the psychological effects related to HIV as a disease. Trial participants found (or expected to find) solace in talking to peers and sharing their problems with people in a similar situation.

...like how we were outside, everyone would advise another. Like the woman I was with, [...] and for her, she told me that 'do you see my phone number, I want you to visit me and we spend the night chatting.' Because everyone, we advise one another. (Naluwugge, Trial 2)

It is also important that when you get them (peers) when you have been with them in research, it is very important that you meet them, you see and understand that 'ok, I am not alone, the friend also is existing like me, then you just continue pushing on life, by may be reducing the worries, may be you could laugh, and say 'ok, I am not alone, but I am with others and still on moving.' (Wilberforce, Trial 3)

In addition, peer support was found to be helpful in maintaining good health seeking and health management behaviors of the participants. Some felt that it was possible for participants to default from taking their medications or to seek healthcare, which was likely to occur in situations of HIV stigma, or where there are misconceptions. Joseph expressed the need for supporting peers who are likely to abandon their treatments (*leaving the focus*) for such reasons, of which he reported to have observed among many peers.

He/she leaves the focus, and they are many. For me there are many I leave with when they were on medications and they say that "mine (HIV) is cured". Yes, there are many not only one, not two, not three. Because for me I move a lot among people, I stay a lot among people, and as you are there, the person calls and tells me "I am fine, for me I have stopped taking the medications, for me mine is cured". Even those I was with at facility M, and one says "my HIV is cured". (Joseph, Trial 1)

Although this research also aimed to include those who might have not continued in care following trial exit, this was not possible due to pragmatic reasons. However, the above finding might suggest a possibility of participants abandoning HIV care and treatment following trial closure. This finding suggests a need for future research to establish rates of linkage to post-trial care for HIV positive participants after exit from the trials. In addition, the finding suggests a need for the continued involvement of researchers in the care of participants after trial exit.

As suggested in the above data, peer support occurred largely as an individual initiative. However, there was a general need expressed by participants for researchers to support this activity. This would involve researchers facilitating group gatherings for peers, to come together, connect and support each other. Group gatherings were assumed to have more advantages over individual networks, in dealing with both the psychological issues and in correcting misconceptions which might exist among trial participants. Many participants supported this view as indicated below.

When you come together, people share with each other how they are doing, the problems they have, so you are able to update your colleague. How you are doing in your home, and you also come to know how your colleague is doing. That is how you even come to know those who died, your colleagues inform you that 'so and so we were with died,' and you come to learn about all those. So now coming together is important because you share ideas and you discuss. So coming together is important, you can do something. (Nabakooza, Trial 2)

... when you are together, a person can say that "for me I suffer from headache in this way" and another also mentions the way it affects him/her. So by the time you combine those responses, you can also realise that may be you are also suffering from the same, and you understand that. (Joel, Trial 1)

Trial participants felt researchers need to take up the responsibility of arranging for peer gatherings. This would not only be helpful in encouraging peer networking, but would also enable researchers to follow-up the participants. In addition, having occasional gatherings would be a good strategy for weaning trial participants from the highly

regarded research care, considering how some participants wished this to be a recurring event.

*... it would be good that they give us a day and we all come back here, so all of you gather and see each other and discuss with the colleagues you have not seen for a long time.
(Nabakooza, Trial 2)*

One thing they would have done and I think, I asked about it here, they would not have forgotten those trainings (group gatherings). May be every three months, or six, and they would call those people they were with, you see? (Joseph, Trial 1)

The above data shows how trial participants highly regarded peer networking and support as a strategy for coping with the challenges experienced during the post-trial period, and to enhance health seeking and management behaviors among peers. The current practices however appeared inadequate, and participants felt they needed to be enhanced by incorporating group gatherings which were seen to have added advantages compared to individual connections. In addition, peer support appeared to address more of the psychological concerns of the participants and not the financial or material needs. These needs were quite significant during the post-trial period and were also not addressed by the research staff as shown in the previous section. Family members and other stakeholders were reported or expected to play a role in addressing these as presented in the following section.

7.4.3 Support from the family and other stakeholders

The family played a role in meeting some of the care needs of trial participants during the post-trial period. These mainly included the emotional, financial and material needs. Although few participants reported being supported by their families, the little support received appeared very helpful in specific situations. For example, Ruth, who did not have a job depended on her family for financial help, especially to raise transport fees to visit the care facility as shown in the quote below.

*Since I started from this way (the city), it was my sister and a few others who knew about it (my HIV positive status), then recently we also informed my father, because I used to encounter transport problems, so I had to inform him the truth why I ask him for money.
(Ruth, Trial 1)*

Similarly, Nandi, who worked far away from her family felt that getting a facility near her family was logical, in order to be able to get her family's support whenever she needed

it. For example, at times when Nandi was not able to collect her routine medications, the family was always available to do that for her.

...even if I have not come to get medicine, I can send somebody, even if I don't have transport, I can send somebody as I have crossed from to go to the other way, he just picks and brings for me. (Nandi, Trial 3)

However, some participants were concerned that even with a good will, some family members were incapable of offering all the support required, especially financially and materially, as these were in most cases also experiencing similar economic situations to those of the participants. Mukhwana explained this situation.

Some families yes they do (support trial participants) but there is a family really you can see, father and the mother they are not the people who can help their children and they don't have anything, so who will help them apart from the leaders. (Mukhwana, Trial 3)

This finding might imply the need for a strategy which includes the family of the participants while attending to the financial needs of trial participants, as was suggested by the participants and research staff. For example, one of the supportive strategies suggested was training trial participants on income generation. Such an activity could also include the family in order to boost the financial capacity of the entire family. Moreover, some of the participants were ill and not able to work meaning that empowering the entire family could be a more viable option in addressing the financial needs of the participants. In addition, this finding may suggest a need to investigate the views of family members on post-trial care of HIV trial participants after leaving the trials.

Overall, these findings imply that although some families supported trial participants, the support offered was minimal and was not likely to meet the diverse care needs of the participants as expressed in the previous sections. This situation is largely attributed to the poor socio-economic status of the family members just like the rest of the population, which limited their ability to address especially the material and financial needs of the participants. These findings suggest the need for facilitating families and involving them in the care of trial participants following trial closure.

With limited support received from the families, and considering that many of their needs were as well not met by the researchers or peers, trial participants suggested that other stakeholders need to get involved in their care during the post-trial period. The main stakeholders suggested included: the government, NGOs, research funders/donors,

and the community, among others. Although no actual support was reported to have been received from such entities, participants felt these would play a big role in addressing some of the challenges they faced during the post-trial period. The majority of participants expressed the need for financial and material support, and the provision of adequate healthcare from the various stakeholders. For example, Nandi suggested the need for the government to provide financial assistance and food support to trial participants, as these were essential in care and treatment as earlier explained.

Those people need transport, feeding, transport is first and feeding is a problem. You find some people feed bad, they don't have food to eat. The government should provide food for them at least. At least every year, at least they serve those people some two, three times a year. People lack food. You find a certain person eats badly but is on that..., you know this medicine without eating very well, staying is a problem. And it needs every time at least you have a sweet in the mouth, or a biscuit or what, yes. So you find some people don't have it, they don't have it, they don't afford. So the government should help them at least such people like three, four times a year to serve them food. (Nandi, Trial 3)

Similarly, other participants also advocated for food support from the government and other stakeholders such as research funders/donors as suggested below.

So I would like, may be on the side of the government to give a hand to such people, because these drugs are strong, without like drinks or food it can cause problems. So I would like, may be the government or the research companies to help these people with giving like food stuffs, like that. (Mukhwana, Trial 3)

So, my request also to the government and the donors, they could also..., to make some of these people who do not have ways of survival, ways of getting food, if there is a way of supporting them also, they could support them also with some food, or ways of getting food meanwhile when they are on treatment. That is my request to the government and to the donors. (Dennison, Trial 3)

In addition to food support, Wilberforce felt participants could also be supported with scholastic and domestic materials, to reduce on their multiple demands. This appeared to be influenced by his previous knowledge or experiences of HIV care as shown in the quote below.

I remember the last time when organization T started, they used to help those people because we have some others who are, as I said earlier that they are not able even to sustain themselves for a day. So organization T used to facilitate with some dry ratio things, like some kind of posho, something like that and some other biscuits, even giving

them blankets and even they used to come up may be if someone has children, they used to have a hand in it, so that they can at least reduce the stress of that somebody who is on treatment... (Wilberforce, Trial 3)

As the above data suggests, the need for financial and/or material support could be approached on a case-by-case basis, with a particular focus on those experiencing ill health or with limited financial abilities. This suggests the need to undertake a financial assessment for the participants, before deciding the rightful support to be provided. Conversely, some participants felt they still required psychological support, to enable them cope with the problems related to the HIV situation in general. For example, some suggested they needed general HIV counselling and support. Such help could be provided by NGO workers, the public healthcare facilities, and/or members of the public such as HIV community support groups. This concern also appeared to be more relevant to Trial 3 participants considering their particular circumstances such as being recently diagnosed for HIV, experiencing ill health, and undergoing significant financial challenges. Wilberforce expressed this concern.

...during those days they used to give in some hand so that at least, they could just talk to them (HIV positive people) and they used to have counsellors who could even move in areas to see how they are doing, they even know their homes and visiting them and encouraging them that 'do not worry, it is not you alone, even others we are also there, maybe we are counsellors but we are also victims, 'so they could just come up like that and could stay for long. (Wilberforce, Trial 3)

Despite being expressed by only one participant, this finding appears to confirm the need for continued psychosocial support for trial participants after trial closure, to enhance coping with the HIV positive diagnosis in general. As stated above, this support is likely to be more relevant to those with limited HIV specific care experiences, which could also include people who acquire HIV during trial participation. This finding further suggests a strong need for the involvement of different stakeholders in the care of HIV post-trial participants.

Trial participants also felt the government had a big role to play in their care by providing adequate resources, for the proper running of the public healthcare facilities. The main emphasis on the role of the government was placed on increasing manpower and medical supplies in the public health facilities, plus support supervision and monitoring of service delivery. Such support was necessary to address some of the healthcare challenges faced by participants such as clinic delays and a lack of adequate medications, especially for treating HIV related illnesses as described in previous

sections. By improving the services in the public healthcare facilities, it is possible to reduce the negative emotional reactions related to trial closure as research staff suggested in the next chapter. Byekwaso expressed some of these opinions in the quote below.

Because when the government posts health workers, it never follows up, they stop at posting the staff. [...] The government needs to address that issue, it will not tell us that it has no health workers yet there is no one to educate our children. It (the government) has no training institutions, it has given them to private investors who demand a lot of money, let the government address it and we get private institutions to follow that up. Let the government see to it that when a child is intelligent and can do healthcare courses, let them go for such courses on government sponsorships, so that we can have many health workers. (Byekwaso, Trial 2)

7.5 Conclusion

Findings in this chapter have highlighted that trial participants encountered numerous challenges during their first year of leaving a trial. These challenges related mainly to how the participants accessed HIV care and treatment, and also to their day-to-day living. The main challenges appeared to emerge from the fact that after leaving the trials, participants required to seek care in the public healthcare system which offered significantly lower standards of care compared to research. The change from research to usual care was experienced as negative and uncomfortable for most participants and these required time and support to adapt to the 'new' care system.

The limited financial abilities and ill health of some participants significantly affected how they accessed care and also addressed their domestic needs. These factors were particularly important to participants since all the care in research was free, while some participants could use the incentives received in research to cater for some of their domestic needs. Trial closure therefore meant that participants required meeting all their domestic needs, in addition to raising their transport costs to facilities, and sometimes purchasing expensive medications. Being ill made the situation more complex as those affected in most cases required more finances to seek healthcare and meet their dietary requirements, yet would most likely be unable to work. Complex challenges such as these left some participants confused and emotionally distressed.

These findings have suggested a critical need for the involvement of researchers in the care of trial participants after trial closure. In addition, the involvement of different stakeholders appears to be very paramount as some of the needs may not easily be

addressed by researches alone. The public healthcare facility staff, the family, and the community could be important stakeholders to target as these are in close contact with trial participants. Since some of the care strategies require finances, those responsible for budgeting for research also need to be involved. Research staff shared similar views on this issue as presented in the next chapter.

The previous and this chapter have looked at the perspectives of trial participants during the trial closure process and have highlighted some of their care expectations, needs, and experiences during the transition journey from research to usual care. The next chapter presents the perspectives of research staff, by describing their views and practices regarding the care of HIV positive trial participants as they undergo the transition process.

CHAPTER 8: FACILITATING TRIAL CLOSURE: ETHICAL, MORAL AND PRACTICAL CONSIDERATIONS

8.1 Introduction

The previous two chapters have shown that transitioning from research to usual care was a complicated process, frequently associated with negative impacts, which raised unique and diverse care needs among the HIV infected trial participants. Most of the care needs were related to the psychological, social-economic and practical challenges that arose during trial closure, linkage to care, and post-trial access to HIV care and treatment. Participants reported that research staff played a key role in enabling the transition process by offering support to them. This chapter provides findings related to the ethical governance of post-trial care as shown in research ethical guidelines and also provides the perspectives of research staff regarding transitioning of HIV trial participants from research to usual care facilities. The chapter describes how post-trial care for included trials was regulated and provides an account of how research staff engaged in various activities to facilitate the transition, and highlights their views on some aspects of post-trial care where improvement is required.

Findings showed that researchers engaged in different activities to prepare trial participants for the closure and to support them during linkage to post-trial care. These activities were based on the ethical and moral considerations of researchers and were generally guided by existing research policies. Preparing trial participants involved: providing relevant information to offer guidance on trial closure, (for example, where participants could access post-trial care), addressing the emotional concerns which arose among participants, and addressing stigma related concerns. In addition, research staff facilitated trial participants to link to post-trial care, in order to maintain continuity of HIV care and treatment. This was mainly done through referral to the public healthcare facilities, and by ensuring continuity of provision of trial drugs. Views were shared on how linkage to post-trial care may be improved, e.g. through a more personalised and directly facilitated approach, involving physical handover of trial participants to their next care providers. Research staff also suggested the need for financial support and empowerment, which was not currently implemented but appeared to be a crucial need for trial participants in the Ugandan context.

After trial exit, there was a need for continued support for the participants while getting established into usual care facilities, and for providing trial feedback to them. Findings suggested that post-trial engagement of the staff with participants was minimal and where it occurred, it largely depended on individual staff initiatives. Although there were

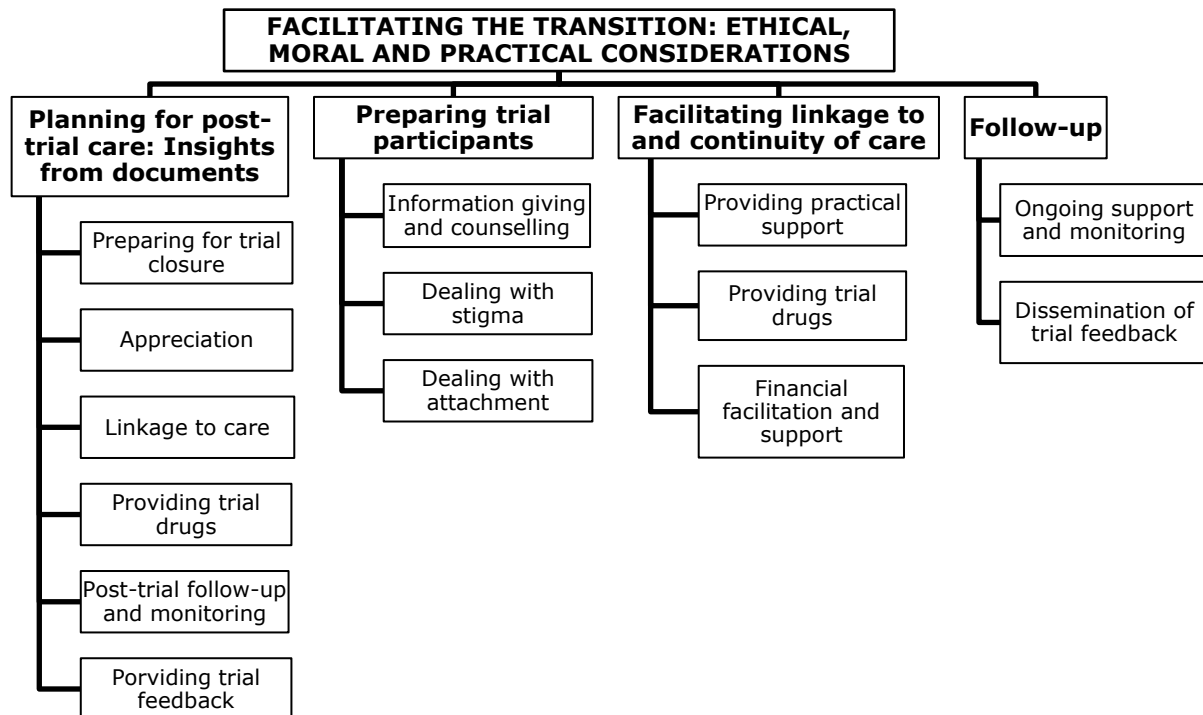
plans for post-trial care reflected in the ethical documents, these mainly concerned the dissemination of trial results and left out other important aspects of care identified by research staff (and trial participants). For example, post-trial clinical follow-up was thought to be very helpful in monitoring for possible side effects from trial interventions and also in offering continued emotional and practical support to participants during the post-trial period. This was also felt as a researcher's ethical responsibility even though not explicitly supported by existing policies.

A review of ethical documents from two²² of the included trials shed some light on how post-trial care is planned and also highlighted on the issues of focus in the current HIV trial closure practice in Uganda. In general, findings in this chapter established a mismatch between what researchers consider 'good' post-trial care practice in HIV trials and the current ethical guidelines as shown from the reviewed documents. To address the diverse post-trial care needs of the participants, a need for involvement of different stakeholders in post-trial care was identified. Since post-trial care activities were guided by ethical policies, research staff recognised a strong need for the ethical authorities to be involved in HIV post-trial care in Uganda, by instituting policies and guidelines on the important aspects of care as recommended in this research.

The findings in this chapter are presented in four main sections. The first section reports on how post-trial care, as set out in relevant ethical documents is governed. The second section describes how trial participants were prepared for the closure. The third section describes the views of research staff on the support provided/required while linking trial participants to post-trial care, and the fourth section reports the perspectives of the staff on post-trial follow-up care. Figure 10 below summarises the presentation of findings in this chapter.

²² Trial 3 was still ongoing by the time of the interviews for this study, therefore, we could not review the ethical guidelines for this trial for ethical reasons

Figure 10: A summary of chapter eight findings



8.2 Planning post-trial care: insights from documents

Documents from Trial 1 and Trial 2 were reviewed to identify any information relating to post-trial care, to provide an insight on how post-trial care is planned for and represented in current research practice. Trial 3 documents were not reviewed due to ethical reasons, since the trial was still ongoing by the time of the current research. The reviewed documents included the general trial protocols, participant information documents, informed consent documents, and the trial closure 'Standard Operating Procedure' (SOP) documents, also sometimes referred to as the Close out 'Manual of Operations'(MOP).

The protocol was recognised as the authoritative and most relevant document in guiding post-trial care. The views from research staff implied that aspects which were not reflected in the protocol were unlikely to be considered for implementation, even though these could be recognised as important. All information within the participant information and the informed consent documents appeared to also be guided by what was contained within the general trial protocol. The MOP document provided specific and detailed guidelines for trial closure, and unlike the protocol which offered general guidelines for all trial sites, the MOP is more contextualised such that for trials which were conducted at different sites, each site was required to develop their own MOP. This implies that the

different aspects of post-trial care as reflected in the protocol could be approached slightly differently across the different sites. However, although detailed in the description of the specific steps to be undertaken while transitioning participants by elaborating on how the specific post-trial care activities could be approached by the trial sites, the MOP²³ did not add new aspects of care not reflected within the protocol. This further showed that the protocol is the most authoritative document in guiding post-trial care.

The information from the reviewed documents provided a picture on the activities which were of focus in HIV trial closure practice in Uganda, and how these were planned. The key issues which were of focus included preparing for the closure, appreciation for trial participation, linkage to post-trial care, provision of trial drugs, post-trial follow-up and monitoring, and providing trial feedback. However, even though the same issues emerged from the perspectives of respondents, the guidelines on these appeared significantly different from the general concerns of the respondents. For example, the guidelines on most aspects were general, not elaborate and inconsistent across the two trials or in the different documents for a given trial. In other cases, the approach to the specific aspects of post-trial care was not considered appropriate for addressing the needs of the participants. The insights from the documents on post-trial care are presented in the following sections.

8.2.1 Preparing for trial closure

The reviewed documents included guidelines on preparing for trial closure. These guidelines related to the required documentation during the closure, information giving to trial participants, and practical activities to be implemented during the closure. Some of the documents required during the closure included a referral form and the trial completion form, although other documents could also be developed. The documents appeared to be specific to individual trials and/or participants and were described in the main documents such as the trial protocols or the trial closure SOPs. The excerpts below represent some of the documentation guidelines.

The following documents should be complete when the patient has exited the trial; exit checklist, client clinical/close out report, exit register. (MOP, Trial 1)

Ensure the following exit visit specific forms have been completed: Form 26
Participant exit Interview form, Participants Clinical Summary report / Participants Referral

²³ The information in the MOP is presented in the relevant aspects of post-trial care in subsequent chapters.

Form, Participants certificate of trial completion, Trial 2 End of Study Form. Trial drug discontinued and discontinuation indicated on the Doctor's follow-up form. Open label TX prescribed and dispensed and prescription indicated on the doctor's follow-up form. All previous and on-going clinical events resolved. Complete and submit all CRFs for final visit (Nurse Follow-up Form, Doctor Follow-up form and blood test results) and event specific report forms as indicated. (MOP, Trial 2)

The reviewed documents also included guidelines on preparing trial participants for the closure. This would be achieved through information giving, aimed at providing general guidance for trial closure and linkage to post-trial care, and attending to the psychosocial needs of the participants. Researchers were required to ensure that exit procedures were understood and also emphasis was put on participants' post-trial care choices, for example, where they wished to go for post-trial care.

Discuss referral of the patient with the patient and the referral centre (as applicable)- The patient's wishes and needs should be assessed to allow the patient to be referred to the most suitable clinic after they exit the trial. (MOP, Trial 1)

Trial 1 also involved a practical activity where trial participants were gathered together with researchers. This gathering was primarily intended to disseminate relevant information on trial closure to the participants.

In early January 2013, the team organised a meeting with participants. At this meeting, there was general review of the trial, and information giving about the exit procedures. A successful question and answer session was part of the programme. Information giving continues at every visit throughout the exit period (14th January 2013 to 31st January 2014). (MOP, Trial 1)

As data from the respondents suggest, coming together was seen as a helpful approach for networking, for saying a proper goodbye, and also for retention of information such as telephone contacts for future networking. In addition, this approach appears to be a good strategy for 'weaning' and although it was reportedly only implemented in Trial 1, respondents from Trial 2 expressed a need for it to be adopted in HIV trial closure practice in Uganda. The need to make assessments for participants' health situations was also highlighted in trial documents, to enable researchers take appropriate actions e.g. offering appropriate treatments or referral to more advanced facilities before exiting them. This information also related to safety monitoring where participants would be screened and those still experiencing ill health or complications would be appropriately managed within research facilities before trial exit or referred to appropriate facilities for further management.

It may be useful to assign patients red, orange and green colours according to their current disease status to allow for planning for final visits and referrals. The exit report can be printed out and may be help with these arrangements. (MOP, Trial 1)

The above information was congruent with what research staff reported and shows concern for trial participants. However, such an approach would not address the concerns or complications which might arise after trial exit, as there were no established mechanisms to monitor for these.

8.2.2 Appreciation

Although limited information existed, the reviewed documents indicated that there were plans made for appreciating the participants for trial participation. This was only reflected in Trial 2 and was to be implemented using a certificate as shown below.

A certificate of trial completion will be issued to each participant at exit to thank them for participating in Trial 2. (MOP, Trial 2)

This information was congruent with the accounts of the respondents. Although some respondents felt this was sufficient, many argued this to be inappropriate for appreciating participants who sacrifice a lot in research. In addition, this information was not reflected in participants' documents, such as the information sheets and the informed consent documents, which could give respect for informed consent. Trial 1 did not include any information regarding appreciation of the participants for their participation.

8.2.3 Linkage to care

Information from documents indicated that the official approach for linking trial participants to post-trial care was through referral, in which trial participants would be offered a referral letter to deliver to the facilities. This information was congruent with that from the respondents, and was clearly reflected in both trials.

Transferring patients back into standard clinical care: *A list of participants with dates of exit will be sent to individual referral/mother centres prior to exit. Sites will be informed that participants will be supplied with drugs enough for 3 months at exit and that their next appointments will be on individual appointment's card at exit. Each participant will be given an exit report to the referral centre but this will be followed by a telephone call to confirm that the patient delivered the report and that the appointment date was noted and recorded in their appointments management system for follow-up. (MOP, Trial 1)*

A clinical summary report will also be the referral form. (This) will be produced in triplicate by the data manager at each site. One copy ---kept by the participant, one ---taken to the ART provider (referral letter) by the participant, one kept in the participant's file. (MOP, Trial 2)

The specific information to be included in the referral forms included participants' health situations, any adverse events from trial participation, any treatments to be continued e.g. for concomitant medications such as for chronic conditions, plus any other relevant information which could be helpful in the management of the participants. Information for future contact such as telephone numbers were also included on the referral forms as reflected in the excerpts below.

Key additional information: *Current clinical status and health (anything of importance that is not recorded in the database but in the participant's clinical notes and that is current), any 'other' concomitant medication (e.g. TB drugs, antihypertensive, etc., that are not included in the report as the database may not always be accurate for these drugs), any allergies or hypersensitivity to any concomitant drugs including suspected CTX – Zidovudine bone marrow suppression, any additional information on pregnancies/infants (for example, HIV status of child) can be added here if necessary. (MOP, Trial 2)*

Nevertheless, data from respondents indicated that linkage to care using referral letters was inappropriate, as it was difficult to provide all relevant information about the participants using this approach. Some information was also included regarding how linkage to care would be confirmed, for example, by using telephone calls as the excerpt below indicated.

Please report how the procedure of transferring to the referral clinic will be organised by this site (e.g. sending list of final visit dates to referral centre, patient arranges the appointment, internally arranged by site staff, etc....), and how it will be verified that an appointment has been made (e.g. returning letter with tear off slip, appointment card, telephoning clinic, etc....). (MOP, Trial 1)

Despite the above recommendations to confirm linkage, data from respondents indicated that these recommendations were unreliable, as in most cases they relied on trial participants, facility staff, or individual research staff, and sometimes would involve costs. Thus the current practice to linkage to post-trial care emerged as a concern in the current study.

8.2.4 Providing trial drugs

Information on provision of trial drugs was somewhat different from the two trials. This information appeared to be dependent on the trial regimen in consideration. For example, Trial 1 which tried participants on 3rd line regimens had specific guidelines on how to provide these as some of these drugs were not available in the public healthcare system. By contrast, Trial 2 tested a drug which was universally available, hence no specific guidelines were provided on this. However, there were similarities regarding the provision of a buffer stock to cater for the time of linkage to care as reflected below.

Patients will be issued with 3 months' supply of drugs when they are exiting the trial. Drugs will be supplied depending on which combination each participant is exited on. (MOP, Trial 1)

The participant will now stop the trial drug and receive a three month prescription of the open label drug (MOP, Trial 2)

As mentioned above, provision of a trial regimen was a major concern for Trial 1 compared to Trial 2. In Trial 1, mechanisms for continuation of providing the trial regimen were required before trial conduct as the excerpt below indicates.

Post-trial treatment: *The drugs²⁴ used in this trial are already licenced or, in the case of drug 3, are likely to be licenced and available in the participating African countries by the time that the first patients complete 144 weeks of trial follow-up. The trial investigators will negotiate with the ministry of Health in each of the participating countries, and obtain an undertaking from them that they would support the ART requirements of the study participants after the trial ends. (Research protocol, Trial 1)*

Trial 1 involved a drug which was unlikely to be unavailable on open market by the time of trial closure. As such mechanisms for ensuring continuity of this were put in place in advance as shown below.

Participants will be educated that continuity of drugs will be at centres where they will be referred. However, those on a combination containing drug R will continue receiving a three monthly supply of the drug until August 2014 from facility J. (MOP, Trial 1)

The above data indicate a commitment among researchers to ensure continuity of providing a trial regimen and was consistent with the views from respondents. By the

²⁴ The names of drugs have been blinded in the excerpt.

time of the interviews, two participants were still receiving a trial regimen from the research facility. In addition, information about continuity of a trial regimen was included in participants' documents as indicated below, further highlighting the importance placed on this aspect of post-trial care.

Post-trial care issues: *I understand that I will be given anti-HIV drugs for up to 3 years (144 weeks) while I am in the Trial 1 study. After the study, my healthcare will be provided by the national health system. (Informed consent document, Trial 1)*

What happens when the research study stops? *After the research stops you will continue to receive your antiretroviral medicines from your current provider and the study team will advise you on further additional TX according to the findings of this study. (Patient information sheet, Trial 2)*

8.2.5 Post-trial follow-up and monitoring

The reviewed documents indicated limited information regarding post-trial follow-up. Where this was done, it appeared to only be targeted at monitoring the possible unwanted effects from trial interventions rather than for the general post-trial care of the participants. The need for monitoring for possible unwanted effects also appeared to be applicable to specific conditions. For example, individuals with ongoing clinical events or those undergoing special conditions such as pregnancy had an indication for follow-up and monitoring following trial closure. These considerations are reflected in the excerpts from MOP documents.

At the exit visit, Exit Interview Form (Form 26, appendix 1) should be completed. Participants with on-going clinical events complete Exit interview form. Give appointment to assess progress or resolution of the event in question. (MOP, Trial 2)

If a participant is pregnant at the exit of the trial, for proper management, facility J team will ensure that the referral centre is informed. If the referral centre does not have an antenatal clinic, facility J team will see to it that the expectant mother is also referred to an antenatal clinic that offers PMTCT services nearby or of her convenience. For easy follow up, facility J will be keeping a diary with all the details of the expecting mother including expected dates of delivery and the antenatal clinic referral. Depending on the outcome of the pregnancy, the facility J team will complete a Pregnancy outcome form.... (MOP, Trial 1)

Although the above guidelines appeared to indicate the need for post-trial follow-up/care, these seemed quite unspecific on the approach and the form. For example, while some documents explained that follow-up was required, these lacked specific

guidelines such as how long this should be done and what it should involve as shown in the excerpt below.

Patients must be followed-up until clinical recovery is complete and laboratory results have returned to normal or baseline, or until the event has stabilized. Follow-up should continue after completion of protocol treatment if necessary (Protocol, Trial 2)

The two trials also appeared to stress the need for follow-up and monitoring differently, with Trial 2 putting more emphasis compared to Trial 1. This further illustrated a lack of explicit and general regulation of this aspect of care in HIV trial closure practice.

8.2.6 Providing trial feedback

Providing trial feedback appeared to be one of the most significant post-trial care aspects emphasised in the reviewed documents. Unlike most aspects of post-trial care, this was also emphasised in both trials and also described in detail, with specific information on how it would be implemented as the excerpts below suggest.

At the participants' meeting on 11 January 2013, participants were informed that once trial results have been released, they will be called in another meeting and given the results. For this reason, the study team will complete another contact form for each participant at exit. This will make it easy for the study team to contact former Trial 1 participants for result dissemination or for any other reasons as deemed necessary. The participants were also told that when trial results come out, Trial 1 study team will visit institutions where participants were recruited from and more likely where they have been referred after exit. The team will give presentations of results to institutional staff who will in turn help in the continued process of disseminating trial results (MOP, Trial 1)

Patients will be informed about the study and the major results through participant meetings. In addition, a letter summarising the study findings and approved timelines for informing participants of the trial results shall be specified (MOP, Trial 2)

This data suggests the commitment researchers had on implementing provision of trial feedback in the HIV trials. In addition to the general trial outcomes, Trial 1 also appeared to have plans of disseminating individual trial feedback to the participants as the excerpt below suggests.

Once facility J receives these results, the team will ensure that a copy of individual results is delivered to the referral centre of exit. The head of the referral centres will be requested to ensure that the participants receive their results as soon as possible and also managed appropriately. Furthermore, the referral centre will be requested to write or call facility J to

confirm that participants received their results individually and where necessary appropriately managed. (MOP, Trial 1)

Although plans to disseminate the individual trial results were in place, this had not been done by the time of the current study, which left trial participants concerned as shown in chapter six above. Similar to the data from research staff, reviewed documents showed how the need to maintain research integrity could have affected the approach to result dissemination. For example, individual results which appeared to be of importance to trial participants such as CD4 counts and viral load would not be provided until a specific time, due to trial requirements as reflected in the excerpt below.

When giving exit presentations to referral centres, Site J team will remind staff that VL (Viral Load) and Resistance results are double blinded throughout the trial. However, at an appropriate time, the institution will provide available viral load and resistance test results to sites prior to patients exiting. However, week 144 results will be provided after all patients have exited the trial. (MOP, Trial 1)

Notwithstanding, despite this aspect being emphasised in the ethics documents, specific concerns arose among trial participants, especially in regard to the timing and types of the feedback as highlighted in chapter six of this research, suggesting a need for evaluation and more improvement on the current practice.

In general, by reviewing the documents, it was clear that post-trial care guidelines were general, not elaborate and inconsistent across the two trials. For example, for the two reviewed protocols, there were brief descriptions of some aspects of post-trial care such as the time for trial closure, plans of how participants would access post-trial care, and plans for dissemination of trial findings. This information also differed among the two trials. For example, in Trial 1, the only post-trial care information in the general protocol²⁵ related to access to the trial regimen after trial closure. On the other hand, the informed consent document provided some information regarding post-trial care, which also related to the provision of the trial regimen, while the participant information sheet provided no information related to post-trial care. Similarly, Trial 2 documents had very limited information, although Trial 2 addressed more and different issues compared to Trial 1. For example, while the issue of post-trial care was reflected by both trials, Trial 2 focused on general care (not only drugs) e.g. care during closure, referral and access to post-trial care in general. Unlike Trial 1, Trial 2 had some information on post-trial care reflected in the participant information sheet, while no information was reflected in the

²⁵ Other ethical documents such as the informed consent forms and participant information sheets were a part of the protocol although the representation of post-trial care issues are presented separately from the general protocol.

informed consent document.

The reviewed documents also highlighted the main focus for post-trial care. As evident from the above excerpts, the main focus for post-trial care related to: linkage to post-trial care (through referral), provision of the trial regimen, and provision of trial feedback, and although some documents indicated guidelines on general post-trial care, this was so limited to address the specific concerns raised by trial participants, as presented in previous chapters. For example, trial participants expressed a need for financial/material support, more facilitation during linkage to care, and post-trial follow-up care and monitoring, which were not clearly represented in the current guidelines. These aspects were also highly supported by research staff as will be elaborated later in this chapter. Although only a few documents were reviewed, these trends are a clear indication of an existing gap in HIV trial closure practice in Uganda, where the current ethical recommendations fail to meet the care needs of trial participants.

The question which arises is why this gap exists. Since the protocol is the official guideline for trial conduct, staff felt that individuals responsible for developing research projects are majorly responsible for identifying and planning for the post-trial care needs of the participants while designing the trials. Specifically, research staff pointed out the need for early projection/identification of participants' post-trial care needs as doing this will ensure that these are planned for during the designing of the trials. In addition, the general research findings seem to suggest a need for involving different stakeholders including potential trial participants and the public in planning for post-trial care. Finally, since the implementation of post-trial care relied on ethical guidelines, the ethics authorities were found to be very key in the planning and implementation of post-trial care, by instituting and enforcing policies on this. The remaining sections in this chapter provide a detailed description of the views of research staff on post-trial care practice in HIV drug trials in Uganda.

8.3 Preparing trial participants

Research staff reported engaging in particular activities to prepare trial participants for the closure. The main goal of preparing trial participants was to: pass on relevant information about the closure, to provide guidance on how and where to seek post-trial care, and to address other concerns which arose during the time of trial closure. The main activities undertaken during preparation of the participants included: information giving, offering psychological support, and activities to address the attachment issues between trial participants and researchers, and peers. These issues are elaborated in the following sections.

8.3.1 Information giving

Preparing for trial closure required research staff to provide relevant information to the participants. This included information about post-trial care, guidance on where to go for care after trial closure and how to access required medications, and allaying anxiety associated to trial closure. Information about post-trial care was usually initiated during trial recruitment and often incorporated within the day today running of the trials. For example, during consent, trial participants were informed about trial closure by disclosing to them the planned period for the trial and any post-trial care plans such as where they would go for care after the trial, or how trial results would be provided. Such information was helpful in eliciting informed consent from participants. Joy explained how this is normally done.

Trial closure starts at the beginning of the study apparently. Because as we start the treatment of patients, we go through the screening, we go through the enrolment, we see them settle in, we prepare them or we tell them that there is time when the study will end so that as we start, as they settle in, they know that there is time and the trial will end. So, by the time we get to the closure, they are already into closure. (Joy, counsellor/health visitor/community mobiliser)

Although information giving on post-trial care was usually initiated during the informed consent process, staff stated that this continued throughout trial conduct. Some staff stated that this information was helpful in enabling participants to keep in mind the reality of trial closure and also to make appropriate arrangements on how to access post-trial care as Destiny explained.

... and even on these daily talks, we normally have health talks when they come in, we keep on reminding them. 'If you have been here for two years, it means you are remaining with one year. April next year we are going to exit you.' So we keep on telling them. So somehow they get to know, it is not like abrupt, 'today is end of the trial, you are going.' (Destiny, nurse)

The above data was congruent with the views of trial participants, who appreciated this approach for keeping them updated about the pending closure. However, such information was not usually intensive during trial conduct. Research staff reported that the intensive preparation for trial closure started on average three months to the planned closure, a period which marked off the trial closure phase as reflected on the Facilitated Transition model. Bernard demonstrated this point in the following quote.

The period (of preparing for trial closure) is inbuilt in our community engagement process, so I don't want to say three months before the trial ends or six months. It is inbuilt. [...] So our post-trial engagement does not start say, when we have seen the last volunteer, its inbuilt we share it, but the bridging activities that take us between when people are seen last for their trial participation and when the results are out, and what happens beyond the results are out is what I actually I would say begins three months before the end of the trial. (Bernard, community liaisons officer)

During the trial closure phase, participants were actively informed of the trial closure processes, received counselling to allay their anxieties about the closure, guided on possible options for post-trial care facilities, and any other information such as plans for dissemination of trial feedback was provided. Although such information varied in form and approach, it was particularly targeted at addressing the care needs of the participants which were likely to arise during the transition. These views are expressed in the quotes below.

Then of course, all the time we have to talk to the patients because some we know also they become a bit anxious, they have been with you for four years, may be for how many years, now somehow the end is coming, so you have to keep preparing them. (Jane, trial coordinator)

Basically counselling is part of it and it is one of the major issues because we would want to prepare them for post-trial time. So we do counsel them, we also provide, like I said we provide referral in case of need, we also go through with them what they think, or what they anticipate to be the challenges they are likely to face. (Bernard, community liaisons officer)

... we do prepare our patients or the participants in the trial both mentally i.e. psychologically and we do also prepare them for the new challenges ... (Alloy, trial coordinator/nurse)

Staff commented that early preparation through information giving was the best approach to address the majority of the post-trial care concerns of trial participants. For example, staff felt that when supported early, trial participants can actively embrace ways of addressing their financial needs and may not suffer the consequences of financial stress after trial exit as Gloria expressed.

I also think the way we can try and solve it (the financial challenge), is right from the beginning when we are recruiting these participants. To gradually keep telling them that when you finish your..., when the study comes to an end, they have to prepare and start

planning. There are many ways of saying it, I am saying it like that but it may not be acceptable to them but there are many ways of putting it. Gradually as we go through the study, so that by the end of the study, at the back of their mind, they have a plan like 'what will I do, how will I buy my opportunistic (infections) drugs,' although we encourage them that 'this will be given, but time will come when you have to do it yourself. (Gloria, nurse, Trial 1)

However, the above view seemed to be an alternative in the context of limited options for meeting the specific care needs of the participants. For example, as has been expressed in previous chapters, material and financial needs emerged as key concerns for participants, for which support was required. Many staff also felt that in addition to providing necessary information, other aspects of care could be incorporated in trial closure practice to support trial participants during trial closure as will be elaborated in the subsequent sections. Furthermore, research staff reported offering psychosocial support, to deal with stigma manifestations which were reported to be a problem among some participants during the closure, a finding also supported by the views of trial participants. The following section describes staff's views on this issue in more detail.

8.3.2 Dealing with HIV stigma

Stigma related concerns were reported to be among the issues which required support during trial closure. These concerns appeared to shape trial participants' choices of post-trial care facilities as shown in chapter six. Such issues were related to the change in the clinic settings, whereby research settings were usually private as opposed to the public facilities where the environment is more exposed. Staff reported providing stigma related support to trial participants during trial closure as expressed below.

Issues of social stigma, because some people say, 'you know people know that we have been with you now when we go back and they don't see us coming to you anymore, they will think either we became HIV infected or we didn't meet your study inclusion criteria.' So those are some of the issues that we discuss with them. (Bernard, community liaisons officer)

Some staff felt that the problem of HIV stigma needed to be addressed to facilitate coping and disclosure, and to enhance access to post-trial care. However, some reported that approaching this issue was challenging, as many participants could not explicitly express this as their concern as Favour noted.

I believe the other issue is stigma, they don't want to be seen at the nearby health centers. They think if they go to those centers they will be seen by village mates, family

members, and the rest of the other people who know them there. They prefer coming this side where no one knows them, where they believe no one will see them. That is another reason, but they hide it, they don't mention it. For them they hide behind the issue of no drugs. (Favour, counsellor/home visitor)

Data suggested that stigma manifestations were more likely to occur among those with limited HIV care experiences, an assumption clearly associated to findings from trial participants, where those with limited HIV care experiences tended to exhibit more HIV stigma tendencies than their counterparts. Research staff supported this view by noting that, people recruited in research with limited HIV specific care experience were more likely to exhibit HIV related stigma at trial closure compared to those with a longer experience.

Actually these naïve participants, stigma is at a high point, yea, because they have not been in care, yea because like for Trial 3, we have really got challenges when especially in time of recruitment we were forced, some participants would love to be close, you close the door, some participants would call you earlier that 'are there many people around,' because of the stigma associated with it. So, patients who have already been in trial (care), their stigma is low, and I think these patients who have just began care, it is much associated with those who are new on treatment, really the stigma is still up. (Alloy, trial coordinator/nurse)

It's mainly new people because like those ones on other studies like study P, for them they have been on drugs, so they are used to the system. Sometimes you find a patient has already disclosed to the entire family and may be to some of the friends. But these ones, them being new, they are just getting used to the condition. Sometimes we fish them from out, they have just tested, they have not yet come to terms with the condition, we start them on drugs, after one year we are exiting them and we are telling them to go back to the village. So that is why they feel like, 'aah, I would rather remain here, with the people who know my challenge.' (Favour, counsellor/home visitor)

The above data suggests a need for identifying people who are likely to experience HIV stigma and to support them accordingly. This concern may also apply to participants who acquire HIV during trial conduct. In addition to HIV stigma, other psychosocial concerns were identified during trial closure. For example, trial participants reporting feeling the loss of valued relationships with research staff and peers. Trial participants suggested mechanisms such as a longer engagement with these after trial exit, to enable them cope with the separation. Research staff also felt that participants required to be supported to deal with the separation from the important relationships, and their views on this issue are presented in the following section.

8.3.3 Dealing with attachment

Although many of the psychological problems reported during/after trial closure could be attributed to the losses associated to trial closure, and to the fears of seeking care in the public health care system, there was a likelihood that the bonds developed during research between researchers and peers also contributed to the emotional reactions. As earlier reported, participants expressed feelings of loss of staff and peer relationships which they considered important. Alloy also shared a related view by reporting that breaking the researcher-participant bond was a challenge for many trial participants.

May be the last challenge would be, the other challenge we have really experienced, these patients don't want to leave the trial, they feel all the time they come back, they come as if, you refer this person, but they feel it's you, they keep on coming to you, you know, as if you didn't refer the person, yea, they always come back, they don't feel like leaving. You say but we have already stopped, but then the person will always come back to you and you have to redirect again ... (Alloy, trial coordinator/nurse)

To specifically address the challenge of attachment and also allow for a gradual termination from trial services, staff reported engaging in activities which were meant to help in breaking the bonds within the researcher-participant relationships, and to also enhance overall coping to the closure. This was described as a 'weaning' process by some staff.

So we start preparing them psychologically because many of our participants get attached to us and they don't want to go away from this kind of care that we have been giving them. So we start preparing them before the really time of closure. (Nsubuga, clinician)

And I also, to make sure people are able to cope, yea we always have a wean off time when we know, when people have really settled back to where we found them before the study, so I know it is an obligation. (Destiny, nurse)

Weaning was assumed to be a helpful strategy for overcoming the negative impacts related to being abruptly discontinued from research care as expressed by trial participants in chapter six. Although the support provided was mainly psychological, some staff reported having some practical activities in relation to weaning. For example, some reported having a gathering with trial participants, a finding also supported by trial participants and from the documents. However, in general, activities related to weaning were not uniformly approached in all included trials. For example, as data from trial participants and the reviewed documents suggest, only Trial 1 engaged in a general gathering. Staff appeared to be in support of having a general get-together as a weaning

strategy, and recommended it to be adopted in HIV trial closure practice as Destiny suggested.

Yea, we can have like a participant meeting, we can meet and like have a party and then send them off, I think that is something we can do and something that can be planned for the studies, so that it is a really send off. Just like if you are leaving an organisation, they really have a send-off party, so that also could, you really see your friend off and it doesn't feel like when someone just disappears. (Destiny, nurse).

In relation to timing, some staff felt that the weaning process needed to go beyond trial closure into the post-trial phase, where trial related care would be gradually terminated, a view also shared by the participants. Although the actual timing for the weaning activities was contested among staff, many suggested that putting into consideration the individual factors of trial participants was necessary. For example, some felt this could go on until trial participants have settled in post-trial care, this being assessed on a case by case basis. Others suggested that weaning should be approached in consideration with other aspects of post-trial care such as provision of trial feedback, assuming that at this point, trial participants would have settled in post-trial care. Some quotes from staff on this are presented below.

First of all, I can't say the researchers or the donors should support these people forever, it is also impossible. May be what I can suggest is to extend sometime after exit, to extend for like a year as we are training them to get used to the system of being exited. [...] At least my suggestion is to extend a little, some little time for them to get used to the system to get exited, the system of being on their own. (Favour, counsellor/home visitor)

Trying to get into contact, trying to get back into contact with them, the whole issue of exiting participants and rolling them out of the trial is a continuous thing. And ideally it should end at the point where you give participants, you inform participants about the results of the trial, of the research that you are undertaking. (Nsubuga, clinician)

This data appears to suggest a need for post-trial follow-up as will be described later in this chapter. However, like other post-trial care activities, weaning had financial implications, which indicates a need for responsible authorities to consider this activity while planning for HIV trials.

8.4 Facilitating linkage to and continuity of care

Findings from chapter six suggested that trial participants experienced significant fears and difficulties during linkage to usual care facilities and these expressed a need to be

supported during the transition process. Research staff reported engaging in activities aimed at providing practical support to trial participants while linking to their post-trial care facilities. In addition, due to the need for continuity of care, and especially to avoid a 'drug holiday' during the transition, staff reported how a continuous supply of the trial medications was maintained during the transition and afterwards. Furthermore, although not practically implemented, staff strongly felt the need for financial/material support, to address the socio-economic needs of the participants after trial closure. These issues are presented in detail in the following sections.

8.4.1 Providing practical support

The need for continuity of care for the HIV positive trial participants required appropriate linkage to post-trial care facilities. Linkage to care was perceived as a researchers' responsibility by many staff, who also felt it was an important aspect of post-trial care in HIV trials as Destiny explained.

I don't know exactly, I don't have somewhere like I have read, but this is what I know as a researcher I am obliged to do. For instance, if I am carrying out a research, and then it comes to an end, I am supposed to know like for instance if this has been a care research, I am supposed to know if these people have gone back to their service care providers and if there is anything that came up during the study and I have..., for instance if I have been managing some conditions, I will make sure I refer them appropriately to where they can be handled properly. (Destiny, nurse)

In addition to recognising it as a researcher's obligation, some staff rationalised the need for appropriate linkage of trial participant to care as their 'duty of care'. Being health care providers, staff felt they were required to safeguard the health of the sick. Some felt that failure to show concern towards trial participants' continued access to care would appear uncaring and exploitative. Hence, the care responsibility emerged as one of the motivating factors for research staff to ensure appropriate linkage of trial participants to care as indicated below.

When we work with these participants, we don't need them just for the sake of getting research information from them, we are also concerned a lot about their care and so it should be a pre-requisite that as a researcher, I guarantee that after getting out of my care, this subject has gotten somebody to continue with their care. So it is so important, it isn't a matter of getting research information, the health of the subject, the health of the participant is supposed to be our concern. So, we should definitely be concerned in that area. (Nsubuga, clinician)

Whilst research staff showed concern towards the need for appropriate linkage of participants to care as evident in the above quotes, the approaches used did not seem satisfactory to both the research staff and the trial participants as earlier indicated. For example, the official approach of linking participants to post-trial care was through referral, where participants were offered with a referral letter to deliver to their post-trial care facilities. This approach was clearly reflected in the reviewed documents and also confirmed by trial participants. Research staff also affirmed to this approach as stated below.

I mentioned about a referral form. So the linkage is providing them with a referral form with the details of their clinical picture which they deliver to the service provider and then it gets filed in their records the other side. (Ivan, trial coordinator)

Practically it ends at giving them referral letters, though usually on the referral letter we are giving, we have contacts, we put our contacts there as well in case the health giver the other side may need more information about what we have written. (Lydia, clinician)

The referral letter was assumed to provide relevant and sufficient details about trial participants as shown in the reviewed documents. This was done to ensure that the clinicians in the referral care facilities were able to understand the clinical picture and other details about the participants, to be able to take on their care. However, this approach implied that trial participants held much of the responsibility of ensuring that they reached the care facilities. As expressed earlier, this approach exposed trial participants to some difficulties while establishing into post-trial care and also raises concerns of confirmation of linkage to care. When asked how they confirmed that participants reported to their post-trial care facilities, staff gave unclear views. For example, some mentioned that they merely assumed participants reached, some would take responsibility to call the care facilities, others relied on receiving feedback from trial participants, while others relied on receiving feedback from the facility staff, either through returning a 'return-slip' provided on the referral form, or through telephone calls. Some views on these issues are presented in the quotes below.

But those who go to other sites, to be honest, there is no way..., we don't follow them up. We give them those exit reports, and we stop there.; Actually we stop there hoping that they will go and present those reports to wherever they are going. (Favour, counsellor/home visitor)

We use to have telephone contacts, because you know these are institutions we were working with, so you would call, because you knew the physician's number. So we would

call them, you say 'I have sent you so and so, please when they come call me.' But most times of course they wouldn't call, we would still call back, to make sure that they have received this patient and the referral form because this is where continuity (of care) will begin. (Jane, trial coordinator)

The above data reveal how confirmation of linkage to care remained ambiguous, and where this was done, it largely based on individual initiatives. Despite some trials emphasizing the need for, and offering guidelines on confirming linkage to care as documents indicated, actual practice of this remained a challenge. This seems to highlight a gap between post-trial regulation and actual practice. However, although these findings seem to expose a lack of a streamlined approach to linkage to care, they also appear to suggest that the need for, and approach to linkage to care could depend on individual participant circumstances. For example, data from trial participants showed that those who returned to their pre-trial care facilities or those who remained at facilities close to research experienced less challenges compared to others. Hence such participants may not require a very rigorous facilitation approach while linking to post-trial care. Research staff also appeared to agree with this view as the following quote suggests.

I must admit since we were co-sharing the care of the participants (with pre-trial care facilities), when we gave them the referrals, we assumed they took them. We didn't go back to the service provider, to check that actually they went back, but since we were..., we are sure they went back because they continued to get their ART and all the other services from there, yes. (Ivan, trial coordinator)

By contrast to the above, participants who are completely detached from their mother facilities, those with ongoing health problems, and those going to new care facilities may require a more facilitated linkage procedure. As suggested by trial participants, a more facilitated linkage, which could involve physical handover of the participants to their facilities was proposed. In addition to assisting trial participants to overcome the likely challenges associated to registration in care, a more facilitated linkage would also be helpful for proper handing over of the participants to health care providers. This would be particularly important for those with complex health problems which may not be adequately explained in the referral, a concern which was also expressed by trial participants. Research staff supported the notion of a more facilitated linkage for some groups of participants as Favour explained.

For example, these patients we work with, some have challenges that we don't write in the exit reports, for example a patient is having psychosocial issues, a patient is having

adherence issues, a patient is having may be some health issues or medical issues, that would be discussed doctor to doctor. So I believe it would be good when we move, we see those health workers, we discuss with them on the way forward of the patient other than giving them exit reports that don't explain more (Favour, counsellor/home visitor)

Although some concerns of linkage to care could be addressed by providing a holistic report to facilities, the above account suggests that physical handover would serve a better purpose. Other staff also supported this view, highlighting its role in enabling the transition process. Moreover, in addition to confirming linkage to care, some staff felt this approach would also be helpful in establishing whether trial participants are receiving adequate and appropriate HIV services. Alloy, a trial coordinator reported a case (not from the current trial), where a post-trial participant was found to be receiving a wrong regimen and felt this would be avoided if participants were physically linked to care.

The above data suggest the need for more facilitation during linkage to post-trial care. However, similar to other aspects of post-trial care, such an approach is likely to involve costs, highlighting the need for planning. In addition, since the process of linkage to care highly relates to staff from post-trial facilities, it was suggested that involving them in the process would further enhance the linkage process. Research staff suggested that involving stakeholders early in the planning of trial closure would improve the collaboration between research and the public care facilities, and would improve the transition journey for the participants as Alloy remarked.

So bringing people on board where we are referring is also important, which has not been there, we do plan other things, we do plan the end of trial as researchers this side, and it is only at the time of exit that we do give them this letter as an introduction, these people are unaware of what else has been happening, we really need to put these people on board before closure. (Alloy, trial coordinator/nurse)

In addition to the benefits of linkage to care, some staff felt involving facility staff in the transition process would be a good indication to the participants that both service providers are working as a team and would possibly eliminate the biases some participants could have about the public care facilities. This would possibly eliminate the fears participants experience during trial closure as shown in previous chapters. Some staff also suggested the need for research institutions to keep potential post-trial facilities updated about the progress of the trials. This would be helpful for them to prepare to receive the participants when trials close, instead of them being taken by surprise as Destiny commented.

Yea also like the other important thing that we always, also could help is may be to make sure that the research organisation keeps in touch with the service providers, updating them on the progress of the study, how the trial participants are doing [...] so that the service provider is also prepared. For instance, Trial 2 had 1200 people taken away from these service providers. So, telling all these 1200 people 'you are going back,' it is an influx to the service providers. (Destiny, nurse, Trial 2)

Some staff also felt that improving service delivery in the public facilities would alleviate some fears among participants and enable linkage to care a more successful and good experience for them. In addition, staff felt the need for public healthcare staff to be more receptive to trial participants who are returning to care. These opinions were also shared by the participants as discussed in the previous chapters.

8.4.2 Providing trial drugs

Continuity of care for HIV positive trial participants was considered to be very crucial and many research staff acknowledged this as their prime responsibility. This aspect of care was also reflected in the reviewed documents, further indicating its relevance in current HIV research practice. To facilitate continuity of care, research staff reported ensuring a continued supply of trial medications for participants during the transition and afterwards. During trial exit, participants were provided with a buffer stock of trial medications, to eliminate any possibility of skipping medication doses during the time of linking to post-trial care. This was especially relevant in maintaining the chain of treatment which is essential in HIV disease management. Nsubuga stated how this was implemented.

...the other thing we do is for research projects where we have been giving participants drugs that they take for example as prophylaxis, at the point of exit, we give them enough drug that can take them for a relatively long period so that even as they try to establish continuity of care they still have drugs with them. (Nsubuga, clinician)

Trial participants affirmed receipt of a buffer stock of trial medications which they found helpful during the transition. Normally, participants received a stock of three months, although special considerations were made depending on individual circumstances. For example, individuals who felt could not report to their care institutions immediately or those the researchers assessed and had special needs such adherence problems could be given a special consideration. In addition to the buffer stock, the need for continuity of care required sustained provision of the trial regimen post-trial. Research staff reported how this was achieved. For example, staff ensured that they advised trial participants

regarding the facilities where such medications were available. This was quite easy for first line HIV treatments and prophylactic medications, since these are widely available in most of the Ugandan public healthcare facilities. However, providing second line medications was more challenging as some were not readily available in the public facilities. For example, in Trial 1 which involved second line HIV treatments, one drug was not available in the public sector, and those who required it continued accessing this from the research site as explained below.

Like, I have been part of two major studies, three, aah one of them was Trial 1, they were using drugs that are not readily available in this country like drug R, and they are still giving them the drugs (at the research facility) up to now, which is like about eight months since the trial was exited. (Wambo, clinician)

You see we were using a drug which was not available that time in Uganda, drug R. So the study said, because they wouldn't just stop giving drugs. [...]... the funders kept sending us the drug, for only those patients who were on that drug because it was not available in Uganda at that time. (Jane, Trial coordinator)

The above data suggest the commitment researchers have to ensure continuity of care, by providing a trial regimen to trial participants. As indicated in the reviewed documents, this commitment sometimes involved donors/funders continuing to supply the drug in question. In other instances, maintaining the supply of the trial regimen required referring trial participants to other centers where such drugs could be available. This sometimes called for the participation of other stakeholders such as the government as data from the documents showed. These findings indicate that although provision of first line regimens may not be a challenge in post-trial care practice in Uganda, this could be for the second or third line regimens.

Similar to other aspects of post-trial care, despite this appearing a major focus in HIV research practice, it appears the mandate and the approach to provision of a trial regimen was not uniform to all trials. This could be attributed to a lack of detailed or explicit guidelines on the issue, and could result into irregularities in its implementation. For example, although no trial participant reported failing to receive the trial regimen following exit in the included trials, some staff reported instances of when this obligation was not fulfilled in previous trials. One staff also reported an incident where a trial participant was given a different regimen upon leaving research. In this case, the problem appeared to be attributed to a communication gap or a lack of collaboration between researchers and the public facility workers.

... there were patients who were on second line but because there was some ignorance, some lady gave birth and then she was put back on first line,... (Alloy, trial coordinator/nurse)

This finding suggests the need for proper linkage of trial participants to post-trial care, confirmation of continuity of the right treatments, collaboration with stakeholders, and post-trial follow-up care as will be elaborated later in this chapter. In addition, the data appears to suggest the need for the improvement of public service delivery, by ensuring that healthcare staff in these facilities are knowledgeable of the current approaches in HIV management. Some staff also felt that if the public health care facilities are well equipped with necessary HIV treatments, it would further enhance continuity of care for trial participants, who would otherwise find access to appropriate care difficult due to socio-economic barriers. This would also improve their overall post-trial care experiences.

My request or appeal is, we argue the government that they really equip those other health centre IVs with nearly all the drugs that are being used to all other hospitals for easy access for our clients. (Prosy, counsellor)

The other thing is if drugs, especially drugs which are not available could be put in those other centres, it could I think help them so that they don't have to feel like they have to stay in a place against their will which is not right. (Wambo, clinician)

Overall, the data presented in this section has suggested that researchers were committed to ensuring provision and continuity of a trial regimen. Although the above data mainly applies to routine HIV mediations, research staff also felt government institutions need to ensure a supply of other medications, especially for treating HIV related infections which was identified as a major challenge for participants with ongoing health concerns, and who were generally economically disadvantaged. Trial participants also expressed these concerns and suggested financial and material support following trial exit, in order to facilitate access to these services. In spite of many staff contesting the idea of providing financial or material support on the basis of research ethics, others strongly recommended it on a moral basis. The views of research staff on this issue are presented in detail in the following section.

8.4.3 Financial facilitation and support

Financial and material support emerged as an important post-trial care need in this research. Views from trial participants suggested a need for financial and sometimes material facilitation to meet their increased social-economic needs which arose after trial

closure. However, although a number of research staff also supported this view, others rejected it. For those who were in support, the reasons and the form of the support also appeared to vary. For example, while some argued such support to be an appreciation or compensation for trial participation, others appeared to view it as a supportive measure to address the economic needs of participants in a low income setting as expressed below.

Let them know that they are doing research in resource limited centres in poor countries, i.e. in Africa and in Uganda in particular. Know that I am going to get a participant from deep in the community, these participants have social problems, may be is a total orphan, may be is an old lady who cannot earn even a dollar a day. (Salif, nurse)

... in most cases these participants they come when they are in a poor shape, so whenever they enter the study with the little token they get from the study, it empowers them to come to a certain level. So when the research is coming to exiting them, it becomes also very difficult for them to cope up with the economic situation in which we are leaving. (Mubiru, nurse)

However, although the above quotes suggest the need for support on a moral basis, the element of compensation/appreciation could not be isolated from the arguments. For example, Mubiru expanded on his reasons for the need for financial support, basing on the participants' contributions to research.

So please, let these donors also think, what will take place after the research has ended. Let them think of the participants. I always compare this with Jesus Christ; these participants are giving in their blood, Jesus also saved the whole world with his blood, so they should not let the blood of our people here go for free. Let them also try to give them some kind of appreciation at the end of the research [...] so at least let them think of something to appreciate the participant. (Mubiru, nurse)

Similarly, Favour elaborated on the need for financial support, which was also closely linked to the need for compensation. Although Favour argued researchers to be sensitive to the contributions of the participants, she also stated that this could be approached on a need by need basis. This further highlights the need for a flexible approach by which this issue could be approached as expressed in the quote below.

Number one, I suggest that these researchers or donors should emphasize on..., the point should not be up to them, for example for them they come with their studies to benefit them as sponsors or researchers, but these patients, little they are considered, they are considered less. For them they give in a lot, they give in samples, they give in time, they

give in everything, but majorly they don't benefit from that. At least after the research, let them be considerate, as in be supported if that person needs support, they are people who don't need support for them they are being taken care of, kind of being given drugs, period. But there are people who surely need care. They come to us, they tell us how they are badly off and all that, but poor we, we have no way we can help them. So me my appeal to researchers is to always at the end of the study to extend some help to those people, because they give in a lot. (Favour, counsellor/home visitor)

Notwithstanding, despite many research staff supporting the idea for compensation or appreciation for research participation, overall, there were varying views expressed by the staff on this issue. The difference in the opinions mainly based on the ethical Vis-à-vis the moral reasoning of the staff. For example, while many supported the idea, some strongly opposed the view of providing support or compensation in monetary terms, as this was attributed to the risk of coercion of trial participants in future research or the current research, if such benefits were disclosed during the informed consent process. Benard shared his view on this issue.

So to me I think the issue of giving a token which ever form it is as long as it does not impact on people's judgement for future research, because we don't want to use material inducements, and then we say communities are willing to participate when actually they are being driven by the desire to get the inducements, the big token that researchers give at the end of their participation. So I think anything reasonable that expresses gratitude for people's participation in biomedical research is a welcome gesture. (Benard, community liaisons officer)

In relation to the above views, staff gave examples of how participants had been appreciated in previous trials. For example, staff reported providing small material gifts such as clothes or a certificate of appreciation to the participants. Such gifts also appeared to be provided on the convenience of the researchers and especially if these fitted within the existing budgets. A similar approach was also adopted in Trial 2, where participants were provided with an appreciation in form of a certificate as data from the documents indicated.

Interestingly, there are staff who did not even recognise the need for trial participants to be compensated or appreciated. Even in situations which participants and some staff provided as reasons for the need for financial benefits, some staff strongly opposed these. For example, while many felt there was need for compensation for the time lost and other inconveniences experienced during trial participation, others still felt it was not an ethical responsibility or even a necessity. In addition, while some based on the poor socio-economic status of the participants to support the need for financial support,

others used the same reasons for arguing against it. Mark defended the position of why financial benefits would even be more unethical in low income contexts.

Interviewer: *How about the time lost for participants, would it be necessary to compensate them for it?*

Respondent: *For me it would be undue influence because the reason the patient will participate..., when you are dealing with patients who are in a poor background, really, really poor below poverty line and you begin talking to them about money which they will get in a study because of this, the reasons they will participate in the study will not be... (Mark, clinician)*

In supporting further why trial participants may not need compensation, Mark felt that some groups of trial participants may not necessitate compensation. For example, for those who join research while ill, they would still require treatment and these would still spend time at healthcare facilities. In such cases, these would not require compensation for time which they would all the same spend elsewhere.

The other thing which I would..., like in HIV clinical trials, I would disagree when the patient's time is being taken is because, in reference to our particular trial is that even if they were not to be here, they would still have to go for care somewhere, and it's not like we are doing them a favor to put them in a study so much, we are also offering them the standard of care which they would actually access somewhere else. So you would not pay..., the government would not pay them to go and receive treatment, they would also be not fair for the government to give them money to receive treatment. (Mark, clinician)

Such views seem to undermine the rights of trial participants and could imply a lack of awareness of the ethical principles among researchers. The view of arguing against financial benefits seemed to be more held by clinicians as opposed to nurses and counsellors. This can be attributed to their training backgrounds, where medicine tends to emphasise more of a rule based (ethics) approach rather than a moral (care) approach to service delivery, which is more emphasised in nursing. However, although the possibility of financial benefits inducing coercion is possible especially among poor communities, drawing from the previous chapters, it is apparent that quality care was central to the need for trial participation instead of other benefits.

To address the financial needs of trial participants, it was relevant that a financial assessment be carried out as also suggested by trial participants. This would be helpful as it would enable an approach based on a need by need basis as suggested above. One staff reported undertaking financial assessments, but reported being disappointed as this

often ended at identifying the financial needs and not addressing them. This resulted into a sense of frustration as expressed below.

There is usually a form we fill, as in to assess the social economic status but we just fill, they power out to us, they tell us how they are staying in grass thatched houses, they have nothing they are earning, as in they don't have any source of income, they are really, really poor, and they tell us, but to be honest, there is nothing done. We show them we were just asking them for our own consumption we are doing nothing, and yet they really need help, more especially that we are exiting them. (Favour, Counsellor/home visitor)

As the data indicate, staff who advocated for financial support felt this would be a good strategy for empowering the vulnerable groups of trial participants, to be able to meet their socio-economic needs following trial exit. Many suggestions were made in which trial participants could be empowered. For example, some staff suggested that participants could be provided with income generating activities, and also trained on financial management issues. To achieve these, there was a need for financial provisions from research. However, even with no funds available, some staff strongly felt financial support could be achieved. For example, staff recommended collaboration with other stakeholders such as local institutions and community groups which can provide financial support to the participants. The quotes below reflect these views.

It may not be money as per se, but I think we look at information and that goes along with training. We can organise a training like once or twice, just to help these people settle in, and then you follow them up, to help these people cope, to help these people do something that will keep them moving. Move around, educate them. You can wake up in the morning go to the garden, go to churches, get involved in community arrangements, they have their arrangements there. (Joy, counsellor)

But having said that, we could also link up with other people; we have SACCOs (Savings And Credit Co-operatives) in these communities, can we encourage our volunteers to save with the SACCOs and make sure that while they participate in the study, even after they have participated in these studies, they can still have something that can keep them in their lives. (Bernard, community liaisons officer)

The above data suggest that although financial support may be contested in research in low income settings due to its ethical implications, many researchers consider it necessary. The data also suggest that in the current HIV research practice, the need for compensation for trial participation is somewhat overlooked. Indeed, this issue was not a focus in the reviewed documents and unlike other aspects of care which research staff explicitly acknowledged as their obligation, compensation for trial participation was not

regarded as such. Instead, the majority of staff tended to advocate for this on a humanitarian point of view. Some staff felt compensation in monetary terms needs to be recognised as an ethical responsibility in research practice, and be provided for during designing of the trials as Salif proposed.

Now my suggestion would be, if a protocol is coming on board, and the researchers are to review that protocol let them read in between lines and on the footnotes, if those points are there, what psycho-social support are they going to give to these patients after their trials? For instance, if they can say that after the trial, for those who are not earning anything a day, for instance those who do not have jobs, at least they can give like \$100 as capital for that participant to go and set off life. For those who are already working, well and good. Let them be appreciated in one way or another. But those who are not working, or they don't have any income, they don't have any social support, or financial support, they are given some income capital to start off something. (Salif, nurse)

8.5 Follow-up

Previous findings revealed that trial participants underwent multiple, and sometimes complex problems during the post-trial period and required support from a number of individuals such as research staff, peers, the family and other stakeholders. The support provided was mainly psychosocial, and was helpful in addressing some of the emotional and/or practical needs of the participants. Some participants also reported being followed up by researchers, for example to change their treatments, which can indicate an aspect of monitoring. Although to a minimal level, research staff also confirmed engaging in some of the above activities to support trial participants after exit from the trials. In addition, provision of trial feedback arose as a concern among trial participants, and although this had not been implemented in any of the included trials by the time of the interviews, research staff confirmed this as an activity planned for and practiced in their institutions. The views of research staff on these issues are presented in more detail in the following sections.

8.5.1 Ongoing support and monitoring

The majority of research staff recognised the need for post-trial follow-up care, support and monitoring of the participants and acknowledged it as a researchers' responsibility. Staff identified a number of reasons why caring for trial participants was essential during the post-trial period. As suggested from previous data, establishing linkage to care and ensuring continuity of HIV treatment for the participants were significant indications for post-trial follow-up. These issues were elaborated on by research staff. For example, many felt post-trial follow-up was necessary to ensure trial participants have been linked to and settled in care. Charlotte represented this view.

It is really very important though we don't actively do it, post follow-up. Because when they go back to their mother clinics, a lot of things change, it is like transitioning. So if you are transitioning, you need to be followed up until you settle in properly. Usually the things which are not there, the tests are not done, so they are not, sometimes they are done but they are not according, like they are not done like when they were in the research study. So they may not understand all these things that are changing though you have prepared them for this time. So the post (trial) follow-up is very important if the funds are there. (Charlotte, counsellor/home visitor)

Some staff felt post-trial follow-up would be helpful in offering ongoing psychosocial support to address some of the issues which arose after trial closure and to monitor the general wellbeing of trial participants.

I believe we are supposed to be following them up, to see how they are coping up, to see the challenges they are facing, and like these Trial 3 patients that we recruited with low CD4s, to find out may be if they have increased, they are rising up, to see generally how they are improving. (Favour, Counsellor/home visitor)

However, the need to monitor for and manage possible side effects from trial interventions emerged as a key indication for post-trial follow-up care. Many staff felt the need to monitor for possible side effects could not possibly be ignored in research practice, since this directly related to their ethical obligations. Particular concerns were raised in relation to the possibility of side effects arising after trial closure, of which researchers could not recognise during trial conduct. This concern is represented in the quotes below.

...there is a possibility of a participant getting an adverse event even after they have received interventional product, there should be an arrangement that these participants can still be followed up. The ideal thing would have been that a participant is totally exited at the point when you don't expect any more adverse events. (Nsubuga, clinician)

It makes a lot of sense to follow them up because for some drugs, the reactions or side effects may come a little later than within the defined study period. So it is important to follow them up and see if anything came up that would still be associated with the drugs, but it is not done. At least we don't do it as an institution. (Wambo, clinician)

And then if anything that comes up, for instance if you are carrying out a research and may be something comes up after the study, I know it is my obligation to further assess and then I have to know if it is because of the participation in the study, and then settle anything that really comes up. (Destiny, nurse)

The above accounts indicate the concerns of research about the safety of the participants even after trial closure. Although some information on this issue was reflected in the documents, this did not clearly imply follow-up or monitoring of the participants after trial exit. The need for follow-up was particularly relevant since research staff felt it was impossible to rule out completely when/if side effects related to trial interventions could occur. This concern also appears to be linked to the ethical obligation of ensuring the safety of research participants, which is a researchers' responsibility. In addition, some staff felt post-trial follow-up and monitoring was required for maintaining the integrity of the research, a concern which trial participants also raised. For example, if deaths occurred among post-trial participants, it would be difficult to clearly establish whether such deaths are related to the trial interventions or not. For some trials, this could have implications on trial outcomes. In addition, some staff felt that post-trial follow-up would be advantageous in future research, by recognising the importance of maintaining relationships between researchers and post-trial participants (or the participating communities), a view also shared by some trial participants.

Despite the great need for post-trial follow-up expressed by the staff, there were contentions regarding the time/form of the follow-up. Unlike trial participants who were suggesting follow-up to take relatively longer periods of time, research staff acknowledged the difficulties in implementing such an activity, putting into consideration resource implications such as time and finances. The majority of staff reflected these concerns while proposing the possible length of the follow-up period as shown below.

Generally linkage to care is a challenge and the follow-up, still you wouldn't follow-up someone for so long. [...]...usually, follow-up is done after say 30 days after the study has exited, there is that extra follow-up that may be done probably at 90 days, but continually it poses a challenge especially when finances have to be incurred. (Elhana, nurse)

I think six months would do, an extra six months after the trial. Because you know it's about feasibility, you can say something but which is not practical... (Wambo, clinician)

I think as it may have cost implications, I think I would think within the first 6 months after exit... (Alloy, trial coordinator/nurse)

On the other hand, similar to suggestions on weaning, some staff felt the follow-up period could be determined by the general progress of the trial. For example, follow-up could continue for as long as trial outcomes have not been conclusively determined

and/or disseminated to the participants. Despite the different views however, on average, follow-up was proposed to continue for 12 months following trial closure as shown in the quotes below.

Probably for a year, for a year. (Charlotte, counsellor/home visitor)

One year (of follow-up) would be ok, but I again it would depend on how the person is getting on. It can be either slightly more, or it could be less if someone is stable. But one year would be ok. (Prosy, counsellor)

Actually, if it were possible, it is post-trial, it would be better that may be you know what is happening after a year. You know for a year at least you know... (Jane, trial coordinator)

I would recommend at least one year. Like someone can say 'come back after six months, and then after one year.' So like you schedule to have people like twice after the exit, I don't think that will be too much. (Destiny, nurse)

Notwithstanding, some staff suggested that individual trial characteristics could be considered while determining the timing for follow-up. Since different trials could pose different risks, some felt it would be irrational to generalise follow-up care to all trials. Assessing for possible risks for a given trial would thus be necessary before determining the need for, and duration of the follow-up as suggested below.

I think you can't generalise that question because there are different types of trials looking at different objectives. There are trials at different phases. If a trial that is ending is a phase one trial, probably phase one or phase two, a longer follow-up would be necessary possibly. If it is a phase three trial, usually most of the adverse experiences must have been observed in the animal studies in the phase one and then in phase two, I wouldn't think it would be applicable to make longer follow-ups when the trial has closed. If it is a phase four that is a post marketing trial, well it could be also designed for a particular period and after that I wouldn't think it would be necessary. So the post-trial follow-up I think would be really important in phase one and to a moderate extent phase two depending on the investigational product. (Ivan, trial coordinator)

In addition, there were special conditions which appeared to demand for special considerations for post-trial follow-up care. These were mainly individual participant factors. For example, individuals who were ill or experienced special conditions such as pregnancy could demand for a longer period of follow-up until their conditions are resolved. These considerations are also reflected in the reviewed documents as earlier reported. However, since the data suggests identifying such issues before trial exit,

recognising these after trial closure may be difficult or even impossible. One staff recognised that it was quite difficult to determine the long term effects of trial interventions, for example in children born during the trial, which may not show up until after the child is about five years of age. Another staff expressed a concern in case the identified problems were not resolved within a reasonable period. This concern closely related to long term conditions which can arise from trial interventions. Handling such issues would indeed pose ethical dilemmas to researchers as implied in the quote below.

I think they will try to probably manage this patient until recovery; if recovery is possible or recovery is expected. Because even renal failure can come as a result of an HIV drug, but with renal failure, recovery is not so much expected. So even then, you are looking at telling someone to follow-up a patient for up to when? You know, you don't know how long this would take. So they can follow them up to a particular extent but I still feel even if they said six months it would end, if they said a year it would still end. You know most of our patients, what disturbs us like I said is the poor health system and the poverty levels are so high, because if you stopped a treatment that a patient can take up, that is not a problem. But you are going to stop a treatment that a patient cannot take up and the healthcare system cannot offer. So, you know, and even if you said that the research would take it on, but for how long? Can it be for life? (Wambo, clinician)

With the enthusiasm shown about the need and rationale for post-trial follow-up, it is surprising that this was not a common practice in all included trials. Basing on the data from trial participants and also from research staff, there was very minimal follow-up/care done after participants were exited from the trials. The reasons for this trend could be blamed on a number of factors, however, similar to other important aspects of post-trial care which were not currently being implemented; this was largely attributed to the lack of a robust focus on the issue. Although there were guidelines that appeared to indicate the need for post-trial follow-up as the documents showed, these seemed quite unspecific on the approach and form of the follow-up. Surprisingly, unlike trial participants who reported some instances of post-trial follow-up, there were very minimal reported by the research staff. Some staff shared their views on the current post-trial follow-up practice as shown below.

Then the responsibility of following them up, actually we have never thought about it. We never thought about it and we just believe that they go, there is nothing done about it, because we never thought about it, we never think that someone can sit back and fails to report to care. (Favour, counsellor/home visitor)

We have not always done this (post-trial follow-up). Well inside me I feel we probably should have, but we have not always done this and I feel it is a very important component

that we should integrate in our research projects to ensure that even as participant have been exited, they are still continuing to receive the appropriate care that they need. So we have not always done this, but I feel there is a need to always do it. (Nsubuga, clinician)

Despite trial participants reporting being followed-up, the data above suggests that research staff had no formal follow-up activities done in the current trials. For the few staff who reported engaging in post-trial follow-up care, this was mainly in reference to previous trials, and thus reporting on previous experiences rather than their experiences/practices in the current trials. Moreover, even in the previous experiences, there was no report of such an activity being actively or systematically planned for. This trend points to a gap in HIV post-trial care practice.

In defending the current practice, some staff explained how 'research doors remained open' for the participants to come in at any time when they wished. Although this information appeared congruent with what some participants reported, it was not consistent to all trials. Moreover, as previously explained, this approach raises concerns of reliability in terms of identifying and addressing the care needs of the participants, since follow-up would mainly depend on the initiative of the participants who could have various limitations. On the other hand, other staff tried to rationalise the lack of follow-up care on the assumption that other partners/stakeholders implemented it. For example, community HIV groups were assumed to play a role in offering post-trial follow-up care and support to the participants. While such an approach could be reasonable, it can raise concerns of reliability of the care, depending on the specific needs of the participants and/or the capacity of these people to address such needs. For example, such groups could possibly address the psychosocial needs, but may not be capable of identifying and managing health related complications.

Overall, these findings expose a mismatch between a need for post-trial follow-up care expressed by trial participants and researchers, and the current practice. Research staff attributed this mismatch to a number of factors, which seem to hinder the implementation of post-trial care in general. These factors related mainly to administrative issues in HIV research in general. As earlier stated, post-trial follow-up activities would require financial costs. Research staff commented how, even with good intentions, various limitations (such as a lack of availability of staff for post-trial care and resource constraints both in research and the public healthcare facilities) could obstruct the implementation of post-trial follow-up care. These findings suggest that the implementation of post-trial follow-up care requires advance planning and preparation.

However, many staff noted that most trials do not consider this aspect in their budgets, which makes it difficult to be incorporated later.

Normally as we have stated before, at least researches they come with their budget with strings attached to it. So when it has ended, it has ended. (Mubiru, Nurse)

The reason as to why it is not done is because the sponsors facilitate the study up to the date of exit, we stop there. (Favour, Counsellor/home visitor)

And then, the other thing we have to put into mind is when you are budgeting, you have budgeted for the study up to the exit, up to the closure. So you don't have more funds to cater for people after this time, may be even the staff have been employed up to that time. All these things keep, really tie us. [...] So even if you wanted, really you can't. (Destiny, nurse)

Similar to trial participants, many staff felt the post-trial phase required recognition as an important phase of the overall research process, and as such plans for post-trial follow-up care should be instituted during trial development. Although the responsibility to plan for post-trial follow-up care largely depended on research administrators as earlier suggested, similar to other post-trial care activities, many staff felt that ethical authorities could play an important role. For example, staff felt if this is made a standard requirement for all trials, it could be even easier for the investigators to reflect it in their budgets with limited criticism from their funders. The quotes below elaborate on this suggestion.

So I would recommend that it is put into policy that every trial conducted, especially clinical trials conducted, they should do a post-trial assessment to know how their patients are doing. (Alloy, trial coordinator/nurse)

If it is an obligation or if it is a policy of an institution, then they can add it (post-trial follow-up) on the budget; it can be added onto the budget and say 'for us we do this, if it is a policy of an institution. (Jane, trial coordinator)

To address some of the post-trial care needs of the participants, research staff also suggested the need to involve other stakeholders. For example, some suggested that monitoring for possible side effects could be done by staff from post-trial facilities, in collaboration with researchers. However, even if such an initiative could be considered helpful and cost effective to researchers, as earlier stated, it could have some setbacks. For example, since the public facility staff may not be very knowledgeable about the specific issues related to trial participants and may not even be well equipped to identify

or manage the possible effects resulting from trial interventions, this could present challenges on the reliability of their care. Additionally, placing such a responsibility on these facilities may impose a financial burden on them as Wambo explained.

*I think the cost implications wouldn't be major because if you are just calling another institution, and you are like 'what happened to our patient', probably it wouldn't be a lot. But probably the cost implications would be in institution that is following up, because probably you would request them to do tests at a rate that is not the normal standard rate, still investigating these drugs, because when you are investigating drugs, probably you check the kidneys, the liver, a little more often than probably the normal standard of care is. So the cost implication would come in the extra monitoring that would be required especially if you are still looking for anything that would come as a result of the drugs.
(Wambo, clinician)*

The above concerns emphasise the need for adequate planning and active involvement of researchers in the post-trial follow-up process. One staff also commented that some collaborators may require financial facilitation, for example, to meet their transport costs while supporting trial participants. These initiatives could possibly reduce on the need and length for post-trial follow-up care by researchers, although may still require costs from them. Overall, many research staff showed enthusiasm in seeing new policies being established/implemented on post-trial follow-up care in HIV research in Uganda. Some wondered why such an important aspect of HIV clinical research had been ignored all this while. Ivan, a trial coordinator expressed how this type of research was really timely. Similarly, Bernard, a community liaisons officer expressed eagerness to see the findings of this research disseminated to relevant stakeholders and highly anticipated new policies coming in place on post-trial follow-up care. Indeed, Benard's account below appears to summarise the core of the research staff's views on post-trial follow-up care.

So I would ask you to share this report with us. And not only with us the foot soldiers I must say, but with our top management because it has cost implications in terms of how we design, conduct, research and also handle post-trial issues. My imagination is time might come when the review boards that approve these studies, the National Council for Science and Technology will now start asking critical questions, 'so you have this protocol, your study period is two years, so what happens after the two years? Can you provide for that, do you have an inbuilt system where people are going to be prepared as time will come and they exit the study. So what happens when they exit the study?' So some of those critical issues will actually go a long way in ensuring that we conduct research in a more ethical way. We do not use people and damp them; we continue to work with them even beyond their participation in the clinical trials. (Bernard, Community liaisons officer)

8.5.2 Dissemination of trial feedback

The need to receive both individual and the general trial feedback was one of main concerns expressed by trial participants as shown in chapter six above. The reviewed documents also appeared to indicate provision of trial feedback as a major focus in current HIV research practice in Uganda. Unlike some aspects of post-trial care, information regarding the plan for provision of trial feedback was disseminated to trial participants during the informed consent process. There was also a general recognition among research staff of the need for dissemination of trial feedback, and the majority acknowledged it as an obligation.

Our obligation as researchers at the exit of a trial, we are supposed to disseminate the findings after the trial ... (Anne, nurse)

For every trial really, for every research, we owe them results and outcomes of the research as participants. (Lydia, clinician)

I still have the obligation of delivering results to all participants which I am still committed and trying to see, get the date when we can call them and we share the results. (Ivan, trial coordinator)

Yes, it is our responsibility to give results. [...] ... it is our obligation and even it is budgeted for, dissemination, we have to disseminate results and we do that. (Destiny, nurse)

Although data indicated that trial feedback had not been disseminated by the time of the interviews in all included trials, plans were underway to implement this. Many staff reported how this activity is implemented in their practice by explaining their plans for providing feedback in the current trials, or their experiences from previous trials.

We also promised them that when the trial results are out, we shall inform the participants about the outcomes of the trial ... (Ivan, trial coordinator)

Yea, we do it, we call them, we call them and disseminate the information. (Jane, trial coordinator)

And also the results, we ensure that our patients at least get to know what came out of their participation in a particular research. (Wambo, clinician)

In addition to being a right for the participants, some staff felt that providing trial feedback was recognition of the efforts of those who participated in research. Some staff

also acknowledged the role trial feedback could play in empowering trial participants in handling their health. For example, knowing trial results could enable them to dispel some misconceptions related to the trial intervention or to research participation in general.

However, despite this being a planned activity, some staff expressed challenges associated to its implementation. For example, some found it challenging to determine which information was appropriate for lay people and how much of the information could be disseminated. One staff was also concerned about the ability of the participants to understand some information, especially when provided in a scientific manner. In addition, some staff expressed concerns in regard to what type of findings to be provided. For example, Destiny felt that in addition to informing them about the overall trial outcomes, it was important to provide detailed information about their participation, such as their trial arms in case of blinded randomised trials, and what implications that might have on their health.

And on top of that we want to tell them because if it was a placebo controlled trial they would like to know which arm they fell and also we try to explain to them if by being on one arm, it exposed them to any risk or good from the results. (Destiny, nurse)

The above view is congruent with the concerns of the participants, where some expressed the need to receive feedback about their treatment arms, and also appears to be related to the recommendation in Trial 1 MOP, which stipulated the plans for providing more individual trial outcomes. However, providing trial feedback in blinded trials appeared to present some ethical concerns. For example, in some trials where blinding was required for a specific period of time, it affected dissemination of certain results in order to maintain the research integrity. In Trial 1, CD4 count for trial participants was double blinded and it was reflected in the documents that this could not be provided when interim findings were being provided to post-trial facilities during the transition process. Some participants also reported this to have been a major inconvenience as they desperately wanted to know their health progress. Another challenge identified in the implementation of feedback dissemination related to problems of locating trial participants once they leave the trials. Research staff expressed this concern by highlighting a possibility of losing contact with participants, since sometimes they change their addresses or telephone contacts.

Some of them relocate, some of them change contacts and, so you fail to link up with them and they can't come, you call them and the number does not go through any more,

you try to find this location where you knew they leaved and they relocated to another place, so it's quite a challenge. (Nsubuga, clinician)

These findings indicate that specific factors could influence how dissemination of trial feedback is implemented in the different trials. Unlike other aspects of post-trial care which were often affected by a lack of funds, providing trial feedback was mainly influenced by other factors, of which the majority related to research regulation. Some of these factors tended to also affect the timing of when feedback would be provided. Indeed, as shown in chapter six, many participants expressed discontent in regard to the timing of providing trial feedback, as they reported not receiving them within the expected time. Accounts of research staff also indicated that although this activity was planned, it had not yet been implemented in all included trials. Destiny pointed out some of the reasons why this activity had been delayed in her trial.

... you know these regulatory issues, because sometimes it depends on which scientific conference we are going to present. So you cannot disseminate results before the scientific conference has..., but we have now been released, we have now disseminated to the ministry of health, and then we are going to the..., people now remaining are these organisations we collaborated with and then the participants. (Destiny, nurse)

Apart from trial participants, findings indicated that trial feedback is disseminated to other stakeholders. The main stakeholders include the national and local research regulatory bodies, the pre-trial and potential post-trial care facilities, and the wider public, through conferences and publications. Such stakeholders are targeted for different reasons. For example, potential post-trial care facilities could be targeted due to the need for continuation of care and monitoring of the participants, while for others, this could relate to ethical reasons and scientific interests. Research staff commented that the local communities also demanded receiving trial feedback, in recognition of their general contribution to research.

8.6 Conclusion

From a researcher's perspective, post-trial care emerged as an important concern for consideration in HIV trials involving HIV infected people in Uganda. Although staff recognised most of the post-trial care aspects expressed by trial participants as important and also as their obligation, the current practice does not consider many of these. The lack of implementation of such important care aspects appeared to emerge from a lack of planning, which was also attributed to the lack of stringent policy guidelines on these. While research administrators have been argued to seriously consider these in HIV research practice, ethics and regulatory authorities have been

identified to have a major role to play. Collaboration with different stakeholders has also been recognised as an important approach to enhancing the implementation of HIV post-trial care in Uganda.

These findings also highlight the need for a wider engagement in debates related to HIV research ethics in low income settings, since various factors in these settings appear to have a significant ethical implication on the implementation of post-trial care. Some of these debates will be explored by relating findings of this research to existing and wider research evidence, which is the focus for the next chapter.

CHAPTER 9: DISCUSSION OF THE STUDY FINDINGS

9.1 Introduction

The findings of the current study suggest that trial closure was often a stressful process for the HIV positive participants, due to the negative psychological, socio-economic and healthcare impacts caused. These impacts were attributed to being stopped from care provided at the research facilities, which was considered to be of significantly higher quality to other available alternatives. The main concerns which arose during the transition from HIV research to usual care facilities are summarised as: the loss of the quality healthcare and valued relationships in research, the need to find and link to alternative care, the need to meet associated increased financial needs, and worries about the effects/outcomes of research participation. These concerns call for a range of care and support strategies from researchers (and other stakeholders). The existing support strategies were generally guided by universal research policies and these did not sufficiently address the context specific care needs of the participants.

This chapter presents a discussion of the ethical, moral, and practical considerations during closure of HIV clinical trials involving HIV positive participants in Uganda. The chapter discusses the main issues arising from this research, in light of the existing policy recommendations on HIV research in general and trial closure specifically, and of the wider literature and debates on research ethics.

The discussion is presented under six main headings. The first section discusses the information and psycho-social support needs of trial participants during the transition process, including consent requirements, strategies to address emotional and social concerns (such as allaying fears and anxiety), and dealing with concerns of HIV stigma and attachment. The second section discusses findings about the need and obligation of researchers to appropriately link trial participants to post-trial care, and to ensure continuity of the appropriate HIV treatments for the participants. This section addresses issues such as the need to link trial participants to appropriate facilities, support trial participants during the linkage process, maintain a continuum of care and treatment during the linkage process, ensure the provision of a trial regimen, and ensure that trial participants are receiving appropriate HIV services. The third section discusses findings about the need for researchers to monitor for possible side effects from trial interventions. The fourth section discusses findings related to concerns about compensation and recognition for research participation, and the need for continued financial support for the 'needy' trial participants. The fifth section reports findings related to the need for, and obligation of, providing feedback of trial findings. The sixth

and final section discusses the role of additional stakeholders in improving post-trial care processes.

9.2 Information and psycho social support needs

This section discusses findings related to the information and psychosocial needs of trial participants and how these were addressed. The main information needs which arose during trial closure included post-trial care arrangements and how and where to seek post-trial care. In addition, emotional concerns such as worry about post-trial care, HIV stigma, and separation from important relationships were significant concerns and are discussed in this section.

9.2.1 Informed discussion of post-trial care arrangements

Findings indicated that trial participants were informed about post-trial care arrangements during the consent process and during trial conduct. However, the information provided appeared limited as the focus was usually on the timing of the closure, where to access post-trial care, and feedback of trial results. The findings showed that some relevant information was not usually provided during consent, especially that which related to financial benefits. This was of concern to some participants who felt such information was relevant to enable them make an informed consent and also to protect their rights.

A review of some ethical documents also revealed a mismatch in the representation of post-trial information. For example, information on disseminating of trial findings and linkage to post-trial care was described in details while limited attention seemed to focus on other aspects such as trial benefits, follow-up and monitoring for side effects, yet these emerged as important to the respondents. Moreover, even for the available information, this was not adequately represented in the documents supposed to elicit consent from the participants such as the participant information and consent forms. Some authors have also expressed similar concerns, where researchers fail to explicitly indicate post-trial care plans in the ethical documents (Ciaranello et al., 2009). The absence of such information especially in the documents used to elicit informed consent from participants raises concerns regarding informed consent practice.

The need for disclosure of post-trial arrangements during the informed consent process has been discussed in literature. Similar to the findings of the current research, Sofaer et al. (2009) highlighted that an informed consent document can be legally binding and can act as a contract between researchers and trial participants for the provision of post-trial care. Other reasons provided in literature for the need to disclose all post-trial care

during consent include: increasing recruitment rates, improving researcher-subject relationships, alleviating participants' post-trial anxieties, and increasing trust in the research (Sofaer et al., 2009). Some of these reasons were important in the current study. Although some researchers in the current study contested the idea of disclosing specific post-trial care aspects (especially those related to financial benefits) due to their potential to cause undue influence on potential participants, previous literature strongly suggests the need for all post-trial care information to be disseminated to the participants during the consent process in a complete and clear manner (Ciaranello et al., 2009; Emanuel et al., 2000; Jefferys, 2013; Sofaer et al., 2009; UNAIDS, 2012a; Wang & Ferraz, 2012; World Medical Association, 2013). In circumstances where a given aspect may not be provided, e.g. where participants will not be provided any financial compensation, this also needs to be disclosed to the participants as this assists in making an informed choice and to avoid unrealistic expectations (Ciaranello et al., 2009). Jefferys (2013) places particular emphasis on the need to explicitly reflect all relevant information in the ethical documents that the participants are supposed to read and sign, e.g. the information sheets and informed consent documents.

The current study highlights important gaps in the dissemination of post-trial care information to participants in practice. These gaps may indicate a lack of streamlined guidance on post-trial care, which various authors have criticised as a weakness in current ethical regulation, where guidelines on the various aspects of post-trial care are inconsistent and/or unclear (Ciaranello et al., 2009; Dainesi & Goldbaum, 2011; Sofaer & Strech, 2011; Wang & Ferraz, 2012).

Although the World Medical Association (2013), which is a world research regulatory authority demands that all post-trial care information be disclosed to participants during the informed consent process (p.2193), it does not provide details of how this should be done. For example, how much detail needs to be disclosed or how this should be handled in lay, low income or low literate populations. Moreover, the guideline also majorly focuses on the need to provide the trial regimen and trial feedback, which leaves a gap in the guidance of the implementation of other post-trial care activities. Similarly, UNCST (2007, 2014a), the research regulating authority in Uganda outlines the importance of continued post-trial care and follow-up following trial closure for 'an appropriate period of time'. However, this also does not provide explicit guidance on, for example, what type of care and for how long this should be done. The current study has provided some helpful insights in this area by suggesting the most important areas of focus for post-trial care and the possible length this could be implemented. Hence, in addition to those activities currently being implemented, the findings suggest the need to: implement a

more facilitated, individual-focused linkage to care process, undertaking post-trial follow-up, monitoring for possible effects from trial interventions, and providing financial support. These issues will be discussed in detail in subsequent sections.

In addition to regulatory issues, a lack of focus on some aspects of post-trial care can be attributed to how the subject is generally understood, and on the importance individuals place on the particular aspects of post-trial care. Generally, post-trial obligations have been understood as the need to provide a trial regimen (Schroeder, 2008), and the majority of debates and inquiry on post-trial care have focused on this aspect (Essack et al., 2010; MacQueen et al., 2007). The current study suggests the need for authors and authorities to understand the complex nature of trial closure involving HIV positive participants in Uganda, and to consider other important care needs for this group while guiding trial closure practice. Due to the role of the ethical authorities in the implementation of post-trial care, additional research exploring the views of ethical bodies will be required to enrich the debates in this area.

9.2.2 Preparing trial participants for the closure

Preparing trial participants for the pending closure emerged as an important activity during the transition process. This mainly involved information giving to: keep participants reminded about the timing of the closure, provide guidance on where participants could seek appropriate HIV services, attend to participants' socio-economic concerns, and provide guidance on follow-up activities and provision of trial feedback. The current study appeared to place much importance on the role of counselling and guidance in addressing the post-trial care needs of the participants. Early preparation of the participants was considered the best way to reduce negative emotional effects associated to trial closure, and to solve the socio-economic concerns of participants who could not be assisted through other means.

Similar to the current study, previous literature supports sharing of relevant information with trial participants during trial closure, as this will be helpful in supporting them to identify and access locally available resources or healthcare services where HIV care can be continued (Sofaer et al., 2009; Stephenson et al., 2008; UNAIDS, 2012a). Other authors have identified a need for adequate provision of linkage to care information following an HIV positive diagnosis, as a mechanism to overcome barriers to linkage to care such as stigma and a lack of knowledge of where to seek HIV services for the newly HIV diagnosed individuals (Ankiersztej-Bartczak et al., 2015; Dombrowski, 2013; Fortenberry, Martinez, Rudy, & Monte, 2012; Tweya et al., 2014). This approach can be equally applicable for trial participants, especially those still experiencing HIV stigma,

those who acquire HIV during research, and those who join research immediately following an HIV positive diagnosis. PMTCT trials (where women may be enrolled in HIV trials immediately after diagnosis), and microbicide and HIV vaccine trials (where participants can become infected during research), could also benefit from such services.

9.2.3 Addressing the emotional concerns arising during trial closure

The current study suggested that trial closure resulted into significant emotional impacts such as worry, fear, and anxiety among trial participants. These were associated to trial closure in general, but specifically attributed to the loss of the quality care provided and the loss of valued relationships in research, the complexities associated to accessing post-trial care in Ugandan public healthcare facilities, and the fear of experiencing unwanted effects from trial interventions. Being a new field of research, limited evidence exists to allow an evaluation of these findings against extant evidence. However, emotional reactions to closure of health related programs have been cited in numerous studies, with the majority reporting fear, anger, loss, sadness, and mourning as major reactions (Fortune, 1987; Fortune et al., 1992; Orgel, 2000).

Loss of the quality care provided in research became an important concern in the current study since research usually offered exceptionally better care compared to the usual care facilities. Research usually offered trial participants timely care, standard medical investigations, all required treatments, and often provided other incentives such as transport reimbursements and sometimes food. The loss of such care was highly important to the participants since the majority were of a low socio-economic status, and some were also experiencing ill health, making them to require more frequent healthcare visits, and yet sometimes these were unable to work due to ill health. In addition, the research environment was more private compared to the public healthcare facilities, which was more important to those still experiencing HIV stigma. Owing to the differences in care provision between research and the public healthcare system in developing countries as Clouse et al. (2010) explain, it is not surprising that the majority of participants in the current study were worried about their access to care following trial exit. Although limited literature exists in this area, some evidence concurs with the findings of the current study by suggesting that during closure of research projects, loss of the quality care is a major concern (Chang, 2002; Stephenson et al., 2008). Some authors who have published in the area of closure of health related programs have recommended the need for psychological support of those involved, to allay their fear and anxiety, and assist them to find options for further access to the required care (Levine et al., 2006; Williams et al., 2006).

Fear associated to the possibility of developing unwanted effects from trial interventions was a significant concern for many trial participants. This was especially important to participants in a blinded trial, which also involved a placebo. At trial closure, all participants in this trial were restarted on the trial medication without clear communication about the likely outcomes, the implications of the trial, or their treatment allocations. This concern called for the need to offer emotional support and to provide relevant and adequate explanation about these concerns, considering that some information could not be disclosed at the time of trial closure due to regulatory reasons. However, these concerns also raised the need for timely and precise provision of trial outcomes (as will be discussed in more details later), and for researchers to monitor²⁶ trial participants during the post-trial period.

The loss of valued relationships especially of the research staff and peers raised a need for dealing with attachment concerns during the transition process. Since the majority of the trials lasted beyond three years, trial participants had developed attachments to researchers and peers, which were difficult to lose following trial closure. Sofaer et al. (2009) assert that trials which run for one year or more tend to create relationships between researchers and participants which become difficult to break, with participants sometimes feeling a sense of abandonment when they end, since they have now come to consider research staff almost as caregivers. This perspective was expressed in the current study by some participants displaying a sense of abandonment at trial closure and some desiring to continue in research.

Respondents in the current study suggested a need for 'weaning' strategies to enable a planned, as opposed to an abrupt cut off from research related care and relationships. This strategy has been suggested by other authors (Harrigan & Walsh, 2003; Wilson et al., 2007), as some evidence indicates that relationships terminated abruptly are more likely to cause negative emotions (Fragkiadaki & Strauss, 2012; Mirabito, 2006; Peck, 2007). However, as the findings of this research suggest, not much attention has been paid in practice to address concerns related to termination of close relationships in research or healthcare, a problem attributed to a lack of guidelines on this issue (Mirabito, 2006; Wilson et al., 2007). Understanding the care needs of trial participants during closure of HIV drug trials in a Ugandan setting by various stakeholders will be a starting point in addressing this concern.

²⁶ This issue is discussed in more details in a later section

9.2.4 Addressing concerns related to HIV stigma

Some participants in the current study still experienced HIV stigma at the time trial closure and afterwards. Experiencing HIV stigma was particularly an issue for those who were relatively new in HIV care compared to those who had spent a longer period, and was likely to negatively affect access to post-trial care. Due to limited existing evidence regarding transitioning from HIV research to care, the impact of HIV stigma towards linkage to care can be examined from literature on linkage to care of HIV patients following an HIV positive diagnosis. Numerous literature suggests that HIV stigma still remains a challenge to linkage to and access to care for the HIV positive people, with the fear of psychosocial consequences mainly blamed for it (Clouse et al., 2010; Fortenberry et al., 2012; Govindasamy, Ford, & Kranzer, 2012; Mugavero, 2011; Nalubega & Evans, 2015; Sayles, Wong, Kinsler, Martins, & Cunningham, 2009; Tweya et al., 2014; UNAIDS, 2012a).

Although the need to address HIV stigma was expressed, the findings suggested that this was still difficult due to the challenge of identifying those affected. Some authors have suggested ways of addressing HIV stigma during HIV research and linkage to usual care, which include stigma reduction strategies such as offering counselling and psychosocial support (Fortenberry et al., 2012; Govindasamy et al., 2012; Tweya et al., 2014). Due to the possibility of some trials involving HIV care naïve participants, it is essential for researchers to be equipped with stigma identification and management strategies to assist those who may be affected during the transition process.

9.3 Facilitating linkage to and continuity of HIV care and treatment

Facilitating the linkage to care process emerged as a key aspect of post-trial care, since the HIV positive participants continued to require access to routine HIV care and treatment. This section discusses findings which relate to the need for, and obligation of, researchers to appropriately link trial participants to care facilities, and to ensure continuity of the appropriate HIV care and treatments. Concerns such as the need to provide practical support and maintain a continuum of care and treatment during the linkage process, and the responsibility to ensure that participants continue to receive the trial regimen and/or other required HIV services are particularly addressed.

9.3.1 Linkage of participants to post-trial care

Linkage to care has been identified as the most important step in ensuring appropriate care and treatment for the HIV infected people following an HIV positive diagnosis (Clouse et al., 2010; Dombrowski, 2013; Fortenberry et al., 2012; Mayer, 2011; Tweya et al., 2014; UNAIDS, 2012a). The 2020 UNAIDS 90-90-90 strategy (UNAIDS, 2014)

which aims to achieve 90% sustained antiretroviral therapy for all HIV infected people will highly require appropriate linkage to care strategies, since HIV treatment essentially relies on appropriate linkage to care processes. In a similar manner, appropriate linkage to and retention in HIV care is essential for the continuity of HIV care and treatment which will contribute to the viral suppression among the patients, thereby contributing in achieving the 2020 UNAIDS 90-90-90 goal.

Linkage of participants to post-trial care was strongly recognised in this research as the researchers' responsibility. Basing on an ethical/moral argument, respondents felt researchers held the obligation of ensuring that trial participants continued to receive care after research studies have been concluded. Previous literature has suggested various reasons for the need or obligation of researchers to provide post-trial care in general (and linkage to care specifically) following research participation. These have included: ethical and moral reasons such as reciprocity; compensating participants for their commitment, inconveniences and risks undertaken during research participation; to avoid exploitation of research participants; because it is a health need; a duty to care as a researchers' role; and to maintain trust and the relationships created during research (Clouse et al., 2010; Dainesi & Goldbaum, 2011; Haire & Jordens, 2015; Merritt & Grady, 2006; Sofaer et al., 2009; UNAIDS, 2012a; Wang & Ferraz, 2012). Although participants in the current research did not express all of these reasons, the findings of the study are consistent with what wider calls in the literature suggest, arguing that linkage to, and continuity of, care after research participation is an essential component of a researchers' responsibility.

Nonetheless, despite recognition of the need for appropriate linkage to care, the current approach did not appear to meet the needs of the participants. The current approach mainly involved providing trial participants with a written report about their research/medical history and then referring them to a care facility of their choice. This approach also appears to be the accepted standard in the ethical guidelines (MacQueen et al., 2007; Rennie & Sugarman, 2009; UNCST, 2007), including those in the reviewed documents. This means in current practice, 'participant-led' (passive) referral remains the most practical approach to linkage to post-trial care. This approach appears to have significant shortcomings. For example, using this approach has a potential of failing to confirm that linkage to care had actually taken place or to address the practical difficulties associated with (re-)registration in care facilities. Both of these challenges were reported in the current study. The findings of the current study highlighted that although referral could be sufficient for some groups of participants, it alone may not be suitable for others. For example, according to this research, those going to completely

new facilities, or those returning to facilities in which they had been detached for a significant period of time may require more facilitation to re-establish in care, while those who retained contact with their facilities could require a less rigorous approach. Hence, these findings indicated the need to assess individual trial/participants' circumstances and needs while linking them to post-trial care.

In addition, the study identified a range of other factors which were of significance to post-trial access to care for the participants. These factors included: a lack of finances e.g. to facilitate travel to facilities, HIV stigma, and other practicalities associated to service provision in the Ugandan public facilities such as clinic delays, a lack of privacy, perceived unwelcoming staff attitudes, and a lack of adequate provision of treatments, especially for opportunistic infections. Although no known study has specifically looked at linkage to care following research participation, other (more general) literature suggests closely related barriers to linkage to care following HIV diagnosis, including: HIV stigma, fear of disclosure, perceptions of being healthy, lack of time, feeling inconvenienced, privacy concerns, lack of support, and mistrust of healthcare workers, among others (Cargill, 2013; Dombrowski, 2013; Fortenberry et al., 2012; Govindasamy et al., 2012; MacKellar et al., 2016; Mugavero, 2011). Such problems have been majorly cited in the low income settings (Clouse et al., 2010; Marks, Gardner, Craw, & Crepaz, 2010; van Rooyen et al., 2013), and have been reported to significantly affect access to care in such settings.

Due the above mentioned barriers, low rates of linkage to care have continued to be a significant problem in the efforts to curb the HIV epidemic. Recent studies have reported significantly low rates of linkage to care following an HIV positive diagnosis. Some of these include a study by MacKellar et al. (2016), which sought to establish linkage to care of patients two years after diagnosis in Swaziland, and established that only 55.5% had enrolled in HIV care. Similarly, a study by Clouse et al. (2014) which assessed the impact of systematic HIV testing on case finding and retention in care in South Africa, established that within one year following an HIV diagnosis, more than 50% of patients were not in HIV specific care. Although the research and the HIV diagnosis contexts differ, some conditions may make these contexts quite related. For example, research participants who acquire HIV during research participation or those who join HIV research immediately following an HIV positive diagnosis could be in a situation similar to those newly diagnosed for HIV, and these could experience related barriers to establishing in post-trial care as those for newly diagnosed individuals.

Despite scanty literature in this field, there are some indications that some participants may not actually engage in care following trial exit. For example, in a study conducted in Zimbabwe and South Africa by Clouse and colleagues (Clouse et al., 2010), to elicit the uptake of additional counselling services and clinical care among women who acquired HIV during the trial, it was established that 18% declined any further care following trial exit. Similarly, in an event organised by TED Talks in the UK in 2012, Boghuma, a medical doctor and researcher in HIV cure research reported about a lady from Cameroon, who, 18 months after completing participation in an HIV clinical trial had not accessed further HIV care and treatment (Boghuma, 2012). This information clearly indicates a need to: (i) evaluate systematically the linkage to care process of trial participants, and (ii) devise better approaches of facilitating linkage to post-trial care for the HIV positive participants.

To facilitate linkage to care, respondents in this study suggested a more facilitated 'researcher-led' linkage process, whereby trial participants are physically linked to the care providers, either by researchers escorting them to their chosen facilities or facilities' staff picking them up from the research sites. Although there is a lack of research about this approach in a research context, various authors have suggested a related model to link HIV positive patients to care following diagnosis. For example, in a paper by Mugavero (2011) entitled 'predictors of late linkage to medical care after a new HIV diagnosis', active referral, which involved patients being accompanied to a care facility yielded better results compared to passive referral, which only involved patients being provided with written information to deliver to the care facilities. Similarly, Gardner et al. (2005), who tested the efficacy of a simple intervention of a more facilitated linkage to care for newly HIV diagnosed patients by following them up after referral, reported that the intervention significantly improved linkage rates compared to passive referral (which only involved providing referral information and no further contact thereafter). This literature suggests that these models could be potentially useful in improving the linkage of trial participants to care and may necessitate testing in a research context.

In addition to the above models, some of the problems likely to affect linkage to/retention in care may require specific supportive approaches. For example, fear of recognition as being HIV positive and fear of stigma can be addressed by counselling and offering psychological support, while financial concerns can be addressed by providing additional financial support. These supportive measures were suggested in the current study and have been discussed in other sections.

As some authors have indicated, there is also a possibility of failure of continuity in care following an HIV positive diagnosis even after an initial linkage (MacKellar et al., 2016; Mugavero, 2011), suggesting that complete linkage to care is not a one off event but rather a process, which continues even after the initial linkage. Findings of this research suggested the need for researchers to continue engaging²⁷ with post-trial participants after an initial reporting to their facilities, to ensure they have settled in care and are receiving appropriate treatments and care, a finding which has been supported by other authors (Gardner et al., 2005; Govindasamy et al., 2012; Mugavero, 2011). Nonetheless, due to limited evidence in the post-trial context, further research is recommended to confirm and also to validate the extent of the need for post-trial engagement of researchers with trial participants.

9.3.2 Provision of trial drugs and maintaining continuity of care

Continuity of HIV care and treatment following research requires continued provision of the correct HIV medications and other services. The need to provide trial medications to post-trial participants has been a global concern among various stakeholders and has dominated much of the debate on post-trial care (Dainesi & Goldbaum, 2012; Grady, 2005a; Haire & Jordens, 2015; Pace et al., 2006; Sofaer et al., 2009). Although many debates have focused on the need to provide trial drugs following research participation, this research has also established that the needs of trial participants in regard to access to post-trial care go beyond the provision of trial drugs. For example, the findings showed that in addition to the trial drugs, continuity of HIV care and treatment required continued provision of other HIV medications (especially those for treating opportunistic infections), and continued psychosocial and financial support. Indeed, in the current study, access to trial drugs did not emerge as the major concern and instead, access to treatments for opportunistic infections, financial challenges, and working practices in the public healthcare facilities were of much concern. These findings appear to concur with those of Stephenson et al. (2008), which is explained in detail in the literature review. However, with very limited research done in this area, these findings only provide an initial step towards more investigation about the needs of HIV positive post-trial participants in low income settings.

This research also established that in order to maintain a continuum of HIV care and treatment during the linkage process, trial participants were provided with a stock of medications (buffer stock). This approach was consistent across all included trials, and was primarily intended to minimise a possibility of trial participants missing medication

²⁷ Post-trial follow-up care will be discussed in a later section

doses, to avoid interrupting their treatment as they made arrangements to report to their care facilities. Although limited literature seems to explicitly indicate the need to provide a buffer stock during linkage to post-trial care (Sofaer et al., 2009), some authors have indicated that in HIV care and management, ART drug interruptions may have negative impacts on the health of the patients (Grady, 2005a; Jefferys, 2013; Wang & Ferraz, 2012). Thus the provision of buffer medication may be of much relevance in trials testing HIV treatment/prophylactic medications.

As already mentioned, the findings of the current study suggested that access to trial medications in trials involving prophylactic or first line HIV regimens did not emerge as the major concern among trial participants. This trend could be attributed to the far greater accessibility of HIV medications in recent years (even in low income settings) as Haire and Jordens (2015) note. However, participants in a trial involving second line regimens reported some challenges regarding access to the trial medications. For example, close to 12 months following trial exit, one participant still accessed her HIV medications at the research facility even when this was very far from her home, which increased her transport costs. This finding is consistent with current literature which has pointed out the possible difficulties in access to second and third line treatments worldwide, although this problem could be more pronounced in the low income settings (Ho, 2010). This finding suggests that researchers may need to pay more attention in making preparations for access to trial medications in trials testing second or third line HIV medications in the low income settings, where these drugs are not yet widely accessible.

In addition to access to the routine HIV medications, access to treatments for opportunistic infections emerged as serious concern for the participants. This concern was associated to the low socio-economic status of the majority of the participants, and also to the lack of availability of these treatments in the Ugandan public healthcare system. This concern was often of much significance to participants who experienced ill health, as these were sometimes unable to work. To promote continuity of access to treatments for opportunistic infections, and to meet other care needs such as transport costs, respondents in this study proposed the need for continued financial support²⁸, a finding also supported in previous literature Grady (2005a).

Hence, the need to maintain a continuum of HIV care and treatment requires that researchers (i) take responsibility to confirm linkage to care, and (ii) also to ensure that the correct treatments can be provided to the participants. This is of particular

²⁸ The need for financial support has been discussed in more details in another section

importance as some healthcare staff in non-research contexts may not be well versed with some HIV medications especially those used in research. For example, a staff in the current study reported about a participant who was tested on a second line regimen but who was later found to be restarted on a first line regimen. Such a concern raises the need for sensitisation/collaboration with facility staff (Wilkinson, Skordis-Worrall, Ajose, & Ford, 2015), and also calls for follow-up²⁹ care of the participants.

One of the key questions related to the provision of HIV post-trial care which arose in this study was the period of time for which post-trial care should continue. On average, findings suggested that post-trial care should continue up to 12 months following trial exit. By this time, it is expected that trial participants will be appropriately linked to, and retained in, alternative care. Various views have been expressed by different commentators regarding the length of period researchers are obliged to continue providing post-trial care. Although these arguments have been mainly based on the issue of provision of trial medications, the majority appear to agree that the researchers' obligation should end when they are sure that trial participants can consistently access trial drugs from alternative sources (Barsdorf et al., 2010; Clouse et al., 2010; Dainesi & Goldbaum, 2012; MacQueen et al., 2007; Wang & Ferraz, 2012), or have an alternative for the trial drugs (Sofaer et al., 2009).

The findings of the current study suggested that the main means of follow-up was thorough telephone communication, which was usually unofficial, and initiated by either the participants or the research staff. Although this approach may be limited in addressing the more practical participants' needs, telephone communication can be a helpful approach in addressing some of the concerns which might arise during the post-trial period. Authors have recommended use of telephone follow-up, to address especially the information and psychosocial needs of clients (Ashengo et al., 2014; Eng et al., 2013; Tweya et al., 2014). Although this approach has mainly been implemented in non-research contexts, it could provide an alternative means of meeting some of the post-trial care needs of the participants. However, complex situations such as monitoring for side effects may require more practical approaches, including physical contacts with researchers and/or collaboration with other stakeholders such as healthcare workers in the public facilities.

In general, the findings of this study underscore the need for new debates on post-trial care to focus on ensuring access to a comprehensive HIV care package, including the provision of trial drugs, treatments for opportunistic infections, and attending to the

²⁹ Follow-up care has been discussed in more details in a later section

psycho-social and financial needs of trial participants. In addition, with the widespread availability now of most first line HIV treatments, it appears to be that trials involving second and third line HIV regimes pose the greatest challenge in regard to the obligation to provide a trial drug.

9.4 Monitoring for unwanted effects from trial interventions

The possibility of negative effects occurring later following trial closure was a major concern in this study. Respondents argued that the researchers' responsibility would not be complete until they are sure no undesired effects can arise from the trial interventions. With no systematic monitoring implemented in current practice, many trial participants felt researchers were not showing much concern about them. Research staff in particular emphasised the need to monitor for side effects, although timing of the follow-up became a concern, given the nature of research which has limited timelines and resources.

Fears of possible side effects from trial interventions have been a major concern for people involved in HIV and other trials as noted in previous research (Emanuel et al., 2000; Haire, 2013; Nalubega & Evans, 2015; Sofaer et al., 2009), and some authors have cited the need to attend to these in trial practice (Emanuel et al., 2000; Ho, 2010). This research established that there were stringent guidelines put in place for identifying and dealing with serious adverse events which occur during trial conduct, however, there appeared to be no plans for monitoring/addressing those effects which could occur after the trials have been closed. Respondents in the current study were particularly concerned about effects which may occur after trial participation, with a possibility of some occurring following trial closure. These findings are similar to those identified by Sofaer et al. (2009), where participants expressed fears of effects arising after trial exit. These participants suggested being followed up for as long a period as possible to capture any likely effects. UNAIDS (2012a) also highlighted this concern and recommended particular focus to be paid on trials which are likely to have long term effects.

Research staff highlighted that it was not necessary to monitor individual trials considering that some may not pose any risks. They suggested the need to address the trials on a case by case basis, since for most trials, it was possible to predict beforehand the potential for causing unwanted effects. These findings suggested the need to assess the individual trial risks and to make appropriate follow-up plans, a view also suggested in previous literature (Emanuel et al., 2000; Ho, 2010; UNAIDS, 2012a; World Medical Association, 2013).

9.5 Financial and other research benefits

The subject of compensation and research benefits was of particular concern in the current study. This section discusses findings related to the need to provide financial and/or other research benefits in HIV clinical trials, giving particular attention to a researchers' ethical obligation to compensate participants for their contributions and inputs in research, and the need to support those in financial need.

9.5.1 Compensation (recognition) for trial participation

The findings of the current study suggested a need for compensation of trial participants, for reward/recognition of their contributions in research, with both categories of respondents acknowledging it strongly as an ethical requirement. These felt HIV trial participants should be compensated for their time spent, the risks undertaken, and also for other inconveniences faced during research participation such as blood collection procedures and frequent clinic visits. The need to compensate participants in research has been extensively debated, with most literature (Draper, Wilson, Flanagan, & Ives, 2009; Grady, 2005b; Kwagala et al., 2010; UNCST, 2007; Wertheimer & Miller, 2008) suggesting similar reasons to those raised in the current study. Despite the majority not having formal employments, participants in the current study were much concerned about the time lost while attending research visits which they could have spent doing other productive activities such as cultivation and tending to their animals. Some of them compared the loss of such time to loss of money, indicating how they indeed valued their time. Similar to the current study, Njue et al. (2015), commended that 'poor' participants required compensation for their time spent during research participation.

However, despite the identified need to compensate trial participants, compensation has neither been systematically applied nor recognised with equal importance in practice, in different trials or research contexts. The findings of this study suggest that the main reason this challenge exists is the absence of clear/streamlined guidelines on compensation and also on the beliefs about risks associated with the practice. Numerous commentators (Grady, 2005b; Kwagala et al., 2010; Largent et al., 2012; Roche et al., 2013) agree with the above findings and have criticised current policies on research regulation for being too generalised and failing to offer proper guidelines on the implementation of compensation in research. The major need identified in both the current study and previous literature is to have somewhat standardised guidelines to regulate compensation.

While the need for compensation was recognised by the majority of research staff, some felt there was risk for undue influence or coercion of the participants. This was particularly important when such compensation was in monetary terms, and especially if these were communicated to the participants during informed consent. However, this viewpoint appears to conflict with the need to disclose all post-trial and other research benefits before consenting to research participation as discussed in an earlier section. Some staff in the current study were also concerned about a higher potential for coercion of trial participants in a low income setting such as Uganda, a concern expressed by numerous authors, who have noted that although the potential for coercion/undue influence of research participants might apply generally, the less economically advantaged may be more at risk (Draper et al., 2009; Grady, 2005b; Kwagala et al., 2010; Largent et al., 2012; McGregor, 2005; Roche et al., 2013; Wertheimer & Miller, 2008). Nonetheless, other authors have highlighted that although financial facilitation/benefits may indeed be of more concern for the low income settings, they still remain very necessary to facilitate clinic attendance which would otherwise be very difficult without such facilitation (Govindasamy et al., 2012; Lowther et al., 2016; Nissen et al., 2012; Tweya et al., 2014).

Grady (2005b), in agreement with the above observation also notes that a lack of financial offer may only further restrict the opportunities of the less privileged to participate in research, while other authors have argued that although monetary benefits may indeed influence research participation, these are not likely to be coercive or to even cause undue influence to research participation (Bentley, 2004; Byrne et al., 2012). These arguments also concur with the findings of the current study, where participants who mainly expressed concerns about the need for compensation explicitly expressed their awareness of the voluntary nature of research, but felt their efforts in research deserved due recognition. Indeed, although money has been cited as a motivation for research participation, a recent systematic review (Nalubega & Evans, 2015) has shown that financial benefits are not a major reason for HIV research participation in the low income settings.

Interestingly, some authors have cited a potential for the socially and economically disadvantaged individuals to be exploited in research, for example by being under compensated (Njue, Kombe, Mwalukore, Molyneux, & Marsh, 2014; Njue et al., 2015). The findings of this research also appear to represent this scenario, whereby those who joined research while ill and were desperate to receive treatment appeared to think they did not deserve compensation. One staff member in the current study also pointed out that non-healthy participants may not necessarily be compensated e.g. for their time,

since they would all the same spend it seeking care for their ailments elsewhere. However, Grady (2005b) contends that both healthy and unhealthy research participants deserve to be compensated equally for their participation.

Other debates regarding financial benefits have mainly centred on what levels/amounts of benefits are acceptable. Although the current study did not offer much insight on this issue, some authors have expressed concerns about the potential for increasing amounts of offers to pose more risks for coercion/undue influence (Bentley, 2004; Largent et al., 2012). There is need for more debates and research on the rightful amounts of research benefits.

To avoid coercion, some staff suggested compensation/appreciation in non-monetary terms, such as using material gifts. Research staff in the current study felt such gifts could be helpful in eliminating biases related to coercion/undue influence. Although the debates regarding the types of benefits have not been so extensive, some authors have suggested that financial compensation is most appropriate where financial costs/losses are involved, while in other circumstances such as appreciation, other forms of non-cash benefits such as food items could be acceptable (Njue et al., 2015). Some authors have suggested that to minimise the risks of coercion/undue influence, there is need to involve other stakeholders such as the participating communities in determining the types and amounts of benefits (CAHR, 2008; Haire & Jordens, 2015), while others suggest that sharing of the intended individual benefits to the entire community could be a good approach (Kwagala et al., 2010). However, trial participants in the current study seemed to prefer individual or family benefits, a finding which has been cited in previous literature (Njue et al., 2015).

Conclusively, the issue of financial benefits in research has presented a relatively controversial debate, with somewhat conflicting views expressed about the subject among various stakeholders. Such conflicts have been to a large extent blamed on the lack of streamlined guidelines on this issue, and/or the lack of a clear understanding of the subject by many stakeholders (Grady, 2005b; Largent et al., 2012; McGregor, 2005; Wertheimer & Miller, 2008). However, although no consensus has been reached on these debates, authors seem to concur that despite the ethical concerns related to financial benefits, the need to compensate trial participants is still genuine (Draper et al., 2009). Many have also agreed with the idea that determining which offer is appropriate for compensation, various stakeholders need to join hands, while others have suggested the need for consideration of the various individual research factors such as the risks involved and the research contexts (Grady, 2005b; UNAIDS, 2012a).

9.5.2 The need for on-going financial support

The findings of the current study indicated that some participants required continued financial support during the transition period, to enable them to meet their increased financial needs and to facilitate their continued access to the required HIV care and treatment services. Such support was particularly important since the majority of the participants were of a low socio-economic status, while others were experiencing ill health and were unable to work. Following the loss of the quality care and the incentives received in research, many participants required support to be able to meet their now increased financial demands, e.g. of purchasing medications for opportunistic infections and facilitating clinic visits. As some authors noted (Govindasamy et al., 2012; Lowther et al., 2016; Nissen et al., 2012; Tweya et al., 2014), financial difficulties can be significant barriers to access to care especially for HIV infected and economically disadvantaged individuals, and some have suggested the need to offer financial support to such, in line with the findings of the current study. In addition, some participants reported using some of the transport reimbursements provided in research to help with their domestic needs, which became more burdensome once the research closed, a finding similar to one reported in a recent study by Lowther et al. (2016). Participants felt researchers or other stakeholders could provide some material support such as foodstuffs or pay fees for the children to solve some of their domestic responsibilities.

However, the need to preserve the ethical integrity by avoiding coercion, yet also to be sensitive to the financial needs of the participants raised an ethical dilemma among research staff. The majority of staff, particularly nurses and those attached to counselling advocated for such continued financial support while others, more especially clinicians were against it. Those advocating for the support felt it was a researchers' moral duty to ensure that participants continued to access quality care by financially empowering them, considering that they were being discharged from higher to lower standards of care. This finding also relates to those from other authors who reported that immediate cut off of the participants from research related care and offering them no support (especially to the very poor) could hinder their access to continued care and may be detrimental to their health (Nissen et al., 2012; Sofaer et al., 2009; Stephenson et al., 2008). Similar to the current study, Stephenson et al. (2008), is in agreement with having some post-trial care budget to specifically provide financial support to those who may be in much need.

On the other hand, those who argued against continued financial support felt this would act as a coercion, especially in the current trials if the benefits were declared during informed consent, or in future research. However, some felt that although researchers

may not necessarily provide direct financial support, they could act as mediators between the participants and other stakeholders such as NGOs and community based organisations, who could provide such support, an approach which Grady (2005a) also supports.

Due to variations in the health and socio-economic situations of the participants, most researchers agreed that financial concerns could be addressed on a case by case basis. On a broader perspective, these issues may be approached slightly differently in the different trial contexts, putting into consideration the geographical setting, the trial characteristics, and individual participant situations. This might therefore imply that for the same trials conducted in different settings, e.g. the low and high income settings, the need for financial support may be more relevant for the low rather than the high income setting. These findings align with the ethics of care theory explained in chapter 2 of this thesis, which supports the notion of a context based approach to research ethics (Beauchamp & Childress, 2001; Fry, 1989; Green, 2012). These findings thus underscore the importance of critically evaluating and putting into consideration the contexts under which research occurs.

9.6 Dissemination of the trial findings

This section discusses findings related to the need/obligation of researchers to provide feedback of trial findings to trial participants. Specifically, views relating to the need for, and the researchers' responsibility to provide feedback, the types of the feedback, and the timing of the feedback are discussed.

9.6.1 *The obligation to disseminate trial feedback*

Both trial participants and research staff in the current study expressed the need for dissemination of trial findings to participants. This was strongly recognised as a researchers' obligation and was reported to be one of the post-trial activities that was implemented in practice. There was also clear representation of the information regarding dissemination of trial results in the ethical documents reviewed, including those used to elicit informed consent from trial participants, reflecting this to be an important aspect of focus in current research practice. These findings appear to be congruent with existing research policy guidelines and debates, which put an emphasis on the need for dissemination of trial outcomes in research practice (Emanuel et al., 2000; Fernandez et al., 2012; Rennie & Sugarman, 2009; UNAIDS, 2012a; World Medical Association, 2013).

Trial participants in the current study expressed a strong need for receiving trial outcomes. This was felt to be helpful in ascertaining the impact of the research on their health, allaying fears and anxieties associated to possible effects of the trial interventions, and enabling them to understand the general outcomes of the trials in regard to the research aim. Numerous research studies have also reported similar concerns from their participants (Cox et al., 2011; Fernandez et al., 2009; Fernandez et al., 2007; Getz et al., 2012; Partridge et al., 2003; Partridge et al., 2009; Sofaer et al., 2009), while in other studies, other stakeholders such as investigators or ethics authorities have considered provision of trial feedback as very important in research practice (Di Blasi et al., 2002; MacNeil & Fernandez, 2007; Rigby & Fernandez, 2005).

9.6.2 Types of trial feedback

Although generally there was an expression for the need to know the more general trial outcomes, participants in the current study expressed a particular concern of receiving more specific personalised trial feedback, especially that which related to their individual trial outcomes, such as how trial participation had affected their personal health. This was a particular concern for participants who joined research while ill, and thus had health concerns/fears. Other participants, particularly those who participated in a double blinded randomised trial wished to be informed about their treatment arms, e.g. whether they were taking placebo or an active drug. These findings draw attention to how individual trial/participant characteristics can influence the priorities for trial feedback.

Similar to the findings of the current study, the need to know more specific trial outcomes such as treatment allocations has been reported in previous research (Armstrong et al., 2013; Cox et al., 2011; Dixon-Woods et al., 2006; Sofaer et al., 2009), while in other studies, participants have expressed the need for more individualised trial outcomes such as the effects of an intervention on an individual's health (health outcomes), or the long term effects of their participation in research (Dixon-Woods et al., 2006; Fernandez et al., 2009). These concerns appear to suggest that trial participants may require both the general and also the more personal trial outcomes, a conclusion similar to what other authors have suggested (Cox et al., 2011; Moutel et al., 2005).

Notwithstanding, various authors have raised concerns of the possibility of harm resulting from a disclosure of specific trial outcomes, such as treatment arms or the more individual trial outcomes, especially in studies with negative outcomes (Armstrong et al., 2013; Dixon-Woods et al., 2006; Dixon-Woods, Tarrant, Jackson, Jones, & Kenyon, 2011; Fernandez et al., 2012; Partridge et al., 2009; Tarrant et al., 2015). In

studies with negative outcomes, disclosure of some information has been reported to result into negative emotional effects such as guilt and fear, which in some studies has been reported to affect future research participation (Armstrong et al., 2013; Partridge et al., 2009). Although this concern was not raised in the current study, the eagerness trial participants showed and the worry expressed in not knowing the outcomes, may be an indication that if negative outcomes arose, this would be harmful to the participants. Researchers have suggested a need for establishing measures such as psychosocial support to address these concerns if, and when these occur (Armstrong et al., 2013; Partridge et al., 2009), while others have argued researchers to approach the provision of individual feedback with caution, to avoid the negative effects (Richards, Ponder, Pharoah, Everest, & Mackay, 2003).

Interestingly however, although studies conducted to assess the views/experiences of participants who participated in studies with negative outcomes reported negative emotions/outcomes, participants in these studies still expressed a significant need to know the outcomes (Dixon-Woods et al., 2011; Schulz et al., 2003). This might suggest that most participants will want to know the trial outcomes irrespective of the outcomes and its likely psychological impact as Shalowitz and Miller (2008) reported. Shalowitz and Miller (2008) therefore, recommend that fear of psychosocial harm should not hinder providing trial feedback to participants except in extreme circumstances, where threat to safety has been identified. However, since the current study did not identify any findings related to possible negative effects of providing trial outcomes, and since the majority of the literature reviewed in this area does not focus on HIV, further research could focus on this aspect in HIV clinical trials.

9.6.3 *Timing of trial feedback*

Particular concerns were raised by trial participants in the current study, in regard to the timing of trial feedback. Although the majority of the interviews were done close to 12 months following closure of two of the included trials, none had yet disseminated the overall trial findings. Participants expressed concerns regarding being kept in suspense regarding the trial outcomes, yet some felt these could have some health implications. Some were particularly concerned about being provided with the trial medications before knowing the trial outcomes, especially with no mechanism of knowing if unwanted effects occurred, as it used to be done during trial conduct. The majority of participants wished to receive the feedback during trial closure or shortly afterwards.

The concern of the need to provide trial feedback in a timely manner has been noted in previous literature (Fernandez, Kodish, Shurin, & Weijer, 2003; Fernandez et al., 2007;

Haire & Jordens, 2015; Sofaer et al., 2009), and similar to existing literature (Fernandez et al., 2007; Sofaer et al., 2009), although participants in the current study acknowledged the fact that feedback may not be available as soon as they could wish due to technical/regulatory issues, they still expected researchers to put effort to provide these in a timely manner. Moreover, some outcomes such as the more individual ones could still be provided at trial closure, while the more general ones may be provided later, as participants in the study by Cox et al. (2011) suggested. Although policy guidelines do not seem to specifically assign the timing for providing trial outcomes, some have suggested the need to provide these to the participants as soon as they are available (UNAIDS, 2012a), while others have suggested a period of at least one year following the closure of data collection (Fernandez et al., 2012).

Although there is general concern for the need for dissemination of trial feedback, and research policies also appear to place a particular interest on this, the evidence in the current study suggests that providing trial feedback is sometimes delayed. The delays in the current study were blamed on various factors. For example, research staff expressed concerns related to research regulation, especially as one trial was still ongoing hence feedback could not be provided in this case, while others commented that the results had to be authenticated and approved by relevant authorities before being disseminated. In one study, existing guidelines also made it clear that some outcomes, which were more personal such as CD4 counts could not be disseminated until after sometime, for research regulatory purposes such as blinding.

Previous literature also reports concerns in the practice of result dissemination, with some authors reporting delays or a lack of provision of trial feedback to participants (Fernandez et al., 2003; Fernandez et al., 2007; Getz et al., 2012). Related to the findings in the current study, authors have reported important barriers to result dissemination, including: the fear of biasing results especially for studies which are still ongoing, failure to locate post-trial participants, fear to distress participants (e.g. for trials with negative outcomes), difficulties in engaging with lay participants, and time, financial or other resource constraints (Di Blasi et al., 2002; Fernandez et al., 2003; MacNeil & Fernandez, 2007; Partridge et al., 2004; Rigby & Fernandez, 2005). Interestingly, costs did not emerge as a barrier for result dissemination in the current study, as this was usually planned for, unlike other post-trial care activities as discussed in previous sections. However, respondents mentioned the possibility of difficulties in locating trial participants in general, as there is a possibility for them to change their address or their telephone contacts.

9.7 Stakeholder involvement

This section discusses findings related to role of other stakeholders in post-trial care. These findings are discussed in light of the need to address the various care needs which arise during the transition process, which may not easily be addressed by the research staff. Social-economic needs are particular concerns which may require the support of other stakeholders, such as the family and community groups and which were of significance in this research. In addition, this section discusses the need and role of the ethics authorities in post-trial care, as these were found to be at the centre of research regulation.

9.7.1 *Involving other stakeholders in post-trial care*

The findings of the current study suggested the need to involve various stakeholders in the different post-trial care aspects which included: the planning of post-trial care, providing psychosocial support, linking participants to care and facilitating continuity of care, follow-up and monitoring, and financial support and empowerment. The stakeholders identified by the findings of the current research include: former or potential trial participants, the community, the family, local and national health systems, local, national, and international NGOs, ethics authorities, and politicians. These would need to collaborate with research sponsors, funders, and researchers to create a more coherent strategy for post-trial care. For example, former/potential trial participants would be helpful in establishing the post-trial care needs/expectations, while other stakeholders would act as advocates/advisers in ascertaining appropriate standards of post-trial care such as finances or other post-trial benefits, offer assurance or partnership in providing post-trial care such as providing trial drugs after the trial, or offer ongoing psychosocial, material, and practical support to the participants.

Various authors and authorities (Dainesi & Goldbaum, 2011, 2012; Grady, 2005a; Haire & Jordens, 2015; Rennie & Sugarman, 2009; UNAIDS, 2012a) have highlighted the importance of involving stakeholders in planning post-trial care. These could contribute to important decisions such as determining contextually appropriate post-trial benefits and in establishing ways of ensuring continuity of care after trial closure. Authors have also pointed out other likely advantages of stakeholder involvement in post-trial care. For example, by involving stakeholders, it would be easier to: understand the needs of trial participants as these might be significantly different from those of the researchers (CAHR, 2008), avoid large financial benefits which can cause undue influence (Kwagala et al., 2010), avoid exploitation of participants by underpayments (Haire & Jordens, 2015), and enhance the overall ethical HIV research conduct (Jefferys, 2013).

The need to involve the participating community has been particularly highlighted in international research conducted in the low income settings, and UNAIDS (2012a) recommends full engagement of participating communities in the planning and implementation of post-trial care. These have highlighted how this does not only show respect for trial participants, but helps in the overall ethical and smooth running of HIV trials in the low income settings, by identifying their needs and concerns. As the current study suggests, involving former trial participants who constitute the participating community could be helpful, as these may have particular expectations in the upcoming trials.

Although findings in the current study suggested the need for the involvement of the different stakeholders in post-trial care, it was difficult to ascertain to what extent these are currently involved in practice, given that this was not an area of focus for this study. Moreover, the fact that many post-trial care needs of the participants were not being addressed suggests relevant stakeholders may not be currently involved in HIV post-trial practice, and that post-trial care has not yet been given the prominence it deserves. Future research can be helpful in establishing which stakeholders, and to what extent these are/should be involved in the planning and implementation of post-trial care in HIV research in Uganda. In addition, existing research has mainly focused on the need to involve stakeholders in planning post-trial care, but not much has been explored in terms of what their actual involvement might be. This is an area that deserves more attention.

9.7.2 *The role of ethics authorities*

Research staff made specific recommendation for research ethics authorities to become more involved in post-trial care, by identifying the need for it to institute and enforce policies, which can address the specific aspects of post-trial care identified in the current study, but which are not currently being implemented. Being the enforcing authorities, the current study suggested that their input would be important, to avoid conflicts between researchers and funders/donors. Research staff in the current study noted that some of the post-trial care activities, for example follow-up and monitoring, which they considered important could not be easily budgeted for, due to fear of donors rejecting their research proposals. By making such post-trial care activities mandatory (standard) for all HIV trials, this would make it easier for researchers to reflect them on their budgets. As Kwagala et al. (2010) suggest, ethics authorities should ensure that post-trial specific guidelines and policies are made on how post-trial care issues e.g. access to treatments should be approached, to enable standardisation of post-trial care for researchers, while Largent et al. (2012) cautions ethics authorities to clarify on issues of

undue influence or coercion. In addition, UNAIDS (2012a) emphasises that the final authority should be upon the ethics review boards, to ensure that only research studies which fulfil the post-trial obligations in their proposals are approved.

9.9 Conclusion

Generally, post-trial care has been understood in terms of providing trial drugs, referral back to routine care, and providing trial feedback. The current research has significantly expanded on the understanding of post-trial care in HIV drug trials in Uganda, by describing trial closure as a process rather than a one off event, and by bringing to light other important aspects of post-trial care, which appear to be of less focus in current practice but require to be incorporated in HIV drug trial closure practice in Uganda.

Findings of this research have demonstrated that to meet the post-trial care needs of HIV positive drug trial participants in Uganda, a comprehensive care strategy is required, which, in addition to the already existing activities, should aim to; address the financial needs of trial participants through financial assessment, support and empowerment, provide practical support during linkage to post-trial care, and offer post-trial follow-up care, monitoring and support. The proposed approach to post-trial care has been demonstrated in the Facilitated Transition Model presented in chapter ten below.

The conclusions drawn in this research suggest that the obligation to provide post-trial care mainly falls on researchers. However, this could be achieved through liaising and collaborating with other stakeholders, to address the pertinent needs of HIV post-trial participants. Ethics authorities also appear to be central to the improvement of HIV post-trial care in Uganda.

CHAPTER 10: SUMMARY AND THEORETICAL INTERPRETATION OF THE RESEARCH FINDINGS

10.1 Introduction

This chapter summarises the main findings of this research, and provides a theoretical interpretation of the key concepts, in view of other existing literature and theories. A theoretical model was developed, which represents the process by which HIV positive trial participants transition from research to usual care facilities and how they are facilitated.

The transition process encompasses the events which occur when an HIV positive trial participant, following planned completion of trial participation, is exited from research and linked to the public healthcare system, to continue accessing the required HIV services. The main events which occur along the process relate to trial participants' care expectations, needs, experiences, and decisions. Although these events appear to occur during the actual closure and after participants have been exited from the trials, this research demonstrated that they are strongly influenced by underlying contextual factors occurring before trial closure. For example, the experiences of care before trial closure (such as care experiences in the public healthcare facilities, care during previous research, and during the conduct of current trials) had an impact on trial participants' post-trial care expectations, experiences and decisions. In addition, the main events which occur during the transition process are largely influenced by individual participant situations before, during, and after trial closure, individual factors such as health status and social-economic situation appeared to have a significant influence on the care needs and experiences of trial participants during the transition process.

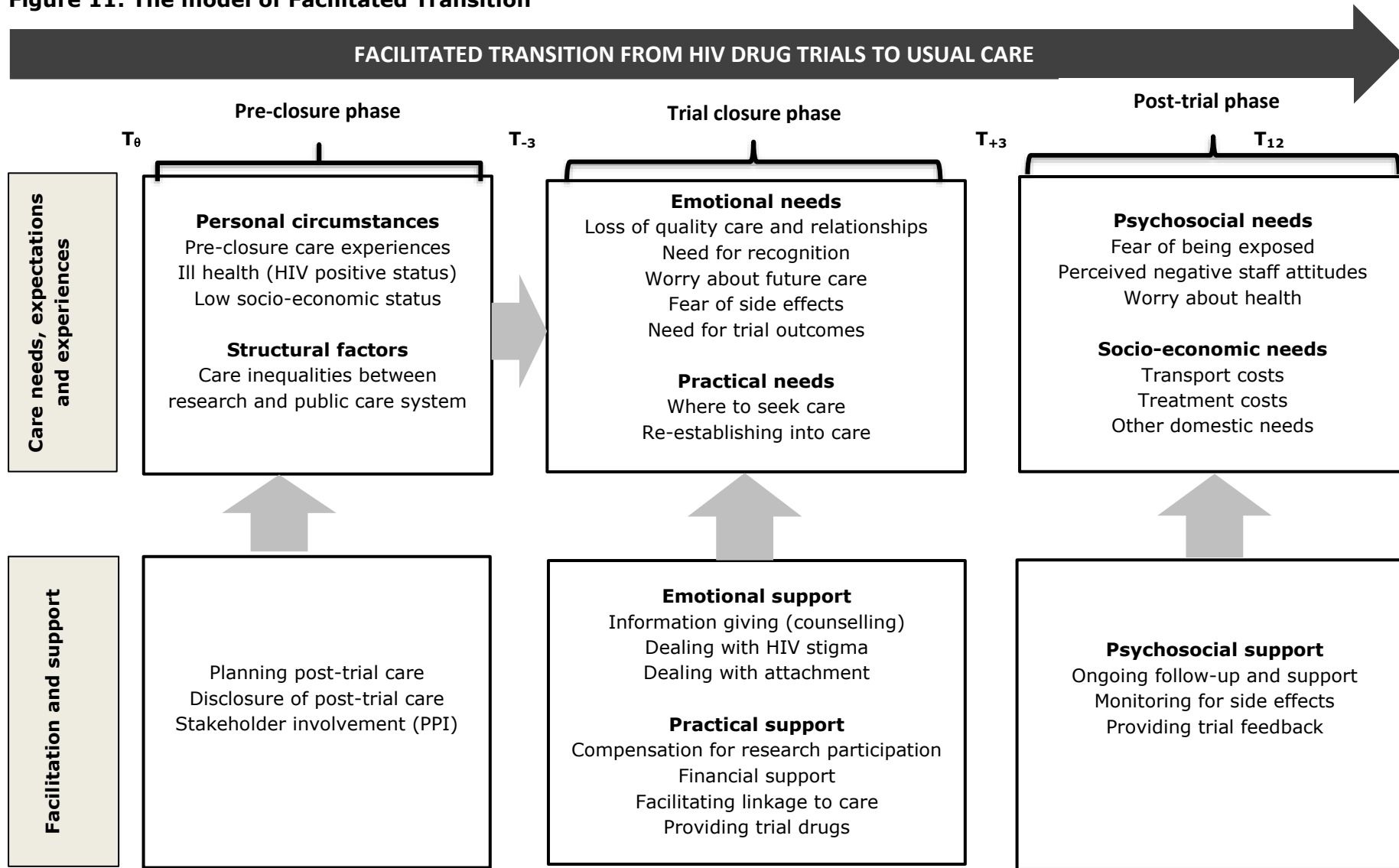
Furthermore, health system and structural factors such as the care delivery gap between research facilities and the Ugandan public healthcare system significantly influenced how trial participants experienced and acted during the transition. The research facilities and the Ugandan public healthcare contexts were described by respondents as 'two different worlds' in terms of service care provision, with research being perceived to offer exceptionally higher standards of care compared to the public healthcare facilities. The main care gaps between these two contexts were identified in: the quality of the general medical care such as the ability to appropriately diagnose and treat HIV related problems, the availability of HIV treatments (especially for opportunistic infections), staff attitudes and approaches towards HIV patients, time management, privacy, and the provision of incentives such as food or transport facilitation. For the majority of trial participants, leaving research meant moving from a more to a less desirable position.

The findings of this study appear to suggest that trial participants move through various phases of the trial closure experience. These phases include: (1) the pre-closure phase which represents events occurring before the actual trial closure but that underpin post-trial care, (2) the trial closure phase which is the active phase of the closure in which trial participants are prepared and exited from the trials, and (3) the post-trial phase which represents events occurring after trial participants have been linked to post-trial care facilities until 12 months later. These phases are demarcated by specific time points, which reflect how the transition process evolves, proceeds and concludes. At the various phases of the process, specific concerns (care needs) arise, being influenced by the various factors explained above. Specific actions are required to support trial participants during these phases. These actions are underpinned by the perceived ethical and moral responsibilities of the research team, and are principally aimed at establishing a continuum of HIV care and treatment after trial closure, promoting positive care experiences for trial participants during the transition, and enabling the settlement and adaptation of trial participants to the care in the public healthcare system. A Facilitated Transition model, which summarises the transition process is explained in more details in the following section.

10.2 The model of Facilitated Transition from HIV drug trials to usual care

The Facilitated Transition model (figure 11 below) represents the transition journey of HIV positive trial participants from research to usual care facilities. The model provides a conceptual framework which helps in the understanding and interpretation of the findings of the current research. It provides important insights on what it means for HIV positive trial participants to leave research in a low income setting, and how they can be supported. A key issue that has been highlighted is the understanding that the process of HIV trial closure involving HIV positive people starts before, and extends beyond, the actual exit of a participant from the trial, as shown in the model. The model reflects the different phases of the transition process, the main concerns and care needs of trial participants, and the actions which may be required to meet the needs of the participants. The model also illustrates how the key issues and phases influence or relate to one another. By illustrating the concerns and needs of the participants, and suggesting possible support approaches to address these, the model can thus be useful for researchers in the planning and provision of post-trial care for HIV positive trial participants in Uganda and related settings. In addition, by illustrating the relationships between the different concepts, the model highlights some propositions for further research in the area of study. The three phases of the model are explained in detail below.

Figure 11: The model of Facilitated Transition



10.2.1 The pre-closure phase

According to the findings of this research, the pre-closure phase consists of the events which occur before the actual exit of the participants from the trials, but which have an impact on post-trial care. This phase represents the underlying contextual factors which influence participants' post-trial care needs, expectations and experiences. These include: participants' pre-closure care expectations and experiences, individual factors such as having ill health and being of a low socio-economic status, plus structural factors such as the inequalities in care provision between research studies and the general health care facilities in Uganda. The pre-closure phase also includes activities undertaken by researchers to prepare the required care. The pre-closure phase starts before or during planning of the trials up to three months to the actual exit of the participant from the trial (**T₀-T-3**).

In this research, the pre-closure events which were relevant to post-trial care included trial participants' experiences of care in previous (or the public) health care facilities, care experiences during participation in previous research studies, and care experiences during the conduct of the current trials. The pre-closure care experiences impacted on the care expectations, experiences, and decision making process of the participants during trial closure, with aspects such as financial benefits, provision of trial feedback, and the choice of post-trial care facilities mostly affected. For example, participants who had received financial benefits from previous research had higher expectations of these in the current trials, while those who did not receive trial feedback from previous research had less expectation of this in the current trials. Although limited, some evidence suggests that previous experiences can play a role in what people may expect in future care (Tarrant, Colman, & Stokes, 2008).

Many participants considered their previous care experiences while deciding where to go for care. They were also largely influenced by the care inequalities between clinical research facilities and the usual care facilities (Clouse et al., 2010) in Uganda. For example, a considerable number of participants expressed fears and anxieties about their care after leaving research, as they were concerned about the 'poor quality' care in the general healthcare system. This finding agrees with previous evidence which indicates that upon closure of healthcare programs, people tend to express concerns about future care (Williams et al., 2003). Due to these concerns, the majority of these participants changed their pre-trial care facilities (to avoid the poor care), and many chose to remain within the facilities attached to research, with expectations of receiving better quality research related care. In contrast, those who reported 'good' care

experiences from their pre-trial care facilities did not express much anxiety about the trial closure and also appeared happy to return to these.

In addition to previous care experiences, the individual life contexts of the participants such as their socio-economic or the health status were important factors in influencing the care expectations, needs and experiences during trial closure. For example, many participants with ongoing infections during trial closure were worried about how they were going to receive care after they left research. These worries were also significantly associated with the poor social-economic status of the participants and the perceived 'poor' quality of care in the Ugandan public healthcare facilities.

The pre-closure phase also involved the preparation for post-trial care by the research team. This mainly included the planning of post-trial care activities such as: how participants will be exited from the research, where they will be linked for post-trial care, how trial drugs will be provided, and when/how trial results will be disseminated. However, despite evidence of planning for post-trial care, this research established that currently, the care planned was not meeting the post-trial needs of the participants. The findings established that although most aspects of post-trial care were reflected in the ethical guidelines, these lacked details of how they could be enacted, they were unspecific to the HIV positive situation and the low income context, and did not accommodate some important aspects of the care needs, weaknesses several authors (Ciaranello et al., 2009; Dainesi & Goldbaum, 2011; Sofaer & Strech, 2011; Wang & Ferraz, 2012) have also identified in research regulation. These findings highlighted the need for adequately identifying and planning for the various post-trial care needs of the participants and suggested the need for involving various stakeholders such as participating communities and the ethics authorities in the planning process.

Lastly, the pre-closure phase involved disclosure of post-trial care plans to the participants during the informed consent process and continued during normal clinic visits. This was particularly an ethical requirement for eliciting an informed consent from the participants as noted in literature (Ciaranello et al., 2009; Jefferys, 2013; World Medical Association, 2013), but was also intended to psychologically prepare the participants for trial closure (Sofaer et al., 2009), which acted as a coping mechanism to the closure for some participants. Understanding this pre-closure phase is highly relevant in predicting the care expectations and needs of trial participants, which can be helpful in the planning and implementation of post-trial care.

10.2.2 The trial closure phase

The trial closure phase describes the events which occur around trial closure, and includes the active trial closure activities such as psychological preparation, and exiting and linking trial participants to post-trial care facilities. The findings of the study suggest that this period begins three months to the planned exit of a participant until three months after the exit (**T-3-T+3**), although the exact time could vary depending on individual circumstances. This research established that during the trial-closure phase, trial participants went through changes which impacted on their psychosocial, economic and emotional wellbeing. Such negative impacts have also been noted in previous trials, being associated to a lack of proper preparation of individuals during closure of healthcare related programs (Hekmatpou et al., 2010). The impacts of the closure upon trial participants were largely associated with the events occurring during the pre-trial phase. For example, perceptions of poor care in the public healthcare facilities, previous research and care experiences, and the care provided during the current trials influenced how trial participants reacted to the closure and how they made their choices, such as where to go for post-trial care (as explained in the above section). In addition, the individual socio-economic and health situations of trial participants were important factors influencing how they reacted to the closure or experienced this phase.

Nonetheless, the impacts of trial closure on the HIV positive trial participants were predominantly negative and were attributed to seven main factors which included: a sense of loss of the quality care in research and of the valued relationships, uncertainty about future care, uncertainty within the decision making process of where to go for post-trial care, fear of difficulties during linkage to post-trial care, the need for recognition for their participation, the fear of possible negative effects from trial interventions, and a lack of awareness of the trial outcomes. These are explained in more detail below.

Loss of the quality care and valued relationships, and the need to find alternatives

Research related care was considered to be of an exceptionally high standard compared with the general care in the Ugandan public healthcare facilities, this being shaped by trial participants' perceptions and previous care experiences in these facilities. The majority of trial participants had been in research for over three years. Losing the high standard of care after such a long time period, and which was unlikely to be matched by the available alternatives was stressful and often created fear and uncertainty among the participants. Loss of quality care in research (Chang, 2002; Stephenson et al., 2008), and the need to find alternative care has been identified as a particular need for

individuals with health related conditions requiring ongoing care, for example after being terminated from care programs (Grady, 2005a; Williams et al., 2003). In addition, as shown in other existing literature (Fragkiadaki & Strauss, 2012; Mirabito, 2006), the relationships developed during the research period left an emotional gap when the research ended. Participants required to make careful considerations while deciding their next care facilities, with factors such as the availability of the trial drug, perceptions of the general care in a facility, the distance to travel, and the fear of HIV stigma playing a major role in this decision making process. Furthermore, some participants were particularly concerned about the difficulties involved while linking to the post-trial care facilities, some of which were 'anticipated' while others were based on experience. As related literature suggests, linking to care e.g. from HIV testing to HIV care (Cargill, 2013; Fortenberry et al., 2012) or from care homes to other alternative facilities (Williams et al., 2003) has been found to constitute remarkable challenges which necessitate facilitation. These findings suggested the need for emotional support for the participants to deal with their emotional concerns, and practical support during linkage and establishing into post-trial care.

The need for recognition (compensation) and financial support

Many trial participants expressed disappointment at not being appreciated or compensated for their efforts to participate in and complete a research trial. Some participants reasoned their need for compensation on (1) an ethical basis, arguing that the risks and inconveniences undertaken in research, and the time lost while attending clinical trial visits deserved compensation, a finding supported by other authors (Draper et al., 2009; Grady, 2005b; Kwagala et al., 2010) as elaborated in the discussion chapter above. Those with previous research experience and those who joined research with good health (and therefore were capable of undertaking productive work) were more likely to express the need for compensation based on the above reasons. On the other hand, some participants expressed the need for compensation (2) based on practical realities (financial support to meet the now increased financial needs after leaving research, such as the purchasing treatments for opportunistic infections, meeting transport costs to facilities, and for some, attending to other domestic needs) also quoted in previous literature (Stephenson et al., 2008).

Participants who joined research while very ill, and those with ongoing ill health at the time of trial exit were likely to express these concerns more than others. These findings suggested the need for consideration of the ethical/moral obligations of researchers, in regard to compensation or offering financial benefits, with particular attention to HIV clinical trials undertaken within low income settings.

Fear of possible side effects and the need to know the trial outcomes

Trial participants expressed fears related to side effects from trial interventions. Some believed that it was risky to leave research with no plans for monitoring for these. These fears were largely associated with the lack of trust in the public healthcare facilities, in adequately identifying and managing these effects if they occurred. The fear of possible side effects was also associated to having left the trials without being informed of the trial outcomes. Some participants strongly expressed the need to know the general trial outcomes such as how the research question was answered, while others expressed the need to know more personal trial outcomes such as how their own health had changed during trial conduct, concerns which have also been quoted from previous studies (Dixon-Woods et al., 2006; Fernandez et al., 2009). Leaving research without knowing trial outcomes increased fears associated with the unwanted effects of the trial interventions, while some participants felt that not knowing the outcomes could be risky in managing their health. Participants who joined research with ill health appeared to desire more the personal trial outcomes while those with good health appeared more interested in the more general outcomes. These findings suggested the need for clear communication and timely provision of trial outcomes. In addition to providing the general trial outcomes as the current guidelines recommend, these findings also suggested the need to put an emphasis on the provision of individual trial outcomes to participants (Cox et al., 2011; Moutel et al., 2005).

10.2.3 The post-trial phase

The post-trial phase describes the events which occur after a trial participant has been linked to post-trial care (approximately three months following trial exit) up to 12 months later (**T₊₃-T₁₂**). This phase relates to how HIV positive trial participants adapted to their post-trial situation, by seeking HIV care and treatment within the Ugandan public healthcare system. Seeking post-trial care for most participants was associated with having to face undesirable conditions such as clinic delays, lack of adequate medications (especially for the treatment of opportunistic infections), lack of privacy, and unwelcoming staff. These conditions appeared to be the direct opposite of those in the research setting where the care was usually of a high standard, with less clinic delays, free and adequate treatment, participants mostly attended to in privacy, and research staff considered very friendly and caring. In addition, during research, participants were provided with incentives such as transport facilitation and sometimes food, which were very helpful to those with a low socioeconomic status, (which were the majority of the participants included in this research).

The change in the care experienced by participants upon leaving research had significant psychosocial, economic and health implications, as has also been observed in previous studies (Stephenson et al., 2008). For example, trial participants now had to find their own transport fees to facilities, had to buy their own breakfast and sometimes required to buy medications (especially for opportunistic infections). In addition, a lack of privacy in the public healthcare facilities was a threat for people's confidentiality, especially to those who still experienced HIV stigma, a situation which was particularly important to those with limited HIV care experience prior to joining research. Furthermore, the negative staff attitudes were unpleasant for the participants and sometimes resulted in poor health management behaviors such as self-medication. Participants with ongoing ill health appeared to be more significantly affected by the transition, as these were unlikely to be working, yet required more finances (e.g. to buy medications or had specific food requirements). Challenges faced in seeking HIV care have been associated to negative impacts in literature, including some individuals withdrawing from care and possible death (MacKellar et al., 2016; Mugavero, 2011). As some authors indicate, engagement of previous healthcare providers with discharged patients can be helpful in improving the health outcome of individuals following closure of health related programs (van Walraven, Mamdani, Fang, & Austin, 2004). Thus, these findings suggest a need for researchers to continue to engage with trial participants after trial exit, to offer ongoing psychological, practical, and health care related support. The need for providing financial and material support was also suggested as discussed in details in the previous chapter.

10.3 Theoretical interpretation of the findings

Based on the main concepts of the study as represented in the Facilitated Transition model above, this section seeks to illuminate the study findings further, by providing a more explanatory theoretical interpretation that also takes account of existing theories, especially in the field of research ethics and care.

The Facilitated Transition model was developed based on the findings of this research, to provide a guide for dealing with the needs/concerns of the trial participants as they transition from HIV research to usual care facilities. The model provides an explanation of the main events occurring during the transition process, and what happens to the participants, and proposes various interventions to address the most pressing concerns of the participants, and to meet their needs. The model centres on the need to provide holistic and person centred care to the participants, by endeavouring to provide specific guidelines on how a particular need may be addressed. The main concerns of the participants across the transition journey were: psychological (emotional), practical, and

socio-economic. These require interventions which can deal with each type of concern, putting into consideration, variations in individual trial/participant circumstances.

According to the findings of this research, Care (facilitation) emerged as a key aspect of the Facilitated Transition model. This care is explained as the activities undertaken by researchers, targeted at addressing the individual needs of the trial participants during the transition process. Due to the care gap which exists between research and the public healthcare facilities in Uganda, and because trial participants are moving from a more to a less desirable context, trial closure raises special care needs among the participants. Although these needs may be common to the majority of the participants, these might significantly vary among them thereby requiring a case by case approach, although in consideration of the general guidelines. Hence in this research, good care would be regarded as 'care that takes into account the underlying contextual factors, i.e. peoples' needs, and their ongoing circumstances, and attempts to support participants as they move through the transition'.

The Facilitated Transition model offers a more person-centred approach to post-trial care, by attempting to account for individual concerns of trial participants which arise along the transition process. The model is dynamic, person-centred, and capable of providing pragmatic solutions to the care needs of trial participants in the contexts in which they may be. The theoretical model considers the need for ethical practice, but within a framework which is flexible and context based, giving room for special considerations, instead of being based on rigid-prescribed guidelines. For example, the two particular contexts underpinning this research (being HIV positive and being in a low income context) appear to require special consideration in trial closure practice, as these appear to expose the participants to certain vulnerabilities.

First, being HIV positive makes research participation (or trial closure) different for the affected person compared to the rest of the population. Some participants leave research when experiencing ill health and thus require continued access to medical care and treatment (especially for HIV related infections). This makes them to worry about their care, first, since they had developed trust in researchers, as the majority tend to improve during research thereby attributing their recovery or improvement in health to the research context. Second, the fear of HIV related stigma is important to the HIV positive trial participants as it might affect access to healthcare and their general social life, including work, and relationships (Govindasamy et al., 2012; Tweya et al., 2014). These factors may be less relevant in research involving HIV negative individuals. Hence

in our approach to post-trial care for this group, we need to consider what HIV positive people need, value and consider important to them.

Similarly, being in a low income setting affects trial closure in two major ways. First, the majority of the participants may be incapable of financing their own treatments and meeting their domestic needs. Research usually offers free and high standard care and treatment, and also provides incentives which may be sometimes used by the economically disadvantaged participants in offsetting some of their domestic needs. Second, the public healthcare services in the low income settings do not match the standards of those in research, as opposed to the high income settings where the differences may be minor and trial closure may not pose significant concerns in this aspect. Hence HIV trial closure in low income settings may call for special consideration.

The study findings indicated that the HIV positive situation and being in a low income setting were key vulnerabilities to the population studied and these exposed the individuals to various health risks. These vulnerabilities call for protection of the participants. By being humanistic (person-centred) while also considering the ethical underpinnings of research, one can offer care which is responsive to the needs of the HIV positive trial participants in a low income setting. This also might mean that the caregiver (in this case the researcher) will be open and ready to understand and act on what the affected individuals need, value and consider important to them (Haegert, 2000).

10.3.1 Relationship of the conceptual model with existing theories and care approaches

The findings of this study indicated that trial closure resulted in negative psychological, socio-economic and healthcare impacts for many trial participants. These concerns were often not being addressed in current trial closure practice, despite being recognised as significant by all groups of study respondents. The main reason provided for not meeting such needs was that they were not reflected as policy requirements, and as such, were often not budgeted for. The main recommendation made in response to this practice gap was the need for ethics authorities to include these needs in research guidelines and thus make them mandatory to all trials, so that funders and researchers will always consider them while planning for the trials. These findings strongly illustrate how current trial closure practice depends on stringent guidelines and regulations, with limited room for flexibility in the application of post-trial care, as reflected in how staff persistently referred to the protocol as the standard guide for any post-trial care activity to be undertaken. In the current study, research staff overwhelmingly supported the need for

offering particular care aspects, e.g. post-trial follow-up, but were often limited by resources. A number of them highlighted how 'their hands were tied' to offer aspects of care which were not planned for, despite these appearing very crucial needs for the HIV positive trial participants.

These findings show that the current approach to trial closure aligns with traditional/dominant moral theories such as Consequentialism, Deontology and Virtue ethics (Beauchamp & Childress, 2001; Held, 2005), (as presented in chapter two). These emphasise universality and impartiality (Bloch & Green, 2006), as a benchmark for research ethics and tend to hold with high regard universal ethical principles such as autonomy, beneficence, justice and non-maleficence. However, as Beauchamp and Childress (2001) observe, although it is possible to produce generalisations about how a given research situation may be approached, these principles may not be exhaustive enough to provide a helpful guideline to all research situations. This renders such an approach problematic as the important participants' needs may not adequately be addressed, as observed in the current research.

Conversely, the proposed Facilitated Transition model suggests a more flexible, context-based approach to post-trial care, and aligns with the Ethics of Care theory, which emphasizes the need for context based approach to research ethics (Beauchamp & Childress, 2001; Gilligan, 2011). The Ethics of Care Theory (discussed in section 2.4.3) provided a useful perspective of looking at the findings of this research, by becoming more sensitive to the contextual factors which can affect post-trial care in the population studied. In the current study, it was noted that many aspects of post-trial care which were important to the respondents were not currently being addressed (and were not supported by policy guidelines). Some of these included the need to: support financially poor participants, offer practical support to those going to new facilities, follow-up participants in trials which have potential for long term side effects, and provide interim and individual trial feedback to participants while awaiting the general feedback.

Related to the ethics of care theory (Green, 2012; Lachman, 2012), the Facilitated Transition model suggests embracing a more person-centred approach to post-trial care, which puts into consideration the needs of individuals, and is capable of moving beyond the bureaucratic, rule-based mechanisms which are currently being implemented. What was remarkable in the current study is the way some research staff portrayed an emotional involvement towards the need to support trial participants in particular aspects as they transitioned. Some reported going beyond policy boundaries and offered individualised care to some participants. For example, Jane, a trial coordinator with a

nursing background reported being concerned about how participants could be coping after they left research. Since follow-up was not an activity budgeted for, Jane sometimes did this as an individual. Similarly, Tina, a nurse, reported how post-trial participants occasionally came by and requested for financial help which she sometimes offered. Carol Gilligan, a proponent of the Ethics of Care theory, expressed in an interview that the Ethics of Care helps one to reason ethical issues with consideration of other prevailing circumstances, which helps them to take responsible actions in relationships (Gilligan, 2011), elements which were portrayed by some researchers in the current study. The Facilitated Transition model is therefore suggestive of a more flexible, care-focused approach, whose centre of interest is the 'human being'.

Another important dimension which emerged as representative of the current post-trial practice was the application of a medically oriented rather than a person-centred model. Current post-trial care guidelines and practice appear to be more aligned to the medical model, which emphasises treatment, clinical outcomes and cure rather than providing holistic care (Fry, 1989; Gonzales, 2014). The findings of the current study indicate that current post-trial guidelines put an emphasis on aspects such as the need to provide trial drugs, referral of participants to care facilities, and provision of trial feedback. Although access to the trial drugs was not found to be a major concern for trial participants in the current study (except for second line regimens), current debates and guidelines still put much emphasis on this aspect as elaborated in the discussion chapter. The approach proposed in the current study as represented by the Facilitated Transition model aligns more with a care (nursing) model. In addition to meeting the above ethical requirements, the proposed approach also recognises other context based factors which appear to affect individuals on a personal (or trial) level, which require consideration in trial closure practice.

According to Gonzales (2014), the medically-oriented approach tends to ignore other circumstances surrounding the patient such as the psychosocial, economic, and cultural aspects of an individual, which play an important part in the clinical presentation of a disease, its treatment, and even in recovery. In relation to the current study, trial participants were affected by numerous psychosocial and economic factors which appeared to be important to their access to post-trial care, even with widespread availability of HIV treatments. Some of them struggled with raising transport costs to get to healthcare facilities, some feared taking HIV treatments without adequate nutrition, some were worried about other domestic and social responsibilities, while others had the fear of HIV stigma. These to a large extent were not being addressed by the current approach to post-trial care. Some participants expressed how failure to meet other

pressing needs in their lives could result into HIV treatment failure, even with good adherence to medications. For example, Wilberforce, who lost his job due to ill health and was not working by the time of the interview, considered psychosocial and economic support an important aspect of post-trial care.

Unlike the medical model, the nursing model (also related to the Ethics of Care theory), is more person-centred and puts into consideration other factors surrounding the individual, with emphasis on their mental, emotional, and physical needs and wellbeing (Gonzales, 2014). This approach enables the carer to focus on the entire person and not only the 'disease', which results in the provision of holistic care, and long term solutions to problems (Fry, 1989). The proposed approach to post-trial care highly aligns with the nursing model, by highlighting the need to comprehensively assess and attend to the diverse and sometimes complex post-trial care needs of HIV positive trial participants in the Ugandan setting. The Facilitated Transition model presented above summarises the most important concerns of the participants and also provides a guideline on how these can be addressed.

Although the understanding of care might include a diverse range of opinions, there are common features which are recognised by different commentators. For example, care strongly involves relationships, a need to alleviate another person's vulnerability, and showing concern, empathy and responsibility for others (Green, 2012). These should also be undertaken within an environment of culture, and society, shaped by political and structural realities (Green, 2012; Lachman, 2012 ; Paulsen, 2011), and also practically implemented (Held, 2005; Paulsen, 2011). The proposed approach, as reflected in the Facilitated Transition model tends to recognise most of the named features of care, by promoting the need to provide individualised support, towards enabling the individuals to meet their psychosocial, economic and healthcare needs. Thus care forms the basis for the Facilitated Transition model.

Because the two approaches (the current bureaucratic, medically-oriented approach, as opposed to the flexible, person-centred approach supported by the model of Facilitated Transition) significantly differ, these to a great extent may conflict, especially when applied concurrently. The findings of the current study appeared to reveal contradicting scenarios which appeared to pose ethical dilemmas. For example, some researchers felt providing person-centred care e.g. by providing financial support to particular participants could be unethical as this would likely result into undue influence for such participants if they were to take part in future research, which would conflict with the principle of autonomy. On another hand, providing interim trial feedback could possibly

conflict with research regulation in some trials, e.g. by exposing some information which was otherwise supposed to be confidential. Some of these instances could also amount to protocol violations. Hence, although the proposed theory recommends the adoption of a more person-centred approach to post-trial care, the potential for ethical conflict cannot be overlooked. Therefore, it is suggested that further research and debates be undertaken in this area.

10.3.2 Transferability of the conceptual model

The model of Facilitated Transition is primarily intended to guide the practice of closure of HIV drug trials involving HIV positive individuals in Uganda, by providing flexible guidelines which can be applied to different HIV drug trial contexts and geographical settings in Uganda. These guidelines can however be applicable in other situations which share related characteristics to the current study which may include: HIV drug trial closure in other low income settings, transitioning of post-trial participants with other chronic illnesses such as cancer, transitioning of individuals hospitalised for long periods and re-establishing into the community/other healthcare settings, and settling of other groups of individuals in the community e.g. from prisons. However, because of its flexibility, some aspects of the model may be more applicable to given situations than to others.

10.4 Conclusion

The model of Facilitated Transition suggested in the current study provides guidelines which are helpful in implementing a person centred approach while providing post-trial care to HIV positive people in a low income setting. This care is human-centred and should put into consideration the participant's everyday care needs, which are essentially influenced by: a pre-existing socio-economic and structural context, needs associated to accessing continued HIV care and treatment, and current practical realities of moving from one and a different care context. The proposed approach to post-trial care is likely to result into favourable outcomes for the participants, such as psychosocial, economic and health wellbeing and positive post-trial experiences.

The proposed approach in this study considers the need to implement research ethics while putting the individual care needs of trial participants at the centre. According to Fry (1989), caring ought to be the foundational value for any ethical theory, and therefore as a moral value it should never be excluded in ethical reasoning. In other words, research ethics in general, and specifically post-trial ethics needs to embrace other perspectives, to adequately meet the post-trial needs of individual participants. After all, as Haegert (2000) comments, meeting the human needs in itself is ethically

fundamental. The findings of this research strongly suggest a need to evaluate the current HIV trial closure practice in Uganda and other related settings. There is also need to test the proposed model in other contexts, for example, on larger samples of participants, from other geographical locations or on other disease situations.

The next and last chapter provides an overall summary of the research, and highlights the key contributions of this research, identifies the main areas of recommendations for improving post-trial practice, further research, and education.

CHAPTER 11: CONCLUSIONS

11.1 Introduction

This last chapter provides a summary of the study findings. First, the key contributions made in the area of HIV drug trial closure in Uganda are presented. The implication of the research findings to policy and practice, the implication for the role of the research nurse, the implication for education, and the implication for future research are also presented. Finally, the study limitations and strengths are explained.

11.2 Summary of the key contributions

The current study aimed to explore how care is perceived and enacted in HIV drug trial closure in Uganda, by addressing the following specific objectives:

1. From the perspective of research participants and research staff, to establish the views, opinions and understandings of the ethical/legal/moral post-trial obligations in HIV drug trials.
2. From the perspective of research staff, to explore the experiences, practices and processes related to care for HIV drug post-trial participants in a low income setting.
3. From the perspective of research participants, to explore the experiences of care at trial closure.
4. From the perspective of research participants, to establish the experiences of transitioning from HIV research to care/community.

This study adopted an interpretive approach and employed a social constructivist grounded theory design, which provided explicit but flexible analytic guidelines, that directed the researcher in data collection, analysis, and conceptualisation (Charmaz, 2006). The study included a total of 21 trial participants and 22 research staff from three HIV drug trials. In addition, relevant ethical documents were reviewed from two of the included trials. Details about the sample and trial characteristics are provided in chapter five of this thesis. Data collection and analysis followed the principles of grounded theory, with data collection and analysis undertaken concurrently, and earlier data informing subsequent data collection. NVivo10 software was used to manage the data.

The findings of this study indicated that trial closure was often stressful for the HIV positive participants, and often resulted in negative psychological, socio-economic and health impacts. The negative effects mainly resulted from being terminated from research related care, which was of significantly higher quality to that provided in the general healthcare system in Uganda. The main concerns which arose during the transition process of participants from HIV drug trials to usual care facilities include: the

loss of the quality care and valued relationships in research, the need to find and link to alternative care facilities, the need to meet the increased financial needs, and worries about the effects/outcomes of research participation. These concerns demanded for a range of additional care and supportive strategies from researchers (and other stakeholders), these being shaped by the perceived ethical and moral obligations of the researchers to the participants. A conceptual model of Facilitated Transition was introduced, to provide a theoretical representation of the research findings. The key contributions of this research in the area of HIV drug trial closure are presented in the sections below.

11.2.1 The meaning of trial closure/post-trial care

Generally, in HIV drug trials involving HIV positive participants, trial closure has been understood as when trial participants are exited from trials, while post-trial care has been assumed to mean: the provision of trial drugs after trial closure, referral of trial participants to alternative facilities, and the provision of trial feedback. The majority of debates and policy guidelines in HIV (and other) research also mainly focus on these areas as researchers' primary post-trial obligations. The current study has significantly expanded on the understanding of trial closure and post-trial care in HIV drug trials involving HIV positive people, by describing trial closure as a process rather than a one off event, and by uncovering other important aspects of post-trial care, which require to be incorporated in HIV drug trial closure debates, policies, and practice. In addition to the already existing aspects of post-trial care mentioned above, this study has also established that post-trial care should include strategies to: assess and address the psychological and socio-economic needs of trial participants, provide practical support during linkage to post-trial care, and offer post-trial follow-up care and monitoring of trial participants. The Facilitated Transition model presented in previous chapter explains the process of transitioning from HIV research to usual care facilities (or the community), and shows how different factors relate and/or influence one another during the process. The model also provides timelines which demarcate the key phases of the transition process, with a specific finding/recommendation that trial closure/post-trial care should end after 12 months following exit of a participant from the trial.

11.2.2 Influence of previous care exposure

This research has established that participants' post-trial care expectations, needs and experiences are strongly influenced by their *pre-trial* care experiences, which may include their care experiences during previous research or within their care facilities or the general healthcare system. For example, in the current study, the care experiences

in the general healthcare facilities or the pre-trial HIV care facilities influenced how trial participants reacted to the closure and made choices of where to go for post-trial care, with those with negative care experiences tending to avoid them, while those with good experiences being more willing to return to these. In addition, participants with prior research experiences showed specific care expectations, for example, of financial benefits in the closure of the current trials. These findings highlighted the importance of understanding potential participants' backgrounds and their expectations and needs of post-trial care, prior to their participation in HIV trials.

11.2.3 Research regulation

The current study has expanded on the exposure of a gap in research regulation in general, whereby current policy guidelines are deemed to be too generalised and fail to emphasise key aspects of research ethics which appear essential to other stakeholders. Specifically, the current research has highlighted a lack of focus on post-trial care in policy regulation, with generic guidelines, which are not specific to HV research and also appear to target a global context. HIV drug trials in the low income settings may face particular challenges as the current study suggests. In addition, even where guidelines exist on some post-trial aspects, these seem to provide very limited information to adequately guide practice. For example, some regulatory bodies point out the importance of continued post-trial care and follow-up following trial closure for an appropriate period of time (UNCST, 2007, 2014a), but do not state what type of care and for how long this should be done. The current study has provided some helpful insights in this area by suggesting the most important areas of focus for post-trial care and the possible length this could be implemented.

In addition, this research has established that limited attention is paid on describing post-trial care in the ethical documents. Most importantly, the information on post-trial care is poorly reflected in the documents required to elicit informed consent from trial participants such as the participant information sheets or the informed consent documents, which highlights a gap in the informed consent process. The findings of this research suggest that disseminating or clarifying post-trial care information to potential participants is an ethical requirement and should be a key part of the informed consent process.

11.2.4 Linkage to care processes

This research shows that in current practice, participants are linked to post-trial care mainly through a patient-led (passive) referral system. Although it was established that

passive referral could be sufficient for some groups of participants, it alone may not be suitable for others. For example, the findings suggested that those going to completely new facilities, or those returning to facilities in which they had been detached for a significant period of time may require more facilitation to re-establish in care, while those who retained contact with their facilities could require a less facilitated approach. A facilitated, researcher-led linkage to care model, involving physical handover was suggested in the current research, and this appeared to align with the models found effective during linkage to care after HIV diagnosis (Mugavero (2011); Gardner et al. (2005). These findings indicated the need to assess individual trial/participants' circumstances and needs while linking them to post-trial care.

While previous debates and deliberations on post-trial access have focused on how post-trial participants can access trial drugs, the current study has highlighted that HIV positive trial participants in a low income setting are also concerned about access to general care, including their relationships with healthcare workers, privacy concerns, and access to treatments for opportunistic infections. These findings exposed how current post-trial care practice does not meet individual participants needs due to its 'medically oriented' approach which focuses on the need to offer medical treatment. The current study suggested a more flexible 'care oriented' approach, represented by the model of Facilitated Transition, targeted at addressing the various care needs of HIV positive trial participants in a low income setting.

This research suggested the need for follow-up care, to support participants psychosocially, to confirm linkage to care, and to establish that participants are continuing with the rightful treatments. An important concern/barrier to post-trial follow-up regards the need for resources such as finances and time. The findings of this study suggest that although researchers may be responsible for ensuring follow-up, this can be done indirectly, e.g. through collaboration with other stakeholders such as healthcare workers in the public facilities where trial participants seek post-trial care, or using telephone communication to reach the participants, as these approaches have been found to be effective in follow-up for other healthcare programs (Ashengo et al., 2014; Eng et al., 2013; Tweya et al., 2014).

11.2.5 Post-trial monitoring

Whilst current policy and debates underscore the importance of monitoring for side effects and addressing these if they occurred, much effort seem to focus on those side effects which occur during trial conduct. There appears to be very limited guidelines or focus on side effects which may occur after participants have been exited from the trials.

The current study has pointed out a need for attention to the side effects which are likely to occur after trial exit. This may be an important issue for intervention trials which have not been extensively studied or where researchers anticipate some long term effects. Whereas there is some recognition for these in some trials, this appears not to be an area of much focus in current policy guidelines, which can leave room for lack of action even in trials where unwanted effects are possible.

11.2.6 Financial and other research benefits

The current study has expanded on the debate concerning financial benefits in research by highlighting that participants in the low income settings desire recognition of their time, commitment, inconveniences and sacrifice in research, and therefore expect to be compensated for these. Although comprehensive literature exists on these issues, much of this has focussed on non-HIV research or included general community views on hypothetical scenarios, unlike the current study which reports the needs and experiences of actual trial participants. The current study has further highlighted that although non-monetary benefits could also be acceptable, for those in a low income setting, financial or food items could be more appreciated as these seem to directly address their immediate needs.

The findings of the current study further suggested that due to their contribution in research, and also due to their socio-economic needs, researchers may have a moral duty to ensure that participants are discharged from the trials with some form of economic support or provide continued financial support to them during the post-trial period, to ensure that they are able to continue their HIV care and treatment even after leaving research. This could be done by researchers specifically budgeting for and funding such an incentive, or in partnership with other stakeholders such as national or local institutions, groups and organisations, which may be available and willing to offer such support.

11.2.7 The need for timely and personal trial outcomes

Although the area of trial feedback has been relatively well studied, this has been primarily in fields other than HIV or in the context of hypothetical scenarios. This appears to be the first study to investigate issues of trial feedback among actual HIV trial participants. The findings established that HIV trial participants want to know the outcomes of the study in order to: ascertain the impact of the research on their own health, allay fears and anxieties associated to possible effects of the trial interventions, and enable them to understand the general outcomes of the trials in regard to the

research aim. While the general outcomes were of interest to the participants, there was a specific need for participants to be informed of more personal outcomes such as treatment arms and health markers such as CD4 count levels. In addition, participants wished to receive trial feedback in a timely manner.

11.2.8 Stakeholder involvement in post-trial care

The need to involve a range of stakeholders in post-trial care of HIV positive participants in Uganda emerged as a key finding in the current study, as the different aspects of post-trial care identified as necessary in this research could not be easily implemented by research staff. The findings suggested the need to involve stakeholders in the different post-trial care aspects including: the planning of post-trial care, providing psychosocial support, linking participants to care and facilitating continuity of care, follow-up and monitoring, and financial support and empowerment. However, ethics authorities appeared to have a key role to play in post-trial care. By their role as the ethics enforcing authorities, the current study suggested that their input would be important by streamlining policy guidelines on post-trial care and enforcing these in HIV research practice.

11.2 Implications of the research findings

The findings of this study provide helpful insights towards the improvement of post-trial care for HIV positive trial participants in Uganda and possibly in other related settings. The model of Facilitated Transition is a major contribution of this research, and provides novel contributions in the field of HIV research. The model offers a flexible framework which can be applied to HIV clinical trials involving HIV positive individuals in low income settings. Since HIV is a global phenomenon, the proposed guidelines to HIV post-trial care should be of interest to local, national and international researchers, research funders and donors, and other concerned bodies and persons in the field of HIV research. Recommendations to improve practice and education, the role of the research nurse, and gaps requiring further research are provided below.

11.3.1 Implications for practice

The need for early planning/budgeting is emphasised in all aspects of post-trial care, as the majority of these require finances to be implemented. Involving different stakeholders, including the public facility workers, the government, local and international organisations, and the participating communities is essential. In addition, due to the likely influence of past care/research experiences, researchers may need to understand the research participation history of the community, and also assess the

post-trial care needs and expectations of the potential participants, to help plan for these.

This research suggests the need to streamline the dissemination of relevant information to the participants. All relevant post-trial care information must be disseminated to potential participants during the informed consent process. Particular attention should be paid in reflecting such information in the documents used to elicit the informed consent from potential participants. Furthermore, the information needs which arise during the trial closure phase and afterwards should be appropriately addressed.

The findings of the study further indicated that various psychosocial concerns arise during trial closure and beyond which require support from researchers and other stakeholders. Researchers should ensure that these concerns are adequately addressed by themselves or through collaboration with other stakeholders. Stigma identification and reduction strategies are required during the transition period, and this may be more important for trial participants who acquire HIV during research and those who join research immediately following HIV diagnosis.

To ensure appropriate linkage of trial participants to their chosen care facilities, this research suggests that researchers employ additional strategies of facilitating the participants, since significant difficulties may be faced during the transition. Those going to new facilities, those who did not retain contact with their facilities during trial conduct, those who acquire HIV during trial conduct, or those joining research before accessing any specific HIV services may require special facilitation. Facilitated linkage to care models such as using physical hand over have been suggested both in literature and in the current study and need to be implemented.

While the need to ensure access to trial medications remains, researchers need to pay more attention in trials testing second or third line regimens, considering the widespread availability of prophylactic and first line HIV medications in many low income settings. However, ensuring access to all HIV services should be targeted, even though this might require the participation of other stakeholders.

The current study also suggests that due the socio-economic burden faced by HIV post-trial participants in Uganda, these may require financial and material support during the transition process. This support may be of particular importance to participants who may be experiencing ill health, or those with no source of income. It might be of great

relevance for researchers to liaise with other stakeholders who may be in position to provide this support.

The need for researchers to continue engaging with post-trial participants after exiting from the trials is a major recommendation of this research. As presented in previous sections, researchers may need to follow-up trial participants for: establishing whether these are appropriately linked to care and are receiving the rightful treatments, are psychosocially and practically supported, and are monitored for possible side effects from trial interventions. Researchers should ensure that follow-up activities are properly planned for during trial set up. As the findings of this study suggest, researchers should engage with post-trial participants for a period of 12 months post-trial at the minimum, although this period can vary depending on the individual needs of the trial/participants. For example, trials which are likely to have long term effects beyond 12 months may require a longer follow-up period. This means that individual trials will require an assessment for potential risks and advance planning on how these will be monitored.

Finally, the findings of the current study suggest the need for ethics authorities to review the need and possibility of inclusion of more post-trial care aspects (in addition to those currently being practiced) such as: a more facilitated linkage to care process, follow-up activities, and financial support. The role of ethics authorities is fundamental in enabling a standardised approach to post-trial care across different HIV drug trials, and will hopefully address the needs of the participants. Ethics authorities should ensure that there is clarity on how specific post-trial care aspects should be approached.

11.3.2 Implications for the role of the research nurse

The role of research nurses is very essential in contributing to the ethical conduct of clinical research (National Institutes of Health Clinical Centre (NIHCC), 2010). Like in clinical care, research nurses interact more frequently and more freely with participants than other research staff, which provides an opportunity for them to support the participants. In addition, nurses are equipped with counselling, care, and support skills which are essential in addressing the care needs of trial participants which arise during the research process, and their significant role has been associated with improved quality of clinical trials (Spilsbury et al., 2008). The current study has identified various post-trial care needs of the participants which are central to the research nurse's role. These include the need for: appropriate and adequate information about post-trial care, psychosocial support and guidance during trial closure, financial assessment and support, guidance on where to seek post-trial care, and ongoing follow-up and support during the post-trial period. Although these may not be done by research nurses alone,

they can contribute towards the post-trial wellbeing of the trial participants. Moreover, the theory developed in this research supports a nurse based model of care, which aims to respond to the various care needs of trial participants during their transition journey. This further emphasises the role of the research nurse in post-trial care.

11.3.3 Implications for education and training

Due to the specific care requirements of research, which require the care provided to research participants to take into account the study requirements as well as clinical indications and patient care needs (Grady and Edgerly, 2009), nurses and other research staff may require additional or specialised training about HIV care in general, HIV research ethics, and more specifically post-trial care. Such training may be incorporated in the pre-practice training programmes for nurses and other professionals, or can be provided as an induction programme before research activities are commenced. In addition, the findings of this research suggested that healthcare workers in the public facilities may be required to offer specialised care to post-trial participants, in an effort to extend post-trial follow-up care and monitoring. This will require that these are trained in some basic research ethics, and also on how they can offer support to the participants when they return to these facilities, depending on the needs of the individual trials. Meeting these training needs may require a collaborative effort between various stakeholders such as the government, the relevant ministries, and the researchers.

11.3.4 Implications for research

The current study generated important propositions to explain the phenomenon of post-trial care in the Ugandan setting. However, since the study employed smaller numbers of participants, a large quantitative study with larger numbers of participants and from various trial and geographical contexts is required, to verify some of the concepts identified in the Facilitated Transition model and their relationships. This will be important to validate the findings of this research and increase their generalisability. The Facilitated Transition model could also be tested in research involving other chronic illnesses such as cancer and Tuberculosis. In addition, the current study undertook a retrospective approach which limited interacting with the participants while undergoing some of the trial closure experiences. Undertaking a longitudinal-prospective study during the transition process will be required, to minimise possible biases such as the recall bias, and to provide a more in-depth understanding of the events as these are assessed around the contexts in which they occur.

To date, there has been no longitudinal prospective research to assess the outcomes of HIV positive drug trial participants following trial exit, despite the likely challenges associated to linkage to care which might affect this process. Research to ascertain the rates of linkage to care, and to assess the health outcomes of post-trial participants following trial exit is required. Additionally, the current study has suggested a researcher-led model of facilitating linkage to care, through mechanisms such as physical support and handover of trial participants to their next care providers, to eliminate possible barriers to linkage and to improve their experiences during the transition process. Such a model has been tested in linkage to care after HIV testing and found effective and could be tested in a research context.

The current study only included post-trial participants and research staff yet other stakeholders have been found to be essential in the transition process. A study to target the views of other key stakeholders, such as the public healthcare facility workers, the family, and ethical bodies on post-trial care is required to understand better the ways in which to support HIV positive drug trial participants in Uganda. Furthermore, although the review of ethical documents generated helpful insights, these were significantly few and covered a limited range of trials. A comprehensive review of ethical documents would be necessary to establish how post-trial care in HIV drug trials is approached among the different trials in Uganda. The need to focus on how post-trial care is reflected in the documents used to elicit informed consent from trial participants is emphasised, to provide a stronger basis for policy recommendations.

Although the topic of financial benefits in research has been widely debated, there is need to deliberate more on the ethical and moral implications of financial benefits in HIV research involving HIV positive participants in low income settings. Further research is required to provide evidence on what is considered appropriate and acceptable amounts of financial incentives in the socio-economically disadvantaged populations. In addition, the need to provide non-financial benefits for compensation of research participation, and the need for continued financial/material support among HIV post-trial participants in low income settings requires further research. A multi-stakeholder approach, involving ethics authorities, researchers, and the communities would be required to contribute to these debates. Similarly, this research has identified a need for the involvement of various stakeholders in post-trial care of HIV positive trial participants in Uganda. Although literature on stakeholder involvement in research exists, much of this has evaluated the role of stakeholders in planning post-trial care. Research on how various stakeholders can be involved in the entire trial closure process is required, including which stakeholders, where, and to what extent these are/should be involved.

Previous research has suggested a possibility of (negative) individual findings causing negative effects to trial participants (Armstrong et al., 2013; Partridge et al., 2009). However, since the current study did not establish this possibility, and since the majority of the literature reviewed in this area does not focus on HIV, further research needs to focus on this aspect in HIV drug trials.

Finally, the current study suggests that the quality of healthcare provided in research facilities (rather than financial benefits) were more desirable by trial participants and may be a major factor for participating in research. Although many debates have focused on the role of financial incentives in influencing research participation especially in low income settings, due to the care gap that exists between research and usual care facilities in these settings, this area merits some attention from commentators. Research assessing the ethical implications of the quality care provided in research in vulnerable populations is mandated to inform ethical research practice in these contexts.

11.3 Study limitations and strengths

11.4.1 Limitations

The study employed a qualitative approach, involving a relatively small sample of participants, to allow an in-depth understanding of the studied phenomenon. Therefore, the data generated represented the views of the studied sample and may not be generalisable, which limits the application of the study findings to the wider population. Nonetheless, the findings provide an initial step in the understanding of post-trial care among HIV positive trial participants in a low income setting, on which further research involving larger samples may draw, to test some of the propositions and relationships among the key concepts as reflected in the Facilitated Transition model.

There was high potential for selection bias in this study, as potential participants were approached through their former research institutions. This meant that only those participants who were easily reachable by the researchers were contacted. In addition, since the sampling technique used was not random, it tended to be exclusive, limiting the inclusion of specific groups of participants, e.g. those who lived very far from research facilities or the hard to reach. As a result, this study only included participants who were in care, leaving out those who might not have accessed further care following trial exit. Further research is required to follow up linkage to care outcomes of a large number of trial participants in selected HIV trials, in a similar context to the current study. Similarly, because potential participants were initially informed about this study by the researchers of the respective included trials, there was potential for the influence

of power, which might have affected participants' choice to participate in research or not. In fact, some potential participants felt that the current study was a continuation of the previous trial, and also felt that I was part of the research team in the previous trials. This might also have affected their responses in the interview, especially as many saw me as an 'insider'. To limit this problem, effort was made to explain to the participants how the current research was different from the previous trials. I also provided my affiliation and explained how the choice to participate was entirely on the participants, and that even if they chose not to participate, their subsequent care would not be affected. Furthermore, my own professional background as an HIV care and research nurse might have influenced how I approached the participants, how I collected and interpreted the data, and how I made the conclusions, as elaborated in the methodology chapter. However, having in mind the potential influence of this factor on the research, I tried to be more pragmatic, by following the principles of grounded theory as much as possible, which might have limited the potential negative impact of my own biases and professional background on the study findings.

The current research was done retrospectively, with some participants being interviewed close to 12 months following trial exit. The data generated relied on the ability of the participants to recall the events which occurred along the transition process, which could affect the findings due to the potential to forget. A similar study, undertaken prospectively might generate more enriching insights into the area of study. In addition, the majority of trial participants had either visited their post-trial care facilities once or twice, while others had not reported to these yet. This might have limited their view of post-trial care experiences. Indeed, there are a number of fears expressed among trial participants about their care in the public healthcare facilities, but which could not be adequately evaluated in the current study since there was limited experiences of the participants in these facilities. A longer term prospective study, lasting for at least 24 months post-trial could provide a broader understanding of participants' post-trial care experiences.

11.4.2 Strengths

In my knowledge, this is the first study to assess the views about post-trial care in HIV drug trials from those closely involved in the research process, i.e. actual trial participants and research staff. Moreover, this study undertook a comprehensive and open approach to understand post-trial care issues, instead of focusing on specific aspects e.g. trial feedback, as many other studies have done. This research provides novel insights in this area on which other researchers can draw to expand on the understanding of post-trial issues in HIV drugs trials. Second, this research adopted a

pragmatic approach, the constructivist grounded theory methodology, which allowed an inductive generation of the key concepts from the data, and also allowed expanding on these through constant comparison, and theoretical sampling and saturation. This approach enabled the generation of outcomes which are grounded in the data, but can also offer an explanatory theory, which helps in the understanding of the transition journey of HIV positive trial participants in a low income setting, from research to usual care.

Although a limited number of participants were included in the study, the study was triangulated, by including different participant groups such as former research participants and research staff. The former trial participants were drawn from three different trials, with different characteristics such as the study objectives and geographical settings, while research staff included different cadres such as clinicians, nurses, counsellors, and home visitors. The study also involved different positions of research staff including trial coordinators and general research staff. In addition, a review of some ethical documents was done. Including a variety of data sources increased the authenticity and trustworthiness of the findings of this study.

Finally, all interviews were conducted either in the English language or Luganda, which is also the native language of the researcher. This means that no translators were required in this research, which minimised possible translation problems. Being fluent in the two languages, the researcher was able to interact freely with the participants and to probe where need arose. This contributed to the generation of rich data.

11.5 Conclusion

This is the first study to determine the perspectives on post-trial care among HIV positive trial participants in a low income setting, from those closely engaged in the research process. This study has provided novel contributions in the area of HIV research ethics and post-trial care in general.

The study has established that trial closure involving HIV positive participants raises significant ethical, moral and practical concerns in the Ugandan context. The findings further demonstrated that current post-trial care practice does not meet all the care needs of the HIV positive trial participants, as existing ethical guidelines on post-trial care seem to put an emphasis on the need to ensure access to trial drugs and provision of trial results, with less attention on other important aspects as revealed in this research. The current approach was viewed to align with the rigid, rule based, bureaucratic approach to research ethics, which emphasises justice, impartiality and

universally applicable principles. In addition, this approach aligned more with the medical model of care, which focuses on treatment of the disease rather than caring for an individual as a whole. The current approach was found to have limitations in addressing the post-trial care needs of HIV positive trial participants in the Ugandan setting.

To meet the post-trial care needs of HIV positive participants in Uganda, a comprehensive strategy was suggested. In addition to the already existing aspects of post-trial care, the new strategy should aim to; address the financial needs of trial participants through financial assessment and support, provide practical support during linkage to post-trial care, and offer post-trial follow-up care, monitoring and support. The proposed approach was represented by the model of Facilitated Transition, which is a novel contribution of this research. The model of Facilitated Transition is a flexible, person centred approach to post-trial care, aimed at implementing research ethics within a context of 'care'. The proposed approach aligns with the ethics of care theory, which values the context in which research ethics is implemented and also values the relationships involved. Furthermore, care being a key tenet of the model of Facilitated Transition, the proposed approach tends to base more on the nursing approach to care, where an individual's various care needs are considered. It is highly recommended that implementing the proposed approach will require involvement of various stakeholders, including researchers, ethics authorities, research funders and donors, public healthcare workers, families, trial participants, and the community. Finally, further research is merited to establish the feasibility of the proposed approach.

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APPENDICES

Appendix 1: Participant information sheets

Information pack for individual interview potential participants

The University of Nottingham,

School of Health Sciences,

Division of Nursing

B Floor, Queen's Medical Centre

Nottingham

NG7 2HA

Title of Study: Care in HIV drug trial closure: perspectives of research participants and research staff in Uganda

Name of Investigator: Sylvia Nalubega, Doctoral Student

Invitation paragraph

Thank you very much for your interest in this study. I am a Doctoral Student at the University of Nottingham and for my thesis I am interested in finding out what happens to research participants when they complete participation in HIV drug trials. Before you decide whether to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends or relatives if you wish. Ask me if there is anything that is not clear or if you would like more information. If you decide that you still wish to take part, you may keep this information sheet. Thank you for reading this.

Background

There is an increase in HIV drug trials conducted in low income countries. After completion of an HIV drug trial, there is a need to ensure that participants (who are HIV positive) continue to access care and treatment, as part of the comprehensive care and management plan for HIV. Some guidelines and policies have been established to guide researchers on how to conduct HIV research, however, there is little guidance on what needs to be done during closure of HIV drug trials. In order to contribute to the ongoing debates and deliberations intended to inform policies to improve HIV research closure

conduct, it is important to find out how the closure process is managed by researchers and how the participants experience the transition period following termination from HIV drug trials. However, to date, there is limited research about the experiences of those who have participated in HIV drug trials, especially looking at the closure period. This study is intended to find out the views, experiences and opinions of people who have participated in HIV drug trials in Uganda, regarding the transition period after completing participation in HIV research, and also to find out how the transition process is facilitated by the researchers.

What does the study involve?

You will be asked to participate in one individual interview. It is likely that each interview will take approximately one hour. The interview will be recorded on an audio-recorder and you may stop the recording at any time that you wish. The audio-recording from the interview will be transcribed by myself and will then be destroyed.

Why have you been chosen?

You have been chosen to participate in this study because you recently participated in an HIV drug trial and you have expressed a desire to be interviewed on your experiences after the study closed. In total, I am hoping to interview 30 people individually.

Do you have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part, you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason.

What does involvement in the study mean to me?

If you agree to take part in this study, you will be asked to provide a day and venue that is suitable for you so that you can be interviewed.

What if something goes wrong?/Who can I complain to?

In case you have a complaint on the way you have been treated either by myself or anything to do with the study, you can initially approach my lead supervisor (Dr. Catrin Evans, Telephone 0115 8230894, E-mail catrin.evans@nottingham.ac.uk). If you are still not satisfied, you should then contact the TASO Research Ethics Committee secretary (Mr. Stephen Okoboi, telephone +256 752 774 152, email okobois@tasouganda.org).

Will my taking part in this study be kept confidential?

All information which is collected about you during the course of the research will be kept on a password protected database and is strictly confidential. Any information about you which leaves the research unit will have your name removed so that you cannot be recognised from it. As part of my studies, I will be expected to share some of my findings with my supervisors but they will be anonymised and you will not be recognised from the findings.

The only exception to this confidentiality will be if you disclose information which raises concerns about your own safety or about your care either within the hospital, care institution or your own home. If any serious concerns arise, I will discuss these with you where possible and if necessary report them to the appropriate person. I will always

make every effort to contact you and discuss with you any need to break confidentiality in this way before contacting anyone else.

What will happen to the results of the research study?

The results of this study will be published in my thesis and may be suitable for publication in professional journals and presentation in professional meetings and conferences. Any publications will maintain your confidentiality and you will not be identified within any report/publication. If you would like a copy of the results from this research, this can be provided to you.

Who is organising and funding the research?

This study is undertaken with the support of the University of Nottingham where I am undertaking my doctoral study. There has been no external funding for this project.

Who has reviewed the study?

This study has been reviewed and approved by the University of Nottingham, Medical School Ethics Committee, UK and The AIDS Support Organisation Institutional Review Committee, Uganda.

Contact for Further Information

Should you require any further information about this study then you can contact me at:

Telephone: 0755257997 (Uganda)

E-mail: ntxsn11@nottingham.ac.uk

LUGANDA

Ekiwandiiko ekinnyonyola ku kunoonyereza kw'abo abayiinsa okwetaba mu kubuziibwa okw'omuuntu omu

Ettendekero ekkulu ery'eNottingham, e Bungereza.

Essomero erisomesa sayansi

Omwariro gwokubiri, kuddwariro lya Kwini

E Nottingham

Bungereza

Omutwe gw'okunoonyereza: Okulabirira mu kuggalawo okunoonyereza ku ddagala ly'akawuka ka Siliimu: ebirowoozo by'abeetaba mu kunoonyereza n'abanoonyereza mu Uganda

Erinnya ly'anoonyereza: Sylvia Nalubega

Ekituundu ekyaniriza

Webale nnyo okulaga nti wandyetaaze okwetaba mu kunoonyereza kuno. Nze ndi muyizi mu ttendekero ekkulu ery'eNottingham, e Bungereza, era kukiwandiiko kyentekeeddwa okufulumya mu kusoma kuno, nandyagadde okumanya ku ebyo ebifa ku abo abeetaba mu kunoonyereza kw'eddagala ly'akawuka ka Siliimu, mukiseera ngabamalirizza okwetaba mu kunoonyereza okwo. Nga tonnaba kusalawo kwetaba mukunoyereza kuno, kyamugaso ggwe okutegeera lwaki okunoonyereza kuno kugeenda okukolebwa era n'ebyo ebinaaba mu kunoonyereza kuno. Nkusaba otwale ku budde okusoma ebiwandikiddwa wammaanga n'obwegendereza era osobola okubiyitamu nemikwano gyo oba ab'oluganda bo bwoba okyagaadde. Osobola okumbuuza singa waliwo ekintu kyonna ekitategerekeka buluungi oba singa wetaaze okumanya ebisingako ku ebyo ebiri mu kiwandiiko kino. Bwoba osazeewo okwetaba mu nunoonyereza kuno, oyiinza okutereka ekiwandiiko kino. Weebale nnyo okusoma ebiwandiiko kino.

Entandikwa

Okunoonyereza ku ddagala lya Siliimu kweyoongedde nnyo mu nsi enjavu. Abantu bwebamala okwetaba mu kunoonyereza ku ddagala lya Siliimu, kyetaagisa okulaba nti abo abeetabye mu kunoonyereza kuno (abo abalina akawuka ka Siliimu) basigala nga bafuna obujjanjabi n'okulabirirwa, nga ebimu ku ebyo ebiteekeddwa okukolebwa abo abalina akawuka ka Siliimu. Waliwo kko kubiwandiiko ebiragirira abo abanoonyereza ku ngeri y'okukwatamu okunoonyereza ku kawuka ka Siliimu, naye, waliwo biwandiiko

bitono nnyo ebyogeera ku ebyo ebitekeeddwa okukolebwa mu kiseera okunoonyereza ku ddagala lya Siliimu nga kukomekkerezebwa. Okusobola okwongera ku ebyo ebikubaganyizibwako ebirowoozo okwongera okulongoosa ku ngeri y'okukomekkereza okunoonyereza kwakawuka ka Siliimu, kyandibadde kiruungi okuwulira okuva eri abanoonyereza ku ngeri gyebakwatamu ekiseera kino, era n'okuwulira ebirowoozo by'abo abetaaba mu kunoonyereza ku nsonga eno. Naye nokutuusa kati, waliwo okunoonyereza kutono nnyo okukwata ku abo abetabye mu kunoonyereza ku ddagala lya Siliimu, okusingira ddala nga bikwata ku kiseera kyokukomekkereza okunoonyereza kuno. Mukunoonyereza kuno, twagaala okumanya ebirowoozo by'abo abetaaba mu kunoonyereza kw'eddagala ly'akawuka ka Siliimu mu Uganda, ebikwata ku siseera kyokukomekkereza okunoonyereza kuno, era n'okumanya ebyo ebibeerawo ng'okunoonyereza kuwedde. Twagala era okumanya okuva eri abanoonyereza, ebyo ebikolebwa mukiseera kino, era n'ebiroowozo byabwe ku kukomekkereza kw'okunoonyereza ku ddagala ly'akawuka ka Siliimu.

Biki ebinabeera mu kunoonyereza kuno?

Ojja kusabibwa okwetaba mu kubuuzibwa okw'omuuntu omu omuluundi gumu. Kiteeberezebwa nti okubuuzibwa kuno kujja kumala essaawa emu. Okubuuzibwa kuno kujja kutekebwa kukuuma kalikooda, era osobola okuyimiriza ka likooda kano obudde bwonna singa okyagaadde. Ebikwatiiddwa ku likooda okuva mu kubuuzibwa bijja kuwandiikibwa nze, oluvannyuma bijja kwononebwa.

Lwaki olooneddwa?

Olooneddwa okwetaba mukunoonyereza kuno kubaanga emabegako awo weetaba mukunoonyereza okwali kukwata kuddagala ly'akawuka ka Siliimu era n'olaga okwagala okubuuzibwa ku ebyo ebyakutuukako nga okunoonyereza okwo kukomekkerezebwa. Awamu, netaaga abaantu 30 okwetaba mu kubuuzibwa okw'omuuntu omu.

Otekeeddwa okwetaba mu kunoonyereza kuno?

Kiri eri ggwe okusalawo okwetaba mukunoonyereza kuno oba nedda. Singa osalawo okwetaaba mukunoonyereza kuno, ojja kuweebwa ekiwandiiko kino okukitereka, era ojja kusabibwa okuteeka omukono oba ekinkumu ku kiwandiiko ekiraga nti okkirizza okwetaba mu kunoonyereza kuno. Siinga osaalawo okwetaba mukunoonyereza kuno, oli wa ddeembe ate okukuvaamu ekiseera kyonna ate nga towadde nsoonga yonna.

Okwetaba mu kunoonyereza kuno kitegeeza ki eri gyendi?

Siinga osalawo okwetaba mukunoonyereza kuno, ojja kusabibwa okuwa olunaku n'ekifo ekikusanyusa ggwe, osobole okubuuzibwa.

Watya nga waliwo ekibi ekintuuseko? Ani gwennyinza oluloopera?

Siinga ofuna okwemulugunya kwonna ku ngeri gyoyisibbwamu nze oba ekintu kyonna ekirala ekikwatagana ku kunoonyereza kuno, okusokeera ddala oyiinza okutuukirira ankulira ku ssomero (Dokita Catrin Evans, essimu +44115 8230894, endagiriro catrin.evans@nottingham.ac.uk). Siinga ate toli mumativu oluvannyuma lw'okutuukirira omukulu oyo, oyiinza okutuukirira omuwandiisi ku kakiiko akalabirira okunoonyereza kuno (Omwami Stephen Okoboi, essimu +256 752 774 152, endagiriro, okobois@tasouganda.org).

Okwetaba kwange mu kunoonyereza kuno kunakuumibwa n'obwekusifu?

Byonna ebikukwatako ebinaaba bikunnganyizibwa mukunoonyereza kuno bijja kuumibwa ku kompyuta eriko ennaamba enkusifu, era bijja kuterekebwa n'obwegendereza obwawaggulu. Ebikukwatako byonna ebinakozesebwa awalala bijja kuba nga biggiddwako erinnya lyo, waleme kubaawo omuntu yenna okusobola okumanya nti bikwata ku ggwe. Ku bimu ebyetagisa mu kusoma kwange, nja kwetagisa okugabana ebimu kubizuliddwa mu kunoonyereza kuno n'aabo abankulira, naye era erinnya lyo lijja kuba nga liggiddwamu.

Engeri yokka obwekusifu buno webuyinza obutakumiibwa wajja kuba ssinga oliko ebiintu by'oyogedde ebiteberezebwa okuba eby'obulabe eri ggwe oba obujjajanjabi bw'ofuna mu ddwaliro, gy'ofunira eddagala, oba awaka. Singa ebifananako bino bibaawo, nja kusooka njogereko naawe bwekiba nga kisoboka era bwekiba kyetagiisa, nja kuloopa bino ku baantu be kikwatako. Ekiseera kyonna, nja kutwala obudde okukutukirira n'okwogeramu naawe obwetaavu bwonna okumenya obwekusifu mu ngeri eno nga ssinnaba kutuukirira muuntu mulala yenna.

Kiki ekinabeera ku bivudde mu kunoonyereza kuno?

Ebinaava mu kunoonyereza kuno bijja kufulumizibwa mu kitabo ky'emisomo gyange era ebimu biyiinza okuba ebiruungi okutekebwa mu bitongole ebye waggulu nemumawaanga agebweeru, era n'ebirala biyiinza okwogerwako mu nkungaana ezitali zimu mu Uganda n'ebweru wa Uganda. Okufulumizibwa kwonna kujja kukuuma obwekusifu era ggwe tojja kuba nga osobola okumanyika mu bino ebinaaba bifulumizibwa. Singa onaaba oyagala okufuna kubino ebivudde mu kunoonyereza kuno, bino bisoboka okukuweebwa.

Ani ateegeka era asasulidde okunoonyereza kuno?

Okunoonyereza kuno kutegekeddwa nokuyambibwako ettendekero ekkulu ery'eNottingham, jensomera. Tewali ssente zivudde walala wonna.

Ani eyetegerezza okunoonyereza kuno?

Okunoonyereza kuno kukebereddwa era nekukkirizibwa akakiiko kekuttendekero ekkulu ery'eNottingham, e Bungereza, n'akakiiko akekukitongole kya TASO mu Uganda.

Siinga njagala okumanya ebisingawo?

Siinga onetaaga okumanya ebisingawo ebikwata ku kunoonyereza kuno, osobola okuntukiirira ku ndagiro eno wammaanga.

Essimu: **0755257997** (Uganda), endagiro **ntxsn11@nottingham.ac.uk**

GISHU

Shiwandeho esheinyonyola khu khuwenzeresa hubo abanayalisa uhugata mu hurebwa hwomunu mutwela

Lisomero likhulu lye Nottingham, lyebulafu.

Lisomero lyeba nasayansi

kumadala ka B , ku likagiyo lya qweni

Nottingham

Ng7 2HA

Kumurwe ku muhulu kwe khuwenzeresaho:hulabirira nga bekalawo muhuwenzeresa hu malesi kekhwukha ha silimu: ebyambaso byabo abegatta mu huwenezersa ne bawenzerisi mu Ukanda

Lisino lyomuwenzerisi: Sylvia Nalubega

Hulanga Abo bakana Khuba mumusomo

Wanyala nabbi khulaka khukana mu huwenezersa khuno. Esese Ndi Umusomi mu Lisomero likhulu lye Nottingham, lyebulafu.nga sheiwandeho sheisi ndi nihurusa mumusomo khuno, nandikanile khumanya ebi amba hubo abegata mu huwenezersa hwe kamalesi ke khawuha ha silimu musawa zoa nga bamalilisa uhugata muhuwenzeresa okhwo.nga ushili khuhawo uhugata mu huwenzerisa khuno , shili sheikumugaso ewewe khutegera lwashina huwenezersa khuno kuza kukolebwa atea ni binaba muhuwenzeresa khuno. Nahusabirie owuyoowe usomee ebiwandihire asiwo ugagenderesa nabbi ela unyala wabibiramo ne abasale oba ba yaya ngawakanile.unyala wareba eshendu shosi shesi uhategerere taa, ne byesiwandikanile humanya ebifuraho beno. Ngaabe wahaliliwo uhugata mumusomo khuno unyala wabiha lupapula luno.

Wanyala nabbi uhusoma biwandiho bino.

Muhuwenzeresa hu malesi ke khaukha ha silimu kwe yongere mu bibala byeasi oba (Bitambi). Abandu nga bamalirere uhugata muhuwenzeresa hu malesi ka silimu. Shikanisibwa hubona bari abegatire mu khuwenzeresa khuno (abalini khaukha ha silimu) barama nga abafuna khukangibwa ni khulabiriwa, sheibenga shitwela khubyo.

Biyamba khu musomo

Waliwo kamakambira and nichimutendela ebye wandihibwa nga kalinihuyeta omuwenzerisi muhuwenza hu khaukha ha silimu. Nenga waliwo biwandihe bifiti nabbi ebikaniha khu bilini-khuholebwa mu bisera byekhuwenzeresa khu malesi ka silimu ngakhumalirizibwa oba nga (khukalibwawo).

Kunyalisa khugataho khu byesi bahupanisaho ebiyambaso khukwongera kungona engeli eye khumalilisa khuwenzeresa khaukha ha silimu, shandi bere shilayi khuwuririsa kwama khu bandu aba wenzeresa enjeli esi bawambamu mubisera byehari (Byekatano).ate ni ku wulira ebiyambaso byabo abegata mu khuwenzeresa hu mulamwa okwo. Nenga paka kuhwolesa sharero eliwo khuwenzeresa hufiti nabbi kuwamba khubo abegatire mu khuwenzeresa hu malesi ka silimu, kufurira ilala nga biwamba khu Bisera byekukalwo khuwenzeresebwa khuno.mukhuwenzeresibwa khuno khukana kumanya ebyambaso byabo abegata mu khuwenzeresa hu malesi ke khaukha ha sillimu mu Uganda., khusenzira hu libanga lyesi bamaliremo nga bekalawko(bamaliliza) khuwenzeresa khuno, ni khumanya ebyo ebi bawo nga byekhuwenzeresa byawe.

Binanu bi naba mu khuwenzeresa khuno?

Banakusaba kwigatta mu kutebebwa nga uliwonyene kumulundu mutwela.

Kusubira khuri kutebewa khuno ku namala isawa indwela. Kutebebwa khuno kunawabisibwa ku kuma ka rikodinga kamakona. Unyanyala wemisa kakuma lwe sukanile. Byesi ku rekodingire kwama mu kutebebwa kane biwandikhe imale ikonegese.

Lwashina Bakhulondele?

Bakhulondele kwigatta khuwenzeresa khuno khuba ayumawo wa bakho mukhuwenzeresa? Ukwaba ukuwamba hu malesi ke khaukha ha silimu ate nga wokyesa khukana khurebebwa khubyo ebye kholakho nga bakhwenzeresaho khumalilizibwa (kwakamisibwa). Atwela ngana abandu asatuu kwigatta mu kutebebwa nga oliwonyene.

Ukana khuba mu khuwenzeresa khuno?

Shili isiiwe khuhalawo khuba mukhuwenzeresa khuno oba taa. Kasita uhalawo khuba mu khuwenzeresa khuno, Kanye bakhuwe shiwandiho shino khubikha, ate unsabibwa khuraho kumuhono khulupapuala khukwokyesa uri wafukyirire kugatta mu khuwenzeresa khuno.

Wade wahalirewo khuba mu khuwenzeresa khuno unyala waruramo ngawakanire esi ukanire wade nga emawo ilomoyosi ta.

Kwigatta mu khuwenzeresa khuno kumanyisa shina esindi?

Nga wafukuyilile kwigatta mu khuwenzersa khuno kane usabibwe khuwa lunakhu ni akhundu oba shifo shei sukana bahureberemo.

Nenga waliwo shini eshi nzolilekho? Nanuu esi nyala nawabakho?

Kasiita uba nilomo yosi mungeri esi bakhubirisiremu, inyala yabese oba shosi eshiholagana ni kumosomo khuno unyala wolelera Omukulu wase (umusawo Catrin Evans, Isimu: 01158230894, E-mail: catrin.evans@nottingham.ac.uk). Kasita oyo abanga wakhuhumatiza taa unyala wolelera uwuwandisi uli khukakyiko ahamba khu bayenzersa aha TASO bamulanga (umukulu Stephen okoboi, isemu yewe: 256 752 774 152, oba umwandihireho Nga u sindiha khu okoboi@tasouganda.org).

Nga nabele mu khusoma khuno mu nashilinda nga shishamma?

Buli kyesi Unaloma mu khuwenzersa khuno ba khukakasa bati kakyibika bulayi khu shuma kyesi umutu akakayanala wa funa nga kali ni lukusa taa, binabaho bulindi bwe kamani .Buli Bubaaha bukuwambaho nga baza kubukozesa akundi ni batusakao lisino lyowo niyo batu baleme kutegera bati niyo iwewe.

Nga shitwela ku byo beyesi ndi kuhola mukhwenzersa khuno ndi nikubolela umuhulu wa se ku bubaaha obu nenga kaneme emubolele nanu wabimata.(kamasina kane kabe nga sikalimu taishina

Ishinaukha ku linda shishama she bubaaha buno shei naba nga wa boherere bubaaha ubulera buwangafu esi bulamu bwowo nga nomenya , oba nga neba khulabiriwa mudwaliro eliyoy, oba engo isi umenya. Kasita isho shibawo kane nganiheho ni nawe nga shasobohere ate nga shetagisire kane indope isi umunu umutufu. Kane ibenga ikutebako kasita imbanga ngana ku ganikako ku bikuwambakho nu mudu ukundi.

Ibiyama Mumusomo khuno Bikholewa Biryena?

Ibyama mu khuwenzersa khuno binarusiwa(binawandihiwa) mushitabo shese shekyimisomo atenga bubaaha bulala buyanyala bwaba bulayi ku butaa mu shitongole ebye angakyi ni mu manambo kebulafu, ni bilala biyanyala byakaniihahoh mu bubusano ne ba bandu abandi. Nenga waberewo khu birusa mubandu khusoma kane baramenga balindire shishama kye lisino lyowo. Nga wakanire ebi nama mu khuwenzersa khuno Kanye bahusindihire.

Nanu urekehere ni nanu ureremomo kama pesa mukhwenzersa khuno?

Khuwenzersa khuno kwarengehebwe ni be li lekero likulu Nottingham esi ndi khu somera kyimisomo kyese ikyisembayo. Imawo umundu uwebulafu ureremo kamapesa taa.

Nanu uwukanya kuwenzeresa khuno?

Kuwenzeresa khuno hu kanyibwa ate hwafukyirisibwa lukyiko lwe lesomero likhulu lye Nottingham, lukyiko lwe lisomero lye basowu ulufuka enzibirisa, ibulafu ni lukyiko lwa TASO mu Uganda.

Nga nakanire khumanya bifuraho ?

Nga abewakanire ku manya bifuraho awo ibi wamba ku khuwenzeresa kuno unyala wa kubira isimu: 0755257997(Uganda)

Oba umuwandihireho umusindihire khu ntxsn11@nottingham.ac.uk

JAPADHOLA

WACHI RE JUMA LAYERE GIFOGIROKI ME

THE UNIVERSITY OF NOTTINGHAM,

SCHOOL OF HEALTH SCIENCES,

DIVISION OF NURSING B FLOOR,

QUEEN'S MEDICAL CENTRE

NOTTINGHAM

NG 72 HA

Wichi fogiroki: Dewo rijuma itemo kumijo yeni maneko kudini ma kelo two twilo ihongo muchowi temo . Ngeri ma juma ifojere kumijjo gi juma judwaro juniyangi iye

Nyingi jadwari: Sylvia Nalubega; jafogiroki ma malo

Wachi majolojo

Afoyo maro meweni i fogiroki me. Abedo ngati masoma iUniversity ma Nottingham aka rendiko Parani madwong. Amito niyang gimatimere rejuma jumiye kineni ochowi temo yeni ma neko kudini ma kelo two twilo, kungi jo. Mafodi I kidyero bedo I fogiroki me, nwango beri Ikuthi Iniyang gimu omiyo fogiroki me Itemo gi gimamako kwonge. Akwayin gimwolo, Iteri hongo Isoma wachi me aka kinyalo ipenji ye wade gi merini mafodi Ikidyero. Kineni idyero niberi Ibedi ifogiroki me inyalo kano papilla mawachi me. afoyini gi kisoma .

Ngeyi Wachi

Nitye mediroki itemo yeni maneko kudini makelo two twilo ipinyi ma nwango noki iye, Kuchowi temo yathi maneko kudini makelo two twilo, mitere ni ju ma jumiye bedo itemo jumidere nwango konyi ma bothi, mamakere kodi chani madwongi ma mediroki gi kongi kodi nyalo kudini maketo two twilo. Giratima nitye mu ochowi chano manyutho juma jufogere ngeri ma timo medo niyangi ikudini makelo two twilo , too nitye chani manoki swa ma nyutho inegeri ma chengo medo myanga Itemo yeni ma neko kadini makelo two twilo. Gima dwongi nwango ngeri ma chowo temo yeni ma neko kudini makelo two twilo itemo iye, kineni mediroki labedo ingeri ma chyego [Chowo] temi yeni ma neko kudin ma kelo two twilo. Dinyomere ni kiri kononi niyangi netiye nyaka ma noki ma nyutho ngeri ma juma Itemo kumijo yeni me jubedo kuchugi temo yeni me, tekiteki mere I hongo manyaka ochiyegi [achowi] temo. Fogiroki me mito nwango ngeri ma juma Itemo kungijo yeni me in Uganda jonyang , jukwoo, kodi juma junyalo medo ingeri ma

woki ihongo ma ochowi iye temo yeni me, aka medo niyang gima jumajutimo medo niyang jutimo.

Medo niyang me la mito ango?

Iamitini idwoki pengi pakadhano achiyeli.

Pejo kisii dhano nyalo tero sawa achiyeli.

Pegiroki me ilamako iluo, aka inyalo gengo mako me ihongo moro jye kineni imito.

Gima omaki me awoni awiro idhudhoki ma amito kachowo alanyiyeko woko gima omaki jye.

Irango Oyerini?

Oyerini imedo niyang me rupiri ini ibedo itemo yathi ma neko kadini ma kelo two twilo aka inyutho kigomba ma mito nyutho gima ingeyo, gima timere minyu temo orumo. Atiye gi geno bedo ipengiroki gi jyi 30 ala bedo ka pejo kissi dhano kende .

Beri ibedi ifogiroki me?

Iwoni Iripo dyero ka ila bedo iye. Ka idyero bedo iye ilamiyini papilla ma wachi me aka ilamitini ikethi chigini mala nyutho ni idyero.

Ki ineni iyere gitemo, itiye gisilwanyi weyo hongo mi inumiti iye jje.

Ini bedo Imedo niyang me nyutho angorani?

Ki Ineni I dyero bedo Imedo nneyo me, Ilakwayini Imiyi delo gi ka bedo ma repo rini ma ilabedo kifogini Iye.

Too kineni nitye gima okedho ma rach?_Nga ma ala ki osa rigo?

Kineni nitye gima kiberi ri ini ingeri ma omakini itye kosa ma amakini iye kosa gima makere gi medongeyo me, kachako inyalo nyutho jabere parani [**Dr. |Catrin Evans. Simo: 01158 230894, E-mail: catrin.evans@noltingham.ac.uk**]. Kineni iwinjo ni ikinwango konyi paka nwango igeno, nwangi andika ma katipa ma TASO , ma mako kumi ngeri ma medo niyangi [**Jadwong, Odoi Okobi, Simo: +25652 774152**], E-mail: okobois@tasouganda.org.

Bedo imedo niyangi me la bedo nyaliling?

Wachi morojye ma ilachoko imedo nyangi me ila kano kakyoko wachi aka ila ngengo Ingeri ma malo ma kunyali meyoroki. Wachi moro jiye ma makere kodi mala woki kama ichoko iye wachi me nyingini kakwany iye aka kisigima makere kodini jiye ila kwanyo iye.

Paka medo ifogiroko gima anwango aripo nyutho jateli parani too labedo ma nyigini ongoye iye.

Nyaka kama ila nyutho iye wachi perini la bedo ka wachi owoki ma nyalo ketho kwoperini idinyo, aka limo bothi me nitiye iye gimorojiye ma nyalo kelopeko ala wacho re jumaripo kineni mitere aka ripere.

Ala temo paka anyalo Nwangini kiri gi pegiroko kodini kineni obedi gima lamitere whodho wachi ma makere kodini mafodi aka nyutho dhano morojiye.

Ango ma la timere gi gimala nwangere?

Gima la woki imedo nyangi me ala wotho indiko parani madwongi aka lanyalere bende wodho ipapila pa juma jumedo ngiyo madwongi kiri gi kama ifojere iye madwongi , giromo ma medo niyangi. Kisi kama wachi ilawodho iye jiye, la kano miroki perini aka ku nyuthi miroki pereni igindiko gigira wacha morojiye. Keneni ila mito gima ilanwango imedo niyang me, ila miyini.

Nga ma chano kiri gi ketho pesa imedo niyang me?

Medo niyang me itemo gikonyo woki i University ma Nottingham kama bedo ka soma iye, kisoma ma mako. Aka ongoye konyi morojiye ma woki kamani jiye.

Jukune ma jumedo luwo fogiroki me

Medo niyang me oluwi aka oyere gi ika kisoma madwong ma Noltingham, ka kisoma manyaboth matelo kitipa mamakere gi medo niyang, woki UK kodi kitipa mamakere gi konyo ju two twilo [TASO] ma Uganda.

Inyalo nwangani keneni inyalo kigomba medo niyangi

Simo: 0755 257997 [Uganda]

E-mail: ntxsnll@noltingham.ac.uk

ATESO

Abunget naka a kiro anu ikamanaro itunga idiope idiope ni itetemonorere ai bega akiro

Esomero loka o'nottingham,

Asioman nako angaleu naka itunga,

Abunget nako amokolian

B Floor, Queens medical centre

Nottingham

NG7 2HA

Akou akirot naka asioman: Aidario naka itunga kalu itetemonorere ikee nuka eseny: aomisio itungakanu itetemonoritotor ikee kede aomisio eswamak nuka asioman naka eseny ko Uganda

Ekior a someroit: Sylvia Nalubega

Nuisukunyunete

Eyalama noi kanuka ijo acamun asioman na. Arai eong asomeroit naka adoketait naka wasia cut [Doctoral]. A siomi eong O'semero loka o'Nottingham ido ibusakinit eong aitolomun aiwadikaet naka asioman kana. kanuangun epuda eong ajenun anyoka iswamanokino itunga nu itetemonorere ikee nuka ekurut loke esenyi akaulo angetakin cut aitetemoonor kesi. Kerok ijo ecamuno abongonokin aingiseta, epolo ijo amisikin apeleikinet naka asioman kana. Kosiom akiro nu etupakinete, epedori ijo aimor kede epapero arenda ipajan kon arai Ikoto ijo. Ingit eong aingiset adiokere kanu ijo imisikit. karai iroko ijo icamunit abongonokin aingiseta, Ipedori ijo aitasal apapula na. Eyalama asioman apapula na.

Esusut

A poloori asioman naka Ikamara kede aitetemoonor kee nuka esenyi kotoma akwapsinei nuka edit akerianut. Konye akaul nuka angetakin aitetemor ekiya, ebusakinit ti aanyun ebe Itunga nu etemorere ikee [nu adekasi eseny] iyatakinete aduwunun amukian keda aidario na ejok. Ejaasi Ikisila ka nu tupitano nu itetenete asiomak anu Ikamunitos iponesio itolosere asioman naka eseny. Konye, ejok ajenun kodoco epone bo ali iswaatar asiomak araibo nu itolosete aingic akiro nu? Erai da bobo na ameda ajenun aomisio nuka itunga kanu opotu itoritotos o'pone asioman kwa ana. Konye, iKidioko nu tupitono kotoma aitetemonor ikee nu. Ka cut kotupitete apak na daunite ituan kotoma asioman kwa angin.

Kanuka aitacaun ikisila ka nu tupitono kotoma asioman naka esenyi, epol ameda adumun aomisio ama ejaasi asiomak nepepe keda itunga nu angetakisi atetemoonor ikee nuka esenyi tetere ajenum epone lo etolosere akiro, osodi bobo aomisio nuka Itonga Kangun akaul naka angetakin aitetemonor ekiya.

Anyooka ejaasi toma asoman na?

Ebunio ailip ijo ajaikin toma abongonokin aingiset kwap idiope itunganan. Eomitai ebe airiamun na edauni esawa ediope. Ebunio ekam akiro nu inera ijo Keda a Cuma Konye Ipedori ijo a palar ainer edio esawa kere. Akiro nu ikanutai ebunio eijililiun, Kosode aiputar kesi kotoma acuuma ngin .

Ka nukinyo kisekuniter ijo?

Kisekunitai ijo ajaikin toma asioma naarai itetemooritere ijo ikee nuka esenyi pacu, ido ipedori ijo ajaatar nomoruna kanu ikamunitos amukian ngin. Itunga 30 ibunio aingitngit kwape idiope idiope.

Biai, ikotokin ijoda ajaikin toma aingisingisio na?

Ipedoori ijo ajaikin arai mum, Karai Iseku ijo ajaikin, Iinakinio ijo apapula na alosit kede, Ido iliopio ijo aicikakin a kan kwape camunet Kon. Karai ijulakin ijo ekaulo do ilacakina ijo, emamei itionis. Mam da itepesenio ijo.

Inyobo ameda adumuni eong?

Karai icam ijo ajaikin toma asioman na ilacakina ijo alimokin eong apaaran, kede aiboisit naka ailajaara kon tetere oni iriamun abongokin angiseta.

Dobo arai emunaaros akiro?/ Ingaibo Ingarakin eong?

Kodolok itunga nu kanukaa arokok kere.

Dr. Catrin Evas. Esimu: 01158 230894

Asadoku naka o'kwam catrin.evans@nottingham.ac.uk

Stephen Okiror Esimu: +256752 774152

Asadoku naka o'kwam: okobois@tasouganda.org

Konye akakiro ebunio aidar Keda aiyeyeya?

Akiro kere nu elomunet amaakon Idario kede aiyeyeya naka okuju. Iputaro ekiror kon tetere mama ejenuno ijo. Karai da emori a kiro nukeda keda nu a polok ka, mam Kesi epote ajenum ekiror kon.

Nu itegelikina bon elomunete arai ilim ijo akiro nu itodunitos abilio naka ekisil arai amamus naka ayuwara kon koma adekis arai orekon. Arai elomutu nu etioko egei eong aimor kesi keda ijo osdi arai ejaun eipud itijenikin eong itungana yen apedorosio. Atam eong adolonokin ijo duc kotoma akero kere nu ipudasi aitijenikin ice itunga akere nu.

Inyobo iswamaikino akiro nu akaul naka asioman kana?

Epote akiro nu aingarakin eong aitolomun aiwakait naka asioman ka. Epodoro da koinono loka asioman itoritete o'kampuni lo itolomonunete akiro aitolomun kero nu tetere ice itunga da siomete, konyo mam elimoro ekon ekiror cut. Eponio da aitemtem akior nu araimuneta nuka ikukulerun nuka asioman. Karai ikoto ijo da aiwadikait ngin ipodori ijo adumun.

Ingai bo itemonokino akiro ido aibo elomutai apiai nu itwasama ka sioman kana?

Esomero loka o Nottingham ngesi ingarakinit eong konye emameete apiai nuka okinga nepe cep da.

Ingaibo inyabukat asioman na?

Esomero loka o'Nottingham, medical school ethics committee, UK nepepe keda erionget loka o'TASO kesi inyabukatos keda acamakin asioman na alosi akonye.

Nebeara kanuka adumun ace kiro koingaren

Karai ikotokin ijo ace kiro koingaren ipedori ijo adolokin eong o'nambai kanu:

Esimu 0755257997

Asaduku naka o'kwam ntxsn11@nottingham.ac.uk

Information pack for focus group discussion potential participants

The University of Nottingham,

School of Health Sciences,

Division of Nursing

B Floor, Queen's Medical Centre

Nottingham

NG7 2HA

Title of Study: Care in HIV drug trial closure: perspectives of research participants and research staff in Uganda

Name of Investigator: Sylvia Nalubega

Invitation paragraph

Thank you very much for your interest in this study. I am a Doctoral Student at the University of Nottingham and for my thesis I am interested in finding out what happens to research participants when they complete participation in HIV drug trials. Before you decide whether to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends or relatives if you wish. Ask me if there is anything that is not clear or if you would like more information. If you decide that you still wish to take part, you may keep this information sheet. Thank you for reading this.

Background

There is an increase in HIV drug trials conducted in low income countries. After completion of an HIV drug trial, there is a need to ensure that participants (who are HIV positive) continue to access care and treatment, as part of the comprehensive care and management plan for HIV. Some guidelines and policies have been established to guide researchers on how to conduct HIV research, however, there is little guidance on what needs to be done during closure of HIV drug trials. In order to contribute to the ongoing debates and deliberations intended to inform policies to improve HIV research closure conduct, it is important to find out how the closure process is managed by researchers and how the participants experience the transition period following termination from HIV drug trials. However, to date, there is limited research about the experiences of those who have participated in HIV drug trials, especially looking at the closure period. This study is intended to find out the views, experiences and opinions of people who have

participated in HIV drug trials in Uganda, regarding the transition period after completing participation in HIV research, and also to find out how the transition process is facilitated by the researchers.

What does the study involve?

You will be asked to participate in one group interview. It is likely that each interview will take approximately one hour. The interview will be recorded on an audio-recorder and you may stop the recording at any time that you wish. The audio-recording from the interview will be transcribed by myself and will then be destroyed.

Why have you been chosen?

You have been chosen to participate in this study because you are working/recently worked in an HIV drug trial and you have expressed a desire to be interviewed on your views about the closure period. In total, I am hoping to interview a maximum of 6 groups with up to a maximum of 10 people in each group.

Do you have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part, you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason.

What does involvement in the study mean to me?

If you agree to take part in this study, you will be asked to provide a day and venue that is suitable for you so that you can be interviewed.

What if something goes wrong?/Who can I complain to?

In case you have a complaint on the way you have been treated either by myself or anything to do with the study, you can initially approach my lead supervisor (Dr. Catrin Evans, Telephone 0115 8230894, E-mail catrin.evans@nottingham.ac.uk). If you are still not satisfied, you should then contact the TASO Research Ethics Committee Secretary (Mr. Stephen Okoboi, telephone +256 752 774 152, email okobois@tasouganda.org).

Will my taking part in this study be kept confidential?

All information which is collected about you during the course of the research will be kept on a password protected database and is strictly confidential. Any information about you which leaves the research unit will have your name removed so that you cannot be recognised from it. As part of my studies, I will be expected to share some of my findings with my supervisors but they will be anonymised and you will not be recognised from the findings.

The only exception to this confidentiality will be if you disclose information which raises concerns about your own safety or the safety of others. If any serious concerns arise, I will discuss these with you where possible and if necessary report them to the

appropriate person. I will always make every effort to contact you and discuss with you any need to break confidentiality in this way before contacting anyone else.

What will happen to the results of the research study?

The results of this study will be published in my thesis and may be suitable for publication in professional journals and presentation in professional meetings and conferences. Any publications will maintain your confidentiality and you will not be identified within any report/publication. If you would like a copy of the results from this research, this can be provided to you.

Who is organising and funding the research?

This study is undertaken with the support of the University of Nottingham where I am undertaking my doctoral study. There has been no external funding for this project.

Who has reviewed the study?

This study has been reviewed and approved by the University of Nottingham, Medical School Ethics Committee, UK and The AIDS Support Organisation Institutional Review Committee, Uganda.

Contact for Further Information

Should you require any further information about this study then you can contact me at:

Telephone: 0755257997 (Uganda)

E-mail: ntxsn11@nottingham.ac.uk

Information pack for key informant interview potential participants

The University of Nottingham,

School of Health Sciences,

Division of Nursing

B Floor, Queen's Medical Centre

Nottingham

NG7 2HA

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Why have you been chosen?

You have been chosen to participate in this study because you are working/recently worked as a study/project coordinator in an HIV drug trial and you have expressed a desire to be interviewed on your views about the closure period. In total, I am hoping to interview a maximum of 6 people for this interview.

Do you have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part, you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason.

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Who has reviewed the study?

This study has been reviewed and approved by the University of Nottingham, Medical School Ethics Committee, UK and The AIDS Support Organisation Institutional Review Committee, Uganda.

Contact for Further Information

Should you require any further information about this study then you can contact me at:

Telephone: 0755257997 (Uganda)

E-mail: ntxsn11@nottingham.ac.uk

Appendix 2: Informed consent forms

Consent form for individual interviews

Title of Study: Care in HIV drug trial closure: perspectives of research participants and research staff in Uganda

REC ref: (to be added after approval given)

Name of Researcher: Sylvia Nalubega

Name of Participant:

Please initial box

1. I confirm that I have read/they have read for me and I understand the information sheet version numberdated..... for the above study and have had the opportunity to ask questions.

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason. I understand that should I withdraw then the information collected so far cannot be erased and that this information may still be used in the project analysis.

3. I understand that relevant sections of my data collected in the study may be looked at by the research group and by other responsible individuals for monitoring and audit purposes. I give permission for these individuals to have access to these records and to collect, store, analyse and publish information obtained from my participation in this study. I understand that my personal details will be kept confidential.

4. I understand that the interview will be audio recorded using an audio recorder device and that anonymous direct quotes from the interview may be used in the study reports.

5. I understand that all data will be anonymous and confidential with the exception of information being revealed during the interview about criminal activity or potential risks to another person or to myself.

6. I understand that information about me recorded during the study will be kept in a secure database. If the data is transferred it will be made anonymous. Data will be kept for 7 years after the study has ended and then securely destroyed.

7. I agree to take part in the above study.

Name of Participant	Date	Signature
_____	_____	_____
Name of Person taking consent	Date	Signature

2 copies: 1 for participant, 1 for the project notes.

LUGANDA

Ekiwandiiko ekiraga okkukkiriza okwetaba mu kunoonyereza

Omutwe gw'okunoonyereza: Okulabirira mu kuggalawo okunoonyereza ku ddagala ly'akawuka ka Siliimu: ebirowoozo by'abeetaba mu kunoonyereza n'abanoonyereza mu Uganda

REC ref: ()

Erinnya ly'anonyereza: Sylvia Nalubega

Erinnya ly'ageenda okwetaba mukunonyereza:

**Teeka mu ka bokisi kano
erinnya lyo mu bufuunze**

.....

1. Nkakasa nti nsomye/bansomedde era ntegeera ekiwandiiko ekinnyonnyola ku kunoonyereza ekya namba.....nga ennaku z'omwezi.....eky'okunonyereza okwo waggulu era nti mpereddwa omukisa okubuuza ebibuuzo
2. Ntegeera nti okwetaba kwange kwa kyeyagalire era nti ndi waddeembe okuva mu kunoonyereza kuno obudde bwonna nga ssiwadde nsoonga yonna. Ntegeera nti singa nva mu kunoonyereza, ebiba bimaze okunkunganyizibwako tebisobola kuggibwawo era nti bino biyiinza okukozesebwa mukumaliriza ekiwandiiko ky'okunoonyereza kuno.
3. Ntegeera nti ebituundu eby'omugaso ku ebyo ebinkunganyiziddwako mu kunonyereza kuno bisobola okukeberekwako na'abo abanoonyereza n'abalala abalina obuyinza obwengeri ezitali zimu olwokurabirira okunonyereza kuno nti kugeenda buluungi. Mpa obuyiinza abantu bano okukozesa ebinkunganyiziddwako, era n'okufuna, okutereka, okwekenneenya, nokufulumya ebinkunganyiziddwako nga neetaba mu kunonyereza kuno. Ntegeera nti ebinkwatako nga nze bijja kuumibwa n'obwekusifu.
4. Ntegeera nti okubuuzebwa kuno kujja kukwatibwa ku likooda era nti ebimu ku ebyo byennayogedde mu kubuuzebwa nga byekusikiddwa biyiinzika okukozesebwa mu kiwandiiko ekinafulumizibwa.
5. Ntegeera nti byonna ebinaava mu kubuziibwa kwenge bijja kukwekebwa era nga byekusifu okujjako ebyo ebinaaba byogeddwa mu kubuuzebwa nga bikwata ku bumenyi bw'amateeka oba obulabe ku muntu omulala oba ku nze.

6. Ntegeera nti ebikwatiiddwa kunze ebitekeeddwa kulikooda mu kunoonyereza kuno bijja kuterekebwa mu kifo ekyekusifu. Singa waliwo ebimu ku ebyo ebinakozesebwa awalala, erinnya lyanze lijja kukwekebwa. Ebinkwatako bijja kuterekebwa okumala emyaka musaanvu nga ebivudde mu kunoonyereza kuno bimaze okufulumizibwa

7. Nsalawo okwetaba mu kunoonyereza okwo waggulu.

Erinnya ly'eyetabye mukunonyereza	ennaku z'omwezi	omunkono
--	------------------------	-----------------

Erinnya ly'anoonyereza	ennaku z'omwezi	omukono
-------------------------------	------------------------	----------------

Copi bbiri: Emu eya eyetabye mukunonyereza, n'eya pulojekiti.

GISHU

Shiwndiho ishokyeasa shiri wafukyirisire khuba mu kuwenzeresa khuno.

Kumurwe ku mukhulu kwe kuwenzeresa kho: Kufayo mu hukalawo khuwenzeresa ku malesi ke khaukha ka silimu: ibyambaso bye abandu abegatta mu khuwenzeresa ni abayenzeresi mu Uganda.

REC ref:

Lisino Iyo muwenzeresi: Sylvia Nalubega.

Lisino Iyo uzakukagata mu khuwenzeresa:

.....

1. Nekakasire ndi nasomere oba basomere mu biwandkho binno Nategerere isibiroma..... ku lunakhu lweshalelo zinaku.....ku mwahaMukwenzeresa kwe isi bawandihire angakayi. ndi ni kumukisa kwesi ba mbere kuteba birebo.
2. Nategerere ndi khuba mu khuwenzeresa khuno samwene ngi ni kukhalawo ate nyala naruramo nga nakanire nga nakhu babolelewa lwshina nduriremo taa. Ni shishindi kasitta indura mu khuwenzeresa khuno nga waliwo bubaaha bwesi mbaweke ke banyala ba busangula taa era bayanyala barama nga barambisa bubaaha obwo mukhuwenzeresa hwabwe.
3. Nategere ndi bubaaha bwesi bandusireho nga bwekumugaso kane buwebwe ba wenzeresi abandi ni abandu abasanire khu bona bari khuwenzeresa khuno khukya bulayi. Mbawa lukusa khu rambisa byesi khukutusileko, ni khunganya, kubiha,ni kwitegelesa bamale aburuse bubaaha kwama mu musomo kwesi nigatiremo. Nategere ndi bubaaha bwose bunabihibwa mu shama.
4. Nategere ndi khurebewa khuno khunarewa ku kuma ka wamba magona. Ni byesi bawambire ni ba bitusira ku kiyandiko kyesi banatusa

5. Nategere ndi bubaaha bwosi kene burame nga bwshishama kurusaho nga Aliwo. Khu menya khwe kamakambira oba nga bulime bulayi isi omundu ukundu nga bu bulamu bwewe mu mutawanaa kumubi.

6. Nategere ndi bubaaha bwose bwesi ba rikodingire mu khwenzeresa khuno kane babubire bulayi.nga barusa kuwenzeresa kane baruseho lisino lyase. Bubaaha obu kane babubihire kyimyaha musanvu nga bamalire kumusomo bamale babwonekese.

7. Nafukirire khuba mu khuwenzeresa ukuli angakyi

_____ _____ _____
Lisina lyo musomi Lunakhu lwe kumwesi kumuhono

_____ _____ _____
Lisino lye muwenzerisi Lunakhu lwe kumwesi kumuhono

JAPADHOLA

Papila maridho yeroki ri juma Oyere gi medo iniyang me

Wichi medo niyang me: Dewo ma bedo i chiyego temo ma yeni maneko kudini makelo two twilo. Ngeri ma juma i temo kumi joo, gi juma judwaro ju niyang iye. Me ila medo kuchowi yere gine.

Nyingi nganti ma medo niyangi: sylvia nalubega

Nyingi nganti ma oyere:

Kethi nyikuta ma chanko

.....

.....

- 1. A ridho ni atyeko kisoma kosa osoma rani aka aniyang kisi gima ondiki ka.....indelo.....ma makere. Gimedo niyang ma wichi mere nitiye malo aka omiyani kiri silwanyi ma penjo

- 2. Atye gi niyang ni bedo parani imedo ngeyo me aniwoni adyero aka anyalo woki iye hongo ma anu miti iye jiye ma akamiyo atonga morojye. Aniyang ni keneni anu weyi, wachi ma achowo miyo kunyali kwanyo aka inyalo oro chowo medo niyang me.

- 3. Atye gi niyangi ni gima makere gi wachi ma alamiyo inyalo neno ikitipa ma rango medo niyang kiri juma jutiye gimeni ma Luwo gi medo yiko ayere gi jumegi ma nyalo nwngo wachi ma omakijye, aka a yere gijo Choko, Kano, medo niyang iye kiri gi wodho gima junwango rijimani jusoma, gima onwangere imedo niyang me. Atye gi ngeyo ni wachi ma makero kodani ila kano [Kunyere].

- 4. A ngeyo ni ila mako dwondani ikisi ngima ala wacho jye aka gima awoni awacho Inyalo oro indiko ma medo niyang me, ingerima kungeyere.

- 5. A niyangini kisi wachi morojye ila kano ma kuwoki igeri ma kuwoki rigimani. Kwanyo woko kiwodho ipapilla madwong kosa ka wachi ma makere kodi gi ma makere marachi ma nyalo kelo teko rejimani kosa ri ani.

- 6. Aniyangi ni wachi ma ila mako itemo medo rango me ila kano kama kinwangere gi jye mani mani kineni wachi me ila kodo kamorojye gima makerekodani jye ila

kwanyo woko. Gima ila mako ka ila kano ma oro abirio. Ka medo niyang me orumo nyaka ti nyieko woko igeri ma jimani juku nyali nwango iye.



7. Ayere gi medo imedo niyang me.

_____	_____	_____
Nyingani	ndelodwe	chingani
_____	_____	_____
Ningi ngata yere yeyiroki	ndelodwe	chinge

Papila me ripo woki aryo [2] achile ri ngata niwang wachi me, mani ri ngata yere.

ATESO

A papula naka acamun abongonokin aingiseta kotoma asioman

Akou akirot naka asioman: Aidario naka itunga kalu itetemonorere ikee nuka eseny: aomisio itungakanu itetemonoritotor ikee kede aomisio eswamak nuka asioman naka eseny ko Uganda

REC ref:

Ekiror loka asioman: Sylvia Nalubega

Ekiror loka abongonokinon akiro:

.....

1. Ketigogong ebe; asiom, arai asiomakin, ido da amisiik eong akiro nu ejaasi toma abunget no onamba..... eraasi aparasia..... kanuka asioman naka okuju ido da abu adum arereng naka aingit aingiseta.

2. Amisiikit eong ebe ajaikin toma asioman na arai namam etacio ido da apedor eong aitwogoun edio sawa, komamei aitepesenio. Amisikit bobo da eong ebe akiro kere nu edaunitai adumun amaka mam elemario karai etwogou eong asioman owaika, ebunio da aitwasam kesi kanuka asioman.

3. Amisiikit eong ebe abunget ace kotoma asioman na ebunio aitosom kanuka atupakinit aingic epone loitosomaere kesi koingaren. Kanuka kangun, kacamakinit eong ijo aswam ngum konye komamei alimor eka ekiror arai ejenunet ka.

4. Acamunit eong da ebe ebunio aikam akiro keda acuma tetere akiro nu itigogongete aomisio nuka asioman kana.

5. Amisiikit eong ebe akiro kere idario kotoma aiyeyeya, emamei da alimor ikiroria dimarai arai ejaasi nu ebelite ekisil arai nu eyaunete amamus ayuara.

6. A misikit eong ebe akiro nu ikamunitos eong ebunio aidar kotoma odula lo arapap ejok noi. Karai ijuli akiro nu ijulio akaul naka aiputar eka kiror. Akiro nu idario adaun ikaru 7 bon akaul kangin komudiarete cut.

7. Acamunit eong ajaikin toma asioman na.



Ekiror k'bongonokinan

aparasia nuka elap

ecikum/esain

Ekiror ka yen ingisingisei

aparasia nuka elap

ecikum/esain

Ikopin iyarei: idiope loka abongonokinan, ediope da loka engisingitan

Consent form for focus group discussions

Title of Study: Care in HIV drug trial closure: perspectives of research participants and research staff in Uganda

REC ref: *(to be added after approval given)*

Name of Researcher: Sylvia Nalubega

Name of Participant:

Please initial box

1. I confirm that I have read and understand the information sheet version numberdated..... for the above study and have had the opportunity to ask questions.

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason. I understand that should I withdraw then the information collected so far cannot be erased and that this information may still be used in the project analysis.

3. I understand that relevant sections of my data collected in the study may be looked at by the research group and by other responsible individuals for monitoring and audit purposes. I give permission for these individuals to have access to these records and to collect, store, analyse and publish information obtained from my participation in this study. I understand that my personal details will be kept confidential.

4. I understand that the focus group will be audio recorded using an audio recorder device and that anonymous direct quotes from the focus group may be used in the study reports.

1. I understand that all data will be anonymous and confidential with the exception of information being revealed during the interview about criminal activity or potential risks to another person or to myself.

2. I agree to maintain the confidentiality of focus group discussions.

3. I understand that confidentiality cannot be guaranteed during the focus group

4. I understand that information about me recorded during the study will be kept in a secure database. If the data is transferred it will be made

anonymous. Data will be kept for 7 years after the study has ended and then securely destroyed.

5. I agree to take part in the above study.

Name of Participant	Date	Signature
_____	_____	_____
Name of Person taking consent	Date	Signature

2 copies: 1 for participant, 1 for the project notes.

Consent form for key informant interviews

Title of Study: Care in HIV drug trial closure: perspectives of research participants and research staff in Uganda

REC ref: ()

Name of Researcher: Sylvia Nalubega

Name of Participant:.....

Please initial box

1. I confirm that I have read and I understand the information sheet version numberdated..... for the above study and have had the opportunity to ask questions.

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason. I understand that should I withdraw then the information collected so far cannot be erased and that this information may still be used in the project analysis.

3. I understand that relevant sections of my data collected in the study may be looked at by the research group and by other responsible individuals for monitoring and audit purposes. I give permission for these individuals to have access to these records and to collect, store, analyse and publish information obtained from my participation in this study. I understand that my personal details will be kept confidential.

4. I understand that the interview will be audio recorded using an audio recorder device and that anonymous direct quotes from the interview may be used in the study reports.

5. I understand that all data will be anonymous and confidential with the exception of information being revealed during the interview about criminal activity or potential risks to another person or to myself.

6. I understand that information about me recorded during the study will be kept in a secure database. If the data is transferred it will be made anonymous. Data will be kept for 7 years after the study has ended and then securely destroyed.

7. I agree to take part in the above study.

Name of Participant	Date	Signature
----------------------------	-------------	------------------

Name of Person taking consent	Date	Signature
--------------------------------------	-------------	------------------

2 copies: 1 for participant, 1 for the project notes.

Appendix 3: Interview guides

Interview schedule for individual interviews

Study Title: Care in HIV drug trial closure: perspectives of research participants and research staff in Uganda

Introduction

- Researcher introduces self and thanks participant for turning up for the interview
- Researcher provides participant with information about the study and ask them to sign the consent form.
- Researcher completes demographic details
- Researcher explains how the audio-recorder works, especially how to turn it off if they wish to do so.
- Researcher emphasizes confidentiality and anonymity issues
- Researcher asks if the participant has any questions to ask

Interview questions and prompts:

1. How did you come to be involved in the research, what motivated you to get involved
 - *What was it like for you when you were in the research*
2. Tell me about what it was like coming to the end of research participation
 - *How did you feel knowing about it*
3. What happened when the research stopped
 - *How were you prepared to leave the research*
 - *How did you feel about the way staff communicated with you*
 - *How did you feel about the information you were given*
4. How do feel about the care/support you were given during this time
 - *How had you expected the care/support to be*
 - *What did you like*
 - *What did you not like*
 - *What could be done better/differently*
5. How has it been like for you since you left the research
 - *Did you continue to access any HIV care services,*
 - *If yes from where,*
 - *If no why*
 - *Any challenges you faced trying to access HIV care and support*

- *How do you feel about the care/treatment you receive now*

6. Any other thoughts/suggestions about this issue

Concluding the interview:

- Researcher switches off the audio-recorder
- Researcher thanks the participant for their contribution
- Researcher asks the participant whether they would like to receive a copy of their interview transcript for verification.

LUGANDA

Endagiriro y'okubuuzibwa kw'omuntu omu

Omutwe gw'okunoonyereza: Okulabirira mu kuggalawo okunoonyereza ku ddagala ly'akawuka ka Siliimu: ebirowoozo by'abeetaba mu kunoonyereza n'abanoonyereza mu Uganda

Okutandika:

- Anoonnyereza yeyanjula era neyebaza ageenda okwetaba mukunoonyereza olw'okujja okubuuzibwa
- Anoonnyereza ategeeza ageenda okwetaba mu kunoonyereza ebikwata ku kunoonyereza era n'amusaba okuteeka omukono ku kiwandiiko ekiraga nti akkirizza okwetaba mu kunoonyereza
- Anoonnyereza awandiika ebikwata ku ageenda okwetaba mu kunoonyereza
- Anoonnyereza annyonyola nga likooda bwekola
- Anoonnyereza ateeka essiira ku bikwata kubwekusifu
- Anoonnyereza abuuza oba ageenda okwetaba mu kunoonyereza alina ekibuuzo kkyonna

Ebibuuzo n'ebiragirira:

1. Wajja otya okutandika okwetaba mukunoonyereza kw'eddagala lya Siliimu, kiki ekyakusikiriza
 - *Kyali kitya bwewali mu kwetaba mukunoonyereza*
2. Mbulira bwekyali ng'okwetabakwo mukunoonyereza kukkomekkerezebwa
 - *Wawulira otya okumanya nti kino kyali kigenda kubeerawo*
3. Kiki ekyabaawo nga okunoonyereza kutuuse kunkomerero
 - *Bakuteekateka batya okuva mu kunoonyereza*
 - *Wawulira otya engeri abanoonyereza gye bakubuliiramu ku bikwaata ku kukkomekkereza okunoonyereza*
 - *Wawulira otya eri ebyo ebyakugambibwa mu kiseera kino*
4. Owulira otya kukulabirirwa/obuyaambi obwakuweebwa mu kiseera kino
 - *Wali osuubidde otya okulabirirwa /obuyaambi buno okuba*
 - *Kiki kyewayagala*
 - *Kiki kyotayagala*
 - *Kiki ekisaniidde okulongosebwamu oba okukolebwa mu njawulo*
5. Obadde otya okuva lwewamala okwetaba mu kunoonyereza
 - *Weyongera okufuna okulabirirwa n'okujjanjabibwa akawuka ka Siliimu*

- *Oba yee, obifunira luddawa*
- *Oba nedda, lwaki*
- *Olina obuzibu bwonna bwewasaanga okufuna okulabirirwa oba okujjanjabibwa*
- *Owulira otya kukulabirirwa n'okujjanjabibwa by'ofuna kati*

6. Olinawo ebirowoozo oba ekintu ekirala kyonna kyoyagala okwogera nga kikwata kunsonga eno

Okukomekkereza okubuuzza:

- Anoonnyereza ajjako likooda
- Anoonnyereza yeebaza eyeetabye mu kunoonyereza olw'okwetaba mu
- Anoonnyereza abuuza eyeetabye mu kunoonyereza oba ayagala okufuna ku kiwandiiko ky'ebyo ebivudde mu kubuuzza kuno ngabiwandikiddwa, okusobola okulaba oba nga by'ebyo byeyayogedde

GISHU

Lukhalala lwe pulani yo Umuyi mirisi

Kumurwe ku mukhulu kwe kuwenzeresa kho: Kufayo (kulabiria) mu hukalawo khuwenzeresa ku malesi ke khaukha ka silimu: ibyambaso bye abandu abegatta mu khuwenzeresa ni abayenzeresi mu Uganda.

Ibiyowa

- Uwenzeresa ekabihaho ate wasima umundu ukwiza mu khuwenzeresa ni hurebewa bibuuzo.
- Uwenzeresa a bolelela umusomi ibi za kuba mu musomo ate amusaba kutako mukono kwolesa nti wafugirire khuba mu musomo.
- Uwenzeresa awandiha ibi wamba ku mundu uza kugatta mu musomo
- Uwenzeresa okyesa umusomi nga barambisa karikoda.
- Uwenzeresa ahukakasa nga bubaaha byeshi shama.
- Uwenzeresa a reba umusomi oba ali kyesi ateba.

Birebo ni bilakira

1 Wegatta oreyna mu musomo khuno ate shina eshe khusenda hu ku bamo.
Shebashiryeye isi we kuba mu musomo kuno

2. Mbolere shebasireyena nga mu malirisa ku musomo kuno kwe khuwenzeresa.
Shina shyesi wakan umanye mu musono khuno.

3. Shina shabawo nga umwenzeresi akamisa

Babarengeha bareye khu mala kumusomo

Mwawulira mureye nga barambi bakaniha isimwe

Mwawulira mureye ku bubaaha bwesi babawa.

4 . Mwawulira mureye igeli isi babalabirira mo mu bisera ebyo.

Abe mwasubire ku balabirira bareye.

Shina shesi wakana

Shina shesi uhakana

Shina ishinyaliwa kuhulewa bulayi

- 5 Shina isibelewo ukwama waleka kumusomo.
Weyongera ku funa bujajabi oba shosi esi abandu bafayo ku ba silimi.
Nga wafuna
Niyo wayena
Nga taa
Buwangafu shina bwesi ufunire nga uwenza bujajabi bwa silimu.
Uwulira ureye ni khulabirira kwesufu ari.
- 6 Uliwo ni bibyambaso byosi khu songa eyi

Kumaliliza birebo

- Uwenzeresa arusaho ka kuma ka rikodinga
- Uwenzeresa asima umusomi lwe kuba mu kuwenzersa khuno
- Uwenzeresa areba umusomi oba akana khufuna ku biwandiho ibi nama mu khuwenzersa khuno naga bamalire kubiwadiha.

JAPADHOLA

Chani ma pegiroki ma kisi rango

Wichi medo niyang me Dewo mabedo ri juma itemo kumi jo yeni maneko kudini ma kelo two twilo kichyego temo.

Ngeri ma juma itemo kungijo gi juma judwaro ju niyangi iye iuganda

Nyuthi roki

- Jarangi nyuthere doko tu foyo juma jumiye bedo imedo niyang me.
- Jarangi miyo juma jubino bedo imedo niyang.
- Gima ondiki ju soma aka la miyo jo kiri papilla mayeroki jo kethi Chingi jo iye.
- Jarangi chowo chain ma nyuthiroki
- Jarangi miyo wachi igeri ma gima mako wachi tiyo iye, tekiteki mere igeri maneko woko, keneni imito.
- Jarangi medo ridho kano wachi ma lamako nyalingling.
- Jarangi penjo juma labedo keneni ju nitye gi pengi morojye.

Pengi gi rango

1. Igeri mene ma inwangere iye itemo yeni, aka ango mu miyini meni ma bedo iye.
 - *Ochale rini nedi minyo ibedo imedo rango me.*
2. Awachi rani ye gima nwango chale minyo wichowo temo yeni.
 - *Nwango iwinjo nedi ngeyo itemo me.*
3. Ango mutimere minyo temo yeni me arumo.
 - *Igeri ango mu omiyini yikiroki minyo iwacho ri ini temo rumo.*
 - *Iwinjo nedi igeri ma ju niyang ju tiyo itemo yeni me nwango ju luwo iye kodini.*
 - *Iwinjo nedi Igeri wachi ma omiyini.*
4. Iwinjo nedi Igeri dewo ikonyi ma omiyini ihongo ma temo me orumo iye.
 - *Ango ma niwango igeno idewo kiri gi konyi*
 - *Ango ma imaro iye*
 - *Ango ma orachi ri ini iye*
 - *Iparo na ango ma inyalo medo timo maberi kosa igeri mu opokere.*
5. Chali ri ini nedi woki ichowi temo yeni me.
 - *Imedere niwango konyo ma makere gi two twilo.*
 - *Ka iyere iniwango, kune?*
 - *Ka iki niwangi konyi, irango.*
 - *Nitye teko ma inwango minyo itemo niwango konyo ma two twilo?*
 - *Iwinjo nedi igeri konyi ma ilimo sawa me.*
6. Initye gi paro morojye kosa gi ma inyalo medo ma makere iwachi me.

Chyengo dwaro me

- Jarangi neko woko chuma ma mako wachi.
- Jarangi foyo ngati mu opegi yeroki kiri gi gima go omiyo.
- Jarangi penjo ngati mu orange kume kinene la kigomba nwango papilla ma pegi roki pere.

ATESO

Epone loitolosoere abongonokin akiro nu aingitngit itunga

Akou akirot naka asioman: Aidario naka itunga kalu itetemonorere ikee nuka eseny: aomisio itungakanu itetemonoritotor ikee kede aomisio eswamak nuka asioman naka eseny ko Uganda

Nu engeunete

- Itodiar ekasioman kosodi aisialamikin yen ebongonokin aingiseta kanuka adolun
- Einakin asioman lo ebongonokin aingiseta akiro nu iwadikitai ikamanara kede asioman ko sodi ailip ngisi aicikakin akan toma araibo nat ecikum
- Ebuni asioman angetakin ace kiro nu ikamunitos... (demographic details)
- Itetemuni asioman epone loiswamaa acuuma na ikami iporotoi, kacut epone loi itudongoroet nesi
- Itigogongi asioman noi akiro nuka aiyeyea ka mamus naka alimori ekiror
- Ingisi asioman abongonokinan arai ejaasi angiseta ace.

Aingiseta

1. Kopone bo ali ilomara ijo toma asioman na ijai ijo toma, inyo iinakini ijo ilomar toma?
 - Ekote bo akiro ai ne ijaar ijo toma asioman ngin?
2. Kolimok eong epone lo ajaatar akiro nepe eyapuuni asioman ngin angetakin?
 - Ipupi bo ijo biai akaul naka ajenun ebe aloset akiro angatakin?
3. Anyoka opotu iswamaunos ijo akaul naka asioman ngin angetakin?
 - Ikapakina bo ijo biai kwa agetakinor asioman ngin?
 - Ipupi bo ijo biai kotoma obone eneratar eswak kede ijo?
 - Ipupi bo ijo biai kotoma akiro nu koponai kolimokinai ijo?
4. Iwomit ioj biai kanuka aidario/ aigange na ainanakinio ijo apakio kangun?
 - Iwomit ijo biai ti abeitor aidario/aigange ngin ajaut?
 - Inyobo ajokikit ijo noi?
 - Ijo bo aronikit ijo noi?
 - Inyobo ti abeit swam ejok araibo ece pone?
5. Biai bo ejaar do kwana ajar ageun ne iwosikina ijo asioman ngin?
 - Kobu ijo otam adumunun aigange naikamanara keda ekurut loka esenyi?
 - Arai ebo, akai bo?
 - Arai mum, inyobo?
 - Anyoka atiokisio kobu ijo kodum kotoma atamit adumun aigarakinio kotoma okurut loka eseny?
 - Ipupi kwana ijo biai kotoma aidario keda aigangio na obu ijo odumununei?
6. Ejaasi ace kiro araibo aomisio nu iwomit ijo ipedori ooni aimor kanu ikamunitos akiro nu?

Angetakin aingitngit

- Ogwetari asioman acuuma na ikami iporotoi
- Isialamakini asioman abongonokinan kanuka abongonokin ejok
- Ingis asioman abononokinan arai ekotokin ngesi da adumun awakikaete nabongonokineta

Interview schedule for focus group discussions

Project Title: Care in HIV drug trial closure: perspectives of research participants and research staff in Uganda

Introduction

- Researcher introduces self and explains about the study
- The group introduces themselves to each other
- The researcher emphasises the focus group ground rules (everything said must be taken as confidential, speaking one at a time, respecting each other's opinions)

Open ended discussion guide

(Flexible open questions will be used to get the group talking; some prompts will also be used)

1. As researchers, what obligations do you have towards research participants during/after completion of an HIV drug trial? (Post-trial obligations).
 - *What is expected of you,*
 - *Whose responsibility is it to ensure that the post-trial responsibilities are fulfilled (e.g. the PI, The coordinators, the research staffs, the funders, etc...)*
2. What is normally done to HIV positive participants when they have completed the research?
 - *How do you prepare them for exit,*
 - *Where do they go for care,*
 - *How do you facilitate them,*
 - *Any follow up care following termination and if yes, for how long,*
 - *What else do you do to them?*
3. As researchers, what are some of the challenges encountered during this period and what suggestions do you have to overcome the challenges?
 - *Any difficulties preparing/transitioning/facilitating participants for exit*
 - *Are you as researchers directly/indirectly affected by closure of the study*
4. In addition to how you support your participants in this institution, and based on your experience, what else would you consider important in transitioning participants?
 - *Things that you feel would be important but are not currently done*
5. Any other thoughts/suggestions about what you would recommend researchers to know or do for HIV positive people leaving research?
 - *Any other thoughts about this topic?*

Conclusion

- Researcher thanks everyone for their time and contributions
- Researcher asks if anyone has any questions
- Researcher reiterates about confidentiality

Interview schedule for key informant interviews

Project Title: Care in HIV drug trial closure: perspectives of research participants and research staff in Uganda

Introduction

- Researcher introduces self and thanks participant for turning up for the interview
- Researcher provides participant with information about the study and asks them to sign the consent form.
- Researcher completes demographic details
- Researcher explains how the audio-recorder works, especially how to turn it off if they wish to do so.
- Researcher emphasizes confidentiality and anonymity issues
- Researcher asks if the participant has any questions to ask

Open ended discussion guide

(Flexible open questions will be used to get the participant talking; some prompts will also be used)

6. As a researcher, what obligations do you have towards research participants during/after completion of an HIV drug trial? (Post-trial obligations).
 - *What is expected of you,*
 - *Whose responsibility is it to ensure that the post-trial responsibilities are fulfilled (e.g. the PI, The coordinators, the research staffs, the funders, etc...)*
7. What is normally done to HIV drug post-trial participants when they have completed the research?
 - *How do you prepare them for exit,*
 - *Where do they go for care,*
 - *How do you facilitate them,*
 - *Any follow up care following termination and if yes, for how long,*
 - *What else do you do to/for them?*
8. As a researcher, what are some of the challenges encountered during this period and what suggestions do you have to overcome the challenges?
 - *Any difficulties preparing/transitioning/facilitating participants for exit*
 - *Are you as a researcher directly/indirectly affected by closure of the study*
9. In addition to how you support your participants in this institution, and based on your experience, what else would you consider important in transitioning participants?
 - *Things that you feel would be important but are not currently done*

10. Any other thoughts/suggestions about what you would recommend researchers to know or do for HIV drug post-trial participants leaving research?
- *Any other thoughts about this topic?*

Conclusion of the interview

- Researcher switches off the audio-recorder
- Researcher thanks the participant for their contribution
- Researcher asks the participant whether they would like to receive a copy of their interview transcript for verification.

Appendix 4: Ethics approval from the University of Nottingham, Research Ethics Committee



Direct line/e-mail
+44 (0) 115 8232561
Louise.Sabir@nottingham.ac.uk
5th August 2014
Sylvia Nalubega
PhD Student
c/o Dr Catrin Evans
Associate Professor
School of Health Sciences
B Floor, South Block Link
Queen's Medical Centre Campus
Nottingham University Hospitals
Nottingham
NG7 2UH

Dear Sylvia

Ethics Reference No: OVSb10072014 SoHS

Study Title: Care in HIV drug trial closure: perspectives of research participants and research staff in Uganda.

Chief Researcher/Supervisors: Dr Catrin Evans, Associate Professor, Karen Cox, Professor of Palliative Care, Nursing, School of Health Sciences.

Lead Researcher/Student: Sylvia Nalubega, PhD Student, Nursing, School of Health Sciences

Duration of Study: 10/2014-08/2015 10mths **No of Subjects:** 75

Thank you for your letter dated 5th August 2014 responding to the issues raised by the Committee and the following revised documents were received:

- FMHS Research Ethics Application form dated 05/08/2014
- Appendix I: Study proposal v2 dated 05/08/2014
- Appendix II: Information pack for individual interview potential participants v2 dated 05/08/2014.
- Appendix III: Information pack for focus group discussion potential participants v2 dated 05/08/2014
- Appendix IV: Consent Form For Individual Interviews Final version 1.0 dated 04/08/2014
- Appendix V: Consent Form For Focus Group Discussions Final version 1.0: 04/08/2014
- Appendix VI: Interview schedule for individual interviews, V2, 05/08/2014
- Appendix VII Interview schedule for focus group discussions V2 dated 05/08/2014
- Appendix VII: Letter of Introduction to Research Institutions, Dr Catrin Evan 25 June 2014

These have been reviewed and are satisfactory and the study is approved.

Approval is given on the understanding that the Conditions of Approval set out below are followed.

1) Please can you submit copies of approval/agreement letters when these have been obtained from:

- a) the TASO REC, Mulago Hospital Complex, Kampala, Uganda.
- b) the Uganda National Council for Science and Technology (UNCST).
- c) the Research Institutions invited to take part.

2) A Favourable opinion is given on the understanding that all appropriate ethical and regulatory permissions are respected and followed in accordance with all local laws of the country in which the study is being conducted and those required by the host organisation/s involved.

3) You must follow the protocol agreed and inform the Committee of any changes using a notification of amendment form (please request a form).

4) You must notify the Chair of any serious or unexpected event.


5) This study is approved for the period of active recruitment requested. The Committee also provides a further 5 year approval for any necessary work to be performed on the study which may arise in the process of publication and peer review.

6) An End of Project Progress Report is completed and returned when the study has finished (Please request a form).

Yours sincerely

Dr Clodagh Dugdale
Chair, Faculty of Medicine & Health Sciences Research Ethics Committee

Appendix 5: Ethics approval from TASO Research Ethics Committee



**The AIDS Support Organisation
TASO (U) Ltd.**

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Website: www.tasouganda.org

26th August 2014

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Fax: 3488 442 613
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WESTERN
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E-mail: western@tasouganda.org

NORTHERN
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Fax: 3471 432 588
E-mail: northern@tasouganda.org

PROJECTS
GRANTS MANAGEMENT UNIT
GLOBAL TRUST
House of Hope, Plot 16, Windsor Lane
P.O. Box 10443, Kampala
Tel: 0414 286 858
E-mail: grants@tasouganda.org

TASO KARAMONJJA PROJECT
Plot 16, Windsor Lane
P.O. Box 10443, Kampala
Tel: 0332 184 792
E-mail: karamonjja@tasouganda.org

Your Ref:

Our Ref: TASOREC/45/14-UG-IRC-009

Sylvia Nalubega,
Division of Nursing,
The University of Nottingham,
ntxsn11@nottingham.ac.uk

Dear Sylvia,

Ref: RESEARCH APPROVAL "CARE IN HIV DRUG TRIAL CLOSURE:
PERSPECTIVES OF RESEARCH PARTICIPANTS AND STAFF IN UGANDA"

Thank you for submitting your responses to queries raised by the reviewers dated 14th August 2014. This is to inform you that your responses dated 25th August 2014 met the requirements of the TASO REC.

TASO REC annual approval has been granted for the regular review research project "Care in HIV Drug Trial Closure: Perspectives of Research Participants and Research Staff in Uganda, Protocol Version 2, 25/08/2014"

This approval is valid until 25th August 2015 after which you will be required to make a request for extension to the Chairperson, TASO REC in case of continuation with research.

The review and approval includes the following:



1. The study protocol
2. Information pack and Informed consent documents
3. Individual, Key informant and focus group discussion interview guides
4. TASO REC Research Review Application and Declaration of Conflict of Interest form
5. Ethics approval by The University of Nottingham

It is a requirement by the TASO REC that you submit the timely annual progress reports.

We recommend that you proceed with the registration of your study by the Uganda National Council of Science and Technology (UNCST) and a copy of UNCST approval should be forwarded to TASO REC before commencement of the study.

Continuing Review application due date (30 days prior to expiration date).

Sincerely,

Mr. Bakanda Celestin,
Chairperson, TASO RESEARCH ETHICS COMMITTEE (REC)
CC: Executive Director, TASO



**The AIDS Support Organisation
TASO (U) Ltd.**

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13th January 2015

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Fax: 0471 432 990
E-mail: northern@tasouganda.org

Your Ref:

Our Ref: TASOIRC/045/13-UG-IRC-009

Sylvia Nalubega,
Division of Nursing,
The University of Nottingham,
ntxsn11@nottingham.ac.uk

Dear Sylvia,

RE: APPROVAL OF AMMENDMENTS TO RESEARCH PROTOCOL
"CARE IN HIV DRUG TRIAL CLOSURE: PERSPECTIVES OF RESEARCH PARTICIPANTS AND STAFF IN UGANDA"

Thank you for submitting a request for amendments to the protocol "Care In Hiv Drug Trial Closure: Perspectives Of Research Participants And Staff In Uganda, Protocol Version 3" as follows:

1. An addition to include a review of some documents such as the research protocols and the informed consent forms in order to retrieve relevant information for the studies considered.
2. An addition of a research setting to include Makerere University-John Hopkins University Research Collaboration (MU-JHU).
3. A revision of Uganda Virus Institute to Medical Research Council-Uganda Virus Research Institute (MRC-UVRI).
4. An amendment to the key informant interviews to mean including a study coordinator of each included study instead of institution.

Following review of amendments to your research protocol, the committee has approved the submitted amendments. The approval covers the following attached documents:

1. Summary of changes from the revised protocol.
2. The TASO REC amendment/modification request form.


We recommend that you proceed with the submission of the amendments to the Uganda National Council of Science and Technology (UNCST).

Sincerely,



Mr. Bakanda Celestin,
Chairperson, TASO RESEARCH ETHICS COMMITTEE (REC)
CC: Executive Director, TASO (U) Limited

Appendix 6: Ethics Clearance from Uganda National Council of Science and Technology



Uganda National Council for Science and Technology

(Established by Act of Parliament of the Republic of Uganda)

Our Ref: SS 3608 10/11/2014

Ms. Sylvia Nalubega
Right Africa
Masaka

Re: Research Approval: Care in HIV Drug Trial Closure: Perspectives of Research Participants and Staff in Uganda

I am pleased to inform you that on **16/09/2014**, the Uganda National Council for Science and Technology (UNCST) approved the above referenced research project. The Approval of the research project is for the period of **16/09/2014 to 16/09/2016**.

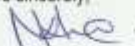
Your research registration number with the UNCST is **SS 3608**. Please, cite this number in all your future correspondences with UNCST in respect of the above research project.

As Principal Investigator of the research project, you are responsible for fulfilling the following requirements of approval:

1. All co-investigators must be kept informed of the status of the research.
2. Changes, amendments, and addenda to the research protocol or the consent form (where applicable) must be submitted to the designated local Institutional Review Committee (IRC) or Lead Agency for re-review and approval prior to the activation of the changes. UNCST must be notified of the approved changes within five working days.
3. For clinical trials, all serious adverse events must be reported promptly to the designated local IRC for review with copies to the National Drug Authority.
4. Unanticipated problems involving risks to research subjects/participants or other must be reported promptly to the UNCST. New information that becomes available which could change the risk/benefit ratio must be submitted promptly for UNCST review.
5. Only approved study procedures are to be implemented. The UNCST may conduct impromptu audits of all study records.
6. A progress report must be submitted electronically to UNCST within four weeks after every 12 months. Failure to do so may result in termination of the research project.

Below is a list of documents approved with this application:

	Document Title	Language	Version	Version Date
1	Research Proposal	English	N/A	N/A
2	Consent Forms	English, Luganda, Gishu, Japadhola, Ateso	2	25/08/2014
3	Interview Schedules	English, Luganda, Gishu, Japadhola, Ateso	2	25/08/2014
4	Informative Pack	English, Luganda, Gishu, Japadhola, Ateso	2	25/08/2014

Yours sincerely,


Winfred Badanga
for: Executive Secretary
UGANDA NATIONAL COUNCIL FOR SCIENCE AND TECHNOLOGY
cc Chair, TASO Research and Ethics Committee

LOCATION/CORRESPONDENCE

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KAMPALA, UGANDA*

COMMUNICATION

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FAX: (256) 414-234579
EMAIL: info@uncst.go.ug
WEBSITE: <http://www.uncst.go.ug>

Appendix 7: Introduction letter from the University of Nottingham



Dr. Catrin Evans,
Faculty of Medicine and Health
Sciences
School of Health Sciences
B Floor, South Block Link
Queen's Medical Centre
Nottingham
NG7 2UH
UK

Tel: +44 (0)115 82 30894
Fax: +44 (0)115 82 31211

catrin.evans@nottingham.ac

.uk
25 June 2014
Dear Sir/Madam,

RE: LETTER OF INTRODUCTION

We are writing to introduce you to Ms Sylvia Nalubega. Sylvia is a Ugandan nurse who has been working in HIV care and research in Uganda for about 8 years. Currently, she is a PhD student at the School of Health Sciences, University of Nottingham, UK. For her PhD research, Sylvia is planning to conduct an interview study, investigating the experiences of former HIV drug trial participants and research staff from Uganda. The study title is: Care in HIV Drug Trial Closures: Perspectives of Research Participants and Research Staff in Uganda. Sylvia's academic supervisors are Professor Karen Cox and Dr. Catrin Evans.

In order to conduct her research, Sylvia will need to be able to contact former HIV drug trial participants and also staff who work in research institutions. Sylvia is interested in speaking with former research participants who have (and who have not) subsequently accessed HIV care services.

This letter is to request your help and cooperation with Sylvia's PhD project. This help would be needed in 3 different ways. First, Sylvia is kindly requesting your permission to allow her to invite your research staff to participate in her study. She is hoping to conduct one to three focus group discussions with research staff and one key informant interview with a coordinator of each study considered. These will not take longer than one hour. Second, she needs help with identifying and approaching former research participants. Lastly, Sylvia will need to review some of the documents pertaining to each included study. These documents may include the study protocol/proposal and the informed consent form. Pertaining to post-trial participants, Sylvia is not requesting access to any personal details of former research participants – but, rather, is requesting

whether your institution might be able to contact them on her behalf (for example, by letter, telephone or a home visit).

As this is a sensitive research area, please rest assured that strict steps will be undertaken to ensure confidentiality and anonymity of both the research participants and the research institution. We would be extremely grateful for your kind support as this study is of particular importance in bringing the voice of key stakeholders in the current debates on HIV drug trial closure in low income settings. Your support will be very essential in achieving this. We will provide detailed feedback on the study findings to all involved so that you can comment on this work.

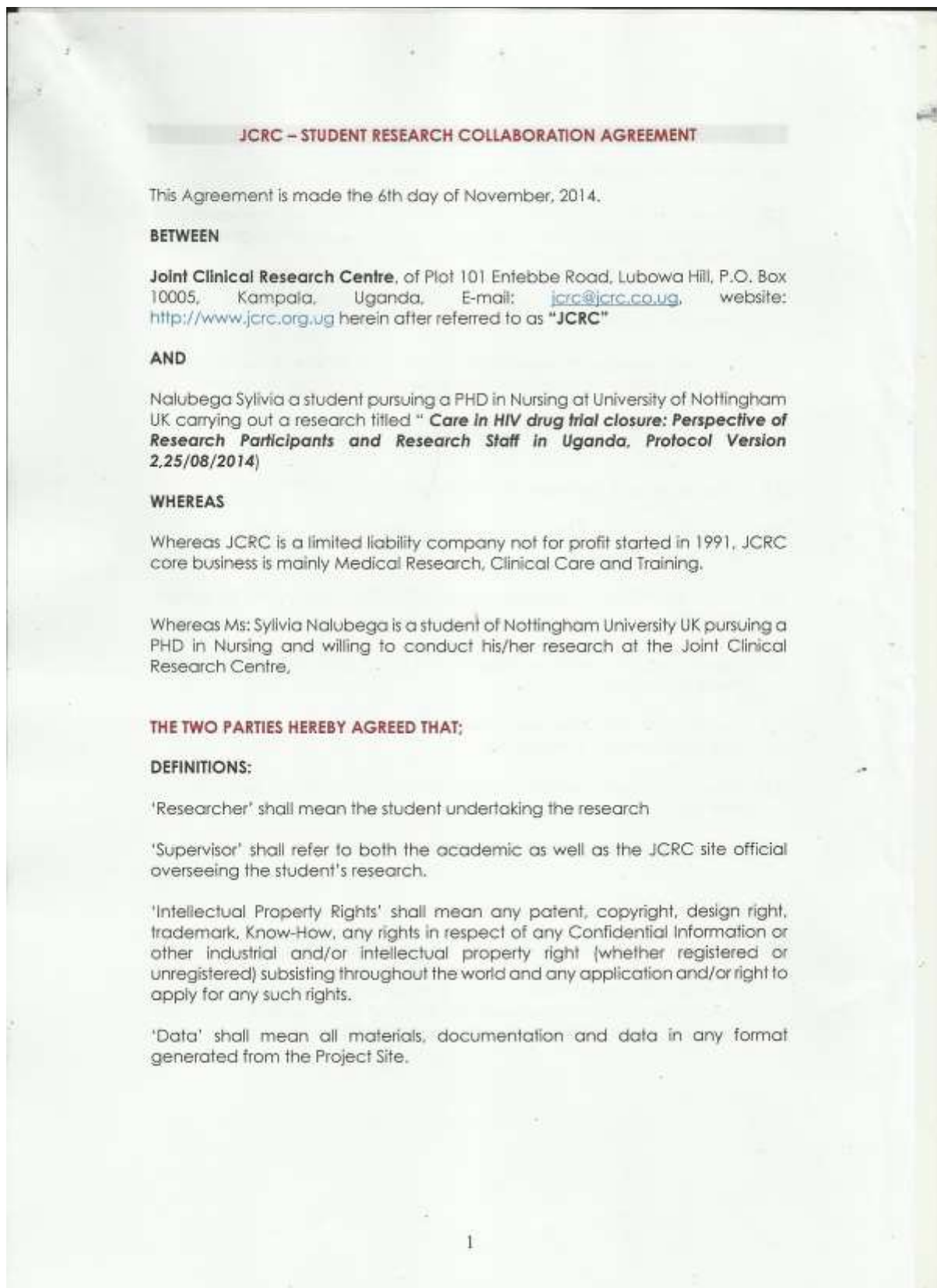
Yours faithfully,

A handwritten signature in cursive script, appearing to read 'Catrin Evans', written in a light grey or blue ink.

Dr. Catrin Evans

Research supervisor

Appendix 8: Permission letter from JCRC



Appendix 9: Permission letter from MRC



MRC

MRC/UVRI Uganda
Research Unit on AIDS

Ms Sylvia Nalubega

c/o
Faculty of Medicine and Health Sciences
School of Health Sciences
Queen's Medical Centre, Nottingham
NG7 2UH, UK

April 10, 2015

Re: PhD Research study entitled: Care in HIV Drug Trial Closures - Perspectives of Research Participants and Research Staff in Uganda.

Dear Ms Nalubega

This letter serves as an agreement from the MRC/UVRI Uganda Research Unit on AIDS for you to carry out data collection for your PhD research investigating the experiences of former HIV drug trial participants and research staff.

We note that your study protocol has been approved by the TASO IRB, UNCST and the University of Nottingham IRB.

Your data collection requirements from the MRC/UVRI site are:

- i) Interviews with up to 10 individuals who participated in the COSTOP trial
- ii) Interviews with the following Research Staff who worked on the COSTOP study:
 - The trial coordinator
 - One Study Doctor
 - One Study Nurse / Counselor
 - One Field Worker

The data collection is expected to take place between April and August 2015, principally out of the MRC Masaka research site. MRC/UVRI research unit staff will assist you in contacting potential participants and you will undertake to cover any costs related to contacting research participants and their attendance for interviews for your study.

While no formal data sharing agreement is necessary, it is expected that the MRC/UVRI Unit will be fully acknowledged in any publication resulting from this research.

Please make contact with the study coordinator of the COSTOP trial, Dr Zac Anywalne (Email: Zacchaeus.Anywalne@mrcuganda.org) for further assistance in commencing your work.

Yours sincerely

A handwritten signature in black ink, appearing to read 'Pontiano Kaleebu'.

Prof Pontiano Kaleebu
Unit Director

MRC/Uganda Virus Research Unit on AIDS | C/O Uganda Virus Research Institute | Plot 51- 59 Nakiwogo Road -
Entebbe | P.O Box 49 Entebbe | Tel: +256 (0) 417 704000 | +256 (0) 312 262910/1 | +256 (0) 752 731733
Email: mrc@mrcuganda.org | Website: www.mrcuganda.org