

From PUBLIC HEALTH SCIENCES
Karolinska Institutet, Stockholm, Sweden

COUNT IN THE YOUNG PEOPLE: HIV VACCINE TRIAL PARTICIPATION IN TANZANIA.

Theodora Mbunda



**Karolinska
Institutet**

Stockholm 2018

All previously published papers were reproduced with permission from the publisher.

Published by Karolinska Institutet.

Printed by Universitetservices US-AB

© Theodora Mbunda, 2018

ISBN 978-91-7831-242-9

COUNT IN THE YOUNG PEOPLE: HIV VACCINE TRIAL PARTICIPATION
IN TANZANIA

THESIS FOR DOCTORAL DEGREE (Ph.D.)

By

Theodora Mbunda

Principal Supervisor:

Associate Professor Asli Kulane
Karolinska Institutet
Department of Public Health Sciences

Opponent:

Professor Peter A. Newman
University of Toronto
Department of Social Works

Co-supervisor(s):

Professor Muhammad Bakari
Muhimbili University of Health and Allied
Sciences
Department of Internal Medicine

Examination Board:

Professor Nawi Ng
Umeå University
Department of Public Health and Clinical
Medicine

Dr Edith A.M Tarimo
Muhimbili University of Health and Allied
Sciences
Department of Nursing Management

Professor Fred Wabwire-Manden
Makerere University
Department of Epidemiology and Biostatistics

Professor Eric Sandström
Karolinska Institutet
Department of Clinical Science and Education

Associate Professor Maja Söderbäck
Mälardalen University
Department of Health, Care and Social Welfare

Professor Anna Thorson
Karolinska Institutet
Department of Public Health Sciences

To my beloved late dad Fr. Dr. Daniel Mbunda and my mentor, the late Dr. Guerino Chalamilla

FOREWORD

My doctoral research investigated the participation of young people in HIV vaccine trials; however, my journey as a researcher started many years back when my late father told me I was going to be a doctor. At the time, I didn't understand what he meant by that. When I graduated from medical school, I thought I had fulfilled my dad's wishes, however that realization faded away as soon as I started working as a medical officer at a youth-friendly IDC. I was responsible for treating youths with sexually transmitted infections including HIV/AIDS, but importantly providing other youngsters with essential yet basic tools for HIV prevention. As a young doctor, I was devastated by the rampant damage to livelihood particularly in young people caused by HIV/AIDS. Advancing to become Monitoring and Evaluation Manager in an HIV care and treatment program in Dar es Salaam gave me the opportunity to see broader complexities of HIV burden, its determinants, dynamics and its prevention strategies, matters that go beyond routine clinical setting of etiology-to-treatment modalities. I quickly jumped onto the research wagon as soon as I heard about HIV vaccine clinical trials at Muhimbili University of Health and Allied Sciences, MUHAS because, by then, I had realized that serving my people as a mere medical doctor would not be sufficient to alleviate the distressing impact of HIV/AIDS. I still consider joining the "HIV sub program" at MUHAS to be one of the best decisions I made as I knew I would be right in the thick of finding solutions to this frightening disease.

My research subject "youth" was carefully chosen not only because this population is the most affected but also 'forgotten' in a sense that most HIV prevention interventions in our settings have been targeting adults, children and pregnant women. Since treating and preventing HIV have always been my top priority, research skills I have acquired during my doctoral training will be put into use in a quest for an effective HIV vaccine through research work in the field of HIV prevention.

ABSTRACT

Background: For nearly four decades, HIV infection has raged across the world; leaving devastation in its wake particularly in sub-Saharan Africa. Even though the use of antiretroviral (ARV) drugs has significantly contributed to lessening HIV/AIDS related morbidity and mortality, their efficacy has had a limited outcome on the cure and prevention of both old and new HIV infections. Like many viral diseases, an effective HIV vaccine is considered the cornerstone for ending the HIV epidemic. The involvement of young people in preventive HIV vaccine clinical trials is fundamental as they are unduly affected by the HIV burden. Whilst new vaccine models continue to be tested for safety, immunogenicity and efficacy, only a few young people join such innovative clinical interventions; highlighting an evolving need for understanding the intricacies of partaking in clinical HIV vaccine trials.

Aim: The overall aim for this thesis was to increase knowledge of factors contributing to recruitment and participation of young people in preventive HIV vaccine trials.

Methods: The thesis encompassed four studies using both qualitative and quantitative methods. Data collection for cross sectional study I was done among 450 youth using questionnaires to assess factors contributing to their willingness to participate in an HIV vaccine trial. Study II used seven focus group discussions to elicit the influence and opinions of members of the community on participation in the trial. In study III, we employed respondent-driven sampling to enlist 600 young female sex workers in a cross-sectional study that assessed willingness to participate in HIV efficacy trials and risk behaviors using questionnaires. In-depth interviews were used in study IV to explore experiences of participating in HIV vaccine trials among 17 young volunteers in a phase I/II HIV vaccine trial, TaMoVac 01.

Results: This thesis identified positive and negative attributes of the willingness of young people to participate in an HIV vaccine trial at several levels of ecological model. At the intrapersonal level, altruism, self-independence in decision making, being in charge of safe sex, having some knowledge of HIV vaccines and regular health check-ups were regarded as positive attributes for joining the trial whereas anxiety about fertility and HIV positivity post vaccination were identified constraints. Looking at the interpersonal level, endorsement of the trial by significant others and support of staff were features of partaking whereas fears of perceived contents of HIV vaccine and mischaracterization of sexual practices were portrayed as impediments. Last but not least, support of regulatory institutions, members of parliament, stigma, and the trial center were elements at the community/institutional level, while substance abuse, unemployment and poverty were structural factors hampering the contribution of young people to HIV vaccine trials.

Conclusion: Youth showed readiness to participate in phase IIa HIV vaccine trial. For most young people, the decision to participate in vaccine trials largely depend on support of members of the community. In contrast, for high-risk young women, this decision largely be their own. Some factors like altruism, support from members of the community and, perceived personal benefit served as positive attributes to participation. Despite such readiness, fertility issues, stigma, poverty were perceived as hurdles needed to be resolved by different stakeholders on individual, community and societal levels for successful participation.

Keywords: Young adults, willingness, participate, recruitment, retention, HIV, vaccine trial, phase I/II, Tanzania

LIST OF SCIENTIFIC PAPERS

- I. Mbunda T, Bakari M, Tarimo EAM, Sandström E, Kulane A. Factors that influence the willingness of young adults in Dar es Salaam, Tanzania, to participate in phase I/II HIV vaccine trials. *Glob Health Action*. 2014; 7: 22853 doi: 10.3402/gha.v7.22853 PMID: 2
- II. Mbunda T, Tarimo EAM, Chalamilla G, Bakari M, Sandström E, Kulane A (2016). The Influence of Community Members on Participation by Youth in an HIV Vaccine Trial in Tanzania. *PLoS ONE* 11(12): e0168660. doi:10.1371/journal.pone.0168660
- III. Mbunda T, Tarimo EAM, Bakari M, Sandström E, Kulane A. Recruitment using Respondent Driven Sampling, risk behaviors assessment and willingness of young Female Sex Workers in Dar es Salaam, Tanzania to participate in HIV vaccine trials.(submitted)
- IV. Mbunda T, Tarimo EAM, Bakari M, Sandström E, Kulane A. Why I am a part of an endeavor to save mankind - Perspectives of young volunteers on participation in an HIV vaccine trial: A qualitative study from Dar es Salaam, Tanzania. (submitted)

CONTENTS

1	BACKGROUND	1
1.1	HIV EPIDEMIOLOGY	1
1.1.1	<i>HIV in the World</i>	1
1.1.2	<i>HIV in Tanzania</i>	3
1.1.3	<i>National response to HIV epidemic</i>	7
1.2	HIV VACCINE DEVELOPMENT AND ITS INITIATIVES	8
1.2.1	<i>Global initiatives</i>	8
1.2.2	<i>Tanzanian initiatives</i>	10
1.3	RATIONALE	10
2	AIM AND OBJECTIVES	11
3	METHODS	12
3.1	SUMMARY OF STUDIES IN THESIS	12
3.2	SETTING	13
3.3	STUDY PARTICIPANTS	13
3.4	STUDY DESIGNS	14
3.4.1	<i>Cross-sectional studies</i>	14
3.4.2	<i>Qualitative studies</i>	15
3.5	DATA COLLECTION TOOLS	16
3.5.1	<i>Structured interviews</i>	16
3.5.2	<i>Focus group discussions</i>	17
3.5.3	<i>In-depth interviews</i>	17
3.6	DATA ANALYSIS	18
3.6.1	<i>Quantitative analysis</i>	18
3.6.2	<i>Qualitative analysis</i>	19
3.7	ETHICAL CONSIDERATIONS	21
4	RESULTS	22
4.1	CONTRIBUTORY FACTORS IN THE RECRUITMENT AND PARTICIPATION OF YOUTH IN PREVENTIVE HIV VACCINE TRIALS	23
4.1.1	<i>Intrapersonal factors</i>	23
4.1.2	<i>Interpersonal factors</i>	26
4.1.3	<i>Community/institutional factors</i>	28
4.1.4	<i>Structural factors</i>	29
5	DISCUSSION	31

5.1	INTRAPERSONAL FACTORS	31
5.1.1	<i>Altruism</i>	31
5.1.2	<i>Perceived personal benefit</i>	32
5.1.3	<i>Vaccine-induced seroreactivity</i>	33
5.2	INTERPERSONAL FACTORS	34
5.2.1	<i>Support from members of the community</i>	34
5.2.2	<i>Mischaracterization of sexual conduct</i>	36
5.3	COMMUNITY/INSTITUTIONAL FACTORS.....	37
5.3.1	<i>Support from research team</i>	37
5.3.2	<i>Support from regulatory institutions</i>	38
5.3.3	<i>Stigma</i>	39
5.4	STRUCTURAL FACTORS	40
5.4.1	<i>Poverty and unemployment</i>	40
5.4.2	<i>Substance abuse</i>	40
5.5	METHODOLOGICAL CONSIDERATION	41
5.5.1	<i>Validity</i>	41
5.5.2	<i>Non-probability sampling</i>	42
5.5.3	<i>Low rate of coupon transfers</i>	43
5.5.4	<i>Incentives</i>	43
5.5.5	<i>Social desirability</i>	43
5.5.6	<i>Trustworthiness/validity</i>	44
6	CONCLUSION	48
7	RECOMMENDATIONS.....	48
8	ACKNOWLEDGEMENTS	49
9	REFERENCES.....	53

LIST OF ABBREVIATIONS

AIDS	Acquired Immunodeficiency Syndrome
ANC	Antenatal clinic
AOR	Adjusted Odds Ratio
ART	Antiretroviral therapy
ARVs	Antiretroviral drugs
CBO	Community Based Organization
CDC	Centres for Diseases Control and Prevention
CI	Confidence Interval
DNA	Deoxyribonucleic acid
EDCTP	European and Developing Countries Clinical Trials Partnership
FGDs	Focus group discussions
FHSPs	Frontline Health Service Providers
FSWs	Female Sex Workers
HIV	Human immunodeficiency virus
HIVIS03	HIV Vaccine Immunogenicity Study 03
HSPs	Health Service Providers
HVTN 702	HIV Vaccine Trials Network 702
IDC	Infectious Diseases Center
IAVI	International AIDS Vaccine Initiative
MSM	Men who have Sex with Men
MoHCDGEC	Ministry of Health, Community Development, Gender, Elderly and Children
MUHAS	Muhimbili University of Health and Allied Sciences
MVA	Modified vaccinia Ankara
NACP	National AIDS Control Program
NGO	Non-government organization
PHC	Population and Housing Census
PMTCT	Prevention of mother to child transmission
RDS	Respondent driven sampling
RDS-SS	Respondent driven sampling-successive sampling

RV 144	Acronym for Thailand HIV vaccine trial
SEM	Socioecological model
STI	Sexually Transmitted Infection
SSA	Sub-Saharan Africa
TACAIDS	Tanzania Commission for AIDS
TFDA	Tanzania Food and Drugs Authority
TaMoVac 01	Tanzania Mozambique Vaccine trial project
UNAIDS	The Joint United Nations Programme on HIV/AIDS
VISP	Vaccine-induced seropositivity
VISR	Vaccine-induced seroreactivity
WHO	World Health Organization
WTP	Willingness to participate

1 BACKGROUND

1.1 HIV EPIDEMIOLOGY

1.1.1 HIV in the World

Since its outbreak three decades ago, Human Immunodeficiency Virus, HIV has relentlessly continued to claim the lives of people as one of the leading causes of morbidity and mortality worldwide, particularly in sub-Saharan Africa, (SSA). The first HIV patients were reported in the United States by Centers for Diseases Control and Prevention, CDC, in 1981 among minority and men having sex with men, MSM, communities. Since then, new cases of HIV have been reported universally¹.

In 2017, UNAIDS estimated that 77.3 million people had been infected by HIV since the start of epidemic, and that 36.9 million people were living with HIV, of which 19.6 million resided in eastern and southern Africa², accounting for 45% of the world's HIV infections³.

Efforts to reach targets of reducing new HIV infections, stigma and discrimination, scaling-up of HIV prevention services, increasing enrolment of HIV-positive children in HIV services by 2020 have been attained to a certain degree³. The global decline in deaths from AIDS-related illness is at its lowest level since the outbreak of the disease in the 1980s due to the more widespread use of ART particularly in SSA the region. But the reduction of AIDS-related mortality has not been quick enough to reach the General Assembly's 2020 milestone³.

The number of new HIV infections globally continued to decline in 2017 yet, progress is far slower than what is required to reach the 2020 milestone of less than 500 000 new infections. The estimates have shown that new infections at all ages declined from a peak of 3.4 million in 1996 to 1.8 million in 2017. Children under the age of 15 years old accounted for 180 000 new infections in 2017³.

Even though the reduction in new HIV infections between 2010 and 2017 was greatest in SSA due to sharp reductions in eastern and southern Africa (30% decline), this region remains the most affected by the HIV epidemic, accounting for 53% of people living with HIV globally. Other regions that have shown HIV decline include the Caribbean (18% decline), Asia and the Pacific (14% decline) while in the Middle East, North Africa, eastern Europe and central Asia, the annual number of new HIV infections has doubled in less than 20 years³.

Women continue to account for a disproportionate percentage of new HIV infections among adults in SSA, representing 59% of the 980 000 new adult HIV infections in 2017³. Every week, around 7 000 young women aged 15 –24 years become infected with HIV globally. In SSA, three in four new infections are among girls aged 15–19 years, and young women aged 15–24 years are twice as likely to be living with HIV than men in 2017². In other parts of the world apart from SSA, men accounted for 63% of the 650 000 new adult

HIV infections in 2017. Globally, there were almost 90 000 more new HIV infections among men than women in 2017³.

Adolescent girls and young women continue to face a disproportionately high risk of HIV infection as a result of gender inequalities, gender-based violence, physiological factors³, insufficient access to sexual and reproductive health services, education, poverty and food insecurity⁴.

HIV infection dominates key populations and their sexual partners. These populations accounted for 47% of new HIV infections globally. Ninety five percent of new HIV infections recorded in eastern Europe, central Asia, the Middle East and North Africa and 16% of new HIV infections in eastern and southern Africa.

Notably, the risk of acquiring HIV is 27 times higher among men who have sex with men, 23 times higher among people who inject drugs, 13 times higher for female sex workers and 12 times higher for transgender women². Several challenges exist in engaging key populations in HIV preventive services because their actions or identities are considered socially or religiously unacceptable, and sometimes punishable under local law. This impairs collection of quality data on the location and size of these populations, their attitudes and practices, their access to HIV services, and the incidence and prevalence of HIV among them in low and high HIV prevalence settings³.

The devastating impact of HIV impinges on social, economic, health and political advancement worldwide but the disease's remarkable impact is most noticeable in low-income countries. It is estimated, for example, that 380 000 people died from AIDS-related illnesses in eastern and southern Africa compared to 13 000 deaths in western and central Europe and North America in 2017². HIV-related deaths in most low-income countries have led to a surge in the number of orphans, street children and children-headed family as well as to poor productivity and economic growth due to reduced manpower.

1.1.1.1 Global HIV response

The initial response to HIV prevention in 1980s was met with resistance, skepticism and stigma among many government officials and the community at large around the globe because of its association with marginalized communities, high morbidity and mortality and sexual transmission¹. From the late-1980s onwards, international organizations began to realize the severity and dire consequences of HIV and hence embarked on worldwide efforts to fight the HIV pandemic by planning coordination meetings and developing strategies, policies and guidelines on the prevention of HIV¹. Following that, a number of international donor-funded agencies, foundations and non-government organizations were created to provide leadership, technical support and expertise in HIV prevention particularly in developing countries. Through such commitment in leadership and resources, most affected countries had established country-specific national HIV/AIDS control programs by 1995 that slowly over time gained local political and communal engagement. Furthermore, in 1998 the

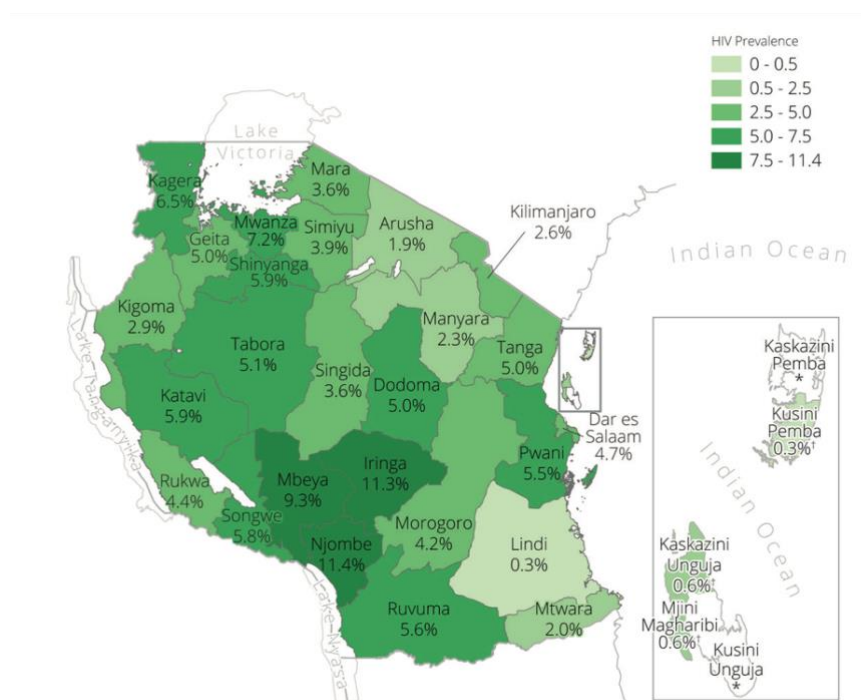
discovery of antiretroviral therapy was a major scientific breakthrough that led to changes in the epidemiology of HIV infection globally¹.

1.1.2 HIV in Tanzania

1.1.2.1 Country profile

The United Republic of Tanzania is located in East Africa (Figure 1). It covers 947 300 square kilometers⁵ with an overall sparse population density of 51 persons per square kilometer, however there are some regions with quite high population densities like Dar es Salaam and Mjini Magharibi⁶. Tanzania is divided into 30 regions: 25 on the mainland and five in Zanzibar. These regions are divided into districts, which are subsequently divided into councils. The councils or local government units administer and provide public services⁵. According to a national census, the total population in 2012 was 44 928 923⁶, with 97% of the population living on the Tanzanian mainland and the rest in Zanzibar⁵. The majority of the population, 71%, live in rural areas, whereas 29% reside in urban areas⁵. Youth aged 15-24 years was found to constitute 19.1% of the total population⁷. The overall sex ratio was about 95 males to every 100 females⁶ and the total fertility rate was 5.5 for women aged between 15 and 49 years⁸. At the national level, the literacy rate among males aged 15 years and above was higher than among females, 83.4% and 73.3% respectively^{9,10}. The gross domestic product (GDP) was TZS 29.5 trillion (Tanzanian shillings), an increase of TZS 4.1 trillion on 2016¹¹. Kiswahili is national language spoken in Tanzania.

Figure 1: Map of Tanzania showing HIV prevalence among adults 15+ by region, 2016-2017.

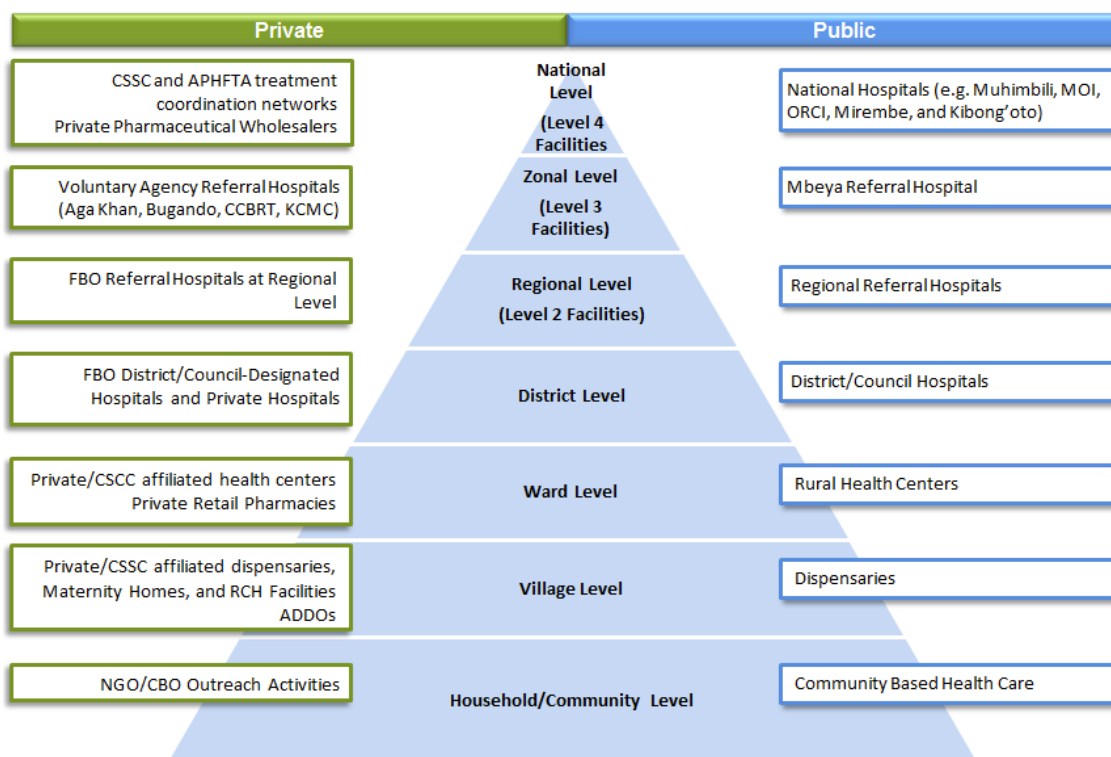


Source: Ministry of Health, Community Development, Gender, Elderly and Children (MoHCDGEC), the Ministry of Health (MoH) Zanzibar, National Bureau of Statistics (NBS) and the Office of Chief Government Statistician (OCGS). Summary Sheet: Preliminary Findings. Tanzania HIV Impact Survey (THIS) 2016-2017.

1.1.2.2 Tanzania health system and HIV services

Tanzania has a well-organized health structure from the community to the national level. Primary health care services constitute the basis of the pyramidal structure of health care services, see Figure 2 below. Community-based health activities focus on health promotion and prevention. Dispensaries provide preventive and curative outpatient services, while health centers admit patients, and sometimes provide surgical services. Council hospitals provide medical and basic surgical services to referred patients. Regional Referral Hospitals provide specialist medical care. Zonal and National Hospitals offer advanced medical care and are teaching hospitals for medical, paramedical and nursing training. The health system is managed at council and regional levels by The Council and Regional Health Management Teams respectively. The Ministry of Health, Community Development, Gender, Elderly and Children, MoHCDGEC, has the overall responsibility over the health and social welfare services. It provides technical guidance to organizations involved in service delivery, mobilizes resources, controls and promotes maintenance of quality standards and sets the policy for social welfare¹².

Figure 2: The health care pyramid in Tanzania (public and private equivalent)



Source: *The United Republic of Tanzania. Health Sector Strategic Plan July 2015 – June 2020, HSSP IV. Reaching All Households with Quality Health Care. Ministry of Health and Social Welfare.*

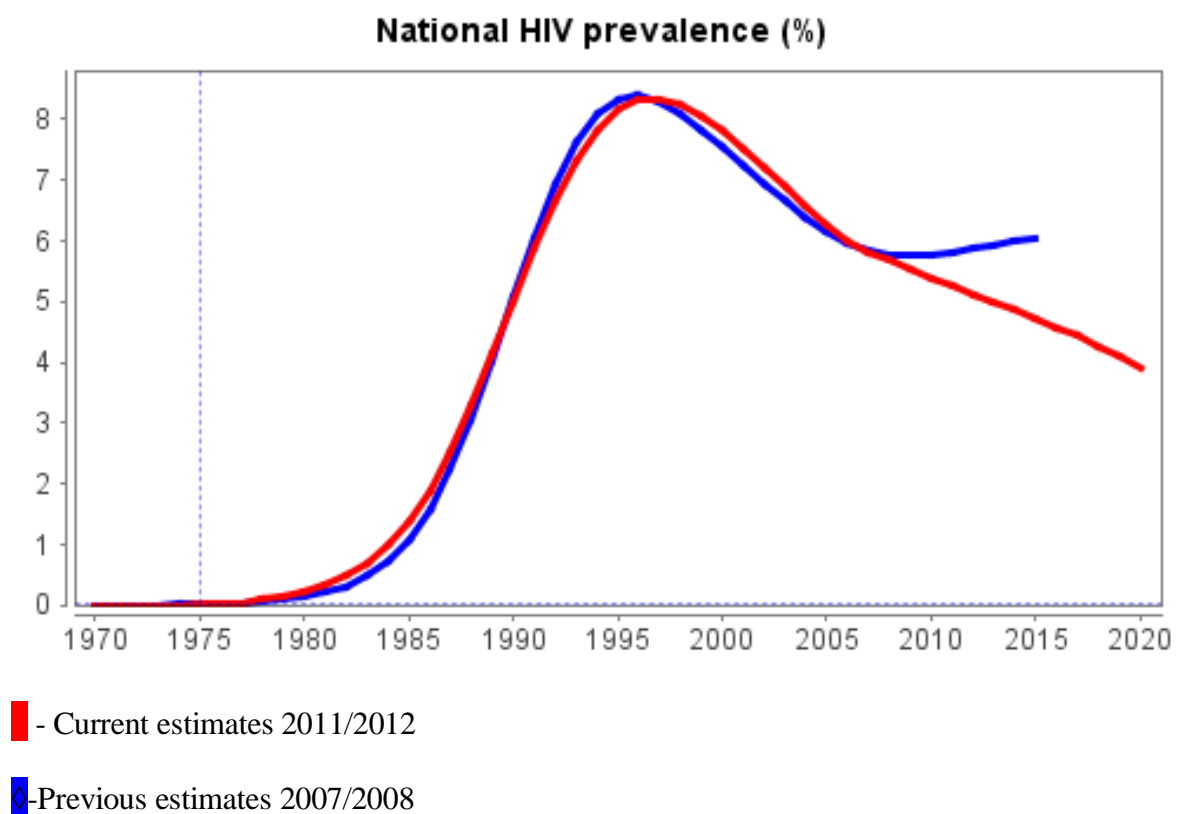
1.1.2.3 HIV/AIDS

HIV has enormously affected Tanzania, like so many other countries. The first HIV patient was reported from northern part of Tanzania, in Kagera region, in 1983. By then, HIV was called ‘slim’ disease due to its characteristic presentation of severe wasting due to diarrhea and dehydration. By December 1986, all mainland regions had reported cases to the Ministry of Health and Social Welfare¹³. HIV infections have spread throughout the country predominantly through unprotected heterosexual intercourse, attributing to 80% of infections, while mother-to-child transmission and blood borne infections account for 18% and 1.8% of all infections respectively¹⁴. The HIV epidemic in Tanzania Mainland is generalized and stable while in Zanzibar islets, it is largely concentrated. The main drivers of the HIV epidemic include risky sexual behaviors such as having unprotected sexual intercourse with concurrent multiple sexual partners, transactional and cross-generational sex, early sexual debut, poor and inconsistent use of condoms, poor HIV knowledge, poverty, poor coverage and access to HIV preventive services¹⁴, and unequal gender norms that perpetuate gender based violence¹⁵. In 2017, UNAIDS reported the total number of people living with HIV was 1.5 million, out of which 120 000 were children under the age of 15, alongside an estimated 32 000 HIV-related deaths. In the same reporting period, 65 000 people were newly diagnosed with HIV infection, 66% of HIV patients were alive and receiving anti-retroviral therapy and only 48% of them were virally suppressed³ The annual incidence of HIV among

adults aged 15 to 64 years in Tanzania was 0.29 percent in 2017¹⁶. The overall national prevalence of HIV among the adult population showed a decreasing trend from 2003 to 2012, see Figure 3 below¹⁴. The Tanzanian HIV impact survey in 2016/2017 reported a further decline in prevalence to 5% among people aged 15 to 64 years, whereas prevalence among young people aged 15 to 24 years was 1.4%. These prevalence estimates vary with sex, age and regions. Among adults 15 years and older, HIV prevalence varies geographically across Tanzania, ranging from 11.4% in Njombe to less than 1% in Lindi and Zanzibar, see Figure 1 above. Overall, women disproportionately bear more of the HIV burden than men, with HIV gender disparity more pronounced among younger adults¹⁶.

The unrelenting impact of HIV in Tanzania has led to serious political, social and economic setbacks in all sectors due to increased HIV/AIDS morbidity and mortality among women and men in their prime years of productivity. As a result, there is poor performance in targeted quality of life indicators, loss of human capital, reduction of income, poverty, disruption of nuclear family structure, enormous strains on extended family due to orphans, and an increased number of households headed by children and widows¹⁷.

Figure 3: Estimated HIV prevalence in Tanzania for the period 1980-2020



Source: HIV/AIDS and STI surveillance report number 23.

1.1.3 National response to HIV epidemic.

The Government of Tanzania has continued to demonstrate great commitment and leadership to the fight against the HIV and AIDS pandemic¹⁴. A major achievement was the establishment of the National AIDS Control Program and the Tanzania Commission for AIDS, TACAIDS, in 1987 and 2001 respectively⁵. TACAIDS took over the role of coordinating, overseeing, and guiding the multi-sectoral response, while the National AIDS Control Program, NACP, remained responsible for leading the health sector responses of the National Multi-sectoral Strategic Framework⁵ covering the period 2013/2014-2017/2018¹⁴. This framework addresses the following fundamental thematic areas; prevention of new adult and child HIV infections, HIV care treatment and support, HIV/AIDS impact mitigation interventions, strengthening local and international partnership in the HIV/AIDS response and monitoring and evaluation of the HIV/AIDS response¹⁴. Additionally, a number of policies and strategies, such as the Global Health Initiative Strategy, the national HIV/AIDS communication Advocacy strategy, the HIV and AIDS care and the Treatment plan and health sector HIV and prevention of mother to child transmission (PMTCT) strategic plan, were developed and aligned to the overall health sector strategic plan to address the epidemic¹⁴. About eight in ten Tanzanian facilities have an HIV testing system, and one-third of all facilities offer HIV/AIDS care and support services. Twenty-eight percent of all facilities provide ART services. More than nine in ten facilities in Tanzania that offer ante natal clinic (ANC) services also provide some PMTCT services while other sexually transmitted infections (STI) services are almost universally available in Tanzanian facilities⁵.

A recent review of the health status of Tanzanians shows some improvement. Over two decades, there has been a downward trend in childhood and maternal mortality rates, improved children's nutritional status and an increase in life expectancy at birth. These improvements primarily resulted from controlling the HIV/AIDS pandemic. This achievement was due to the provision of life-long anti-retroviral drugs and the presence of effective vaccination programs⁵. Despite the gains, there are some challenges ahead in HIV prevention. HIV prevalence is decreasing slowly, key populations (who inject drugs, sex workers and men who have sex with men) do not receive enough attention and women remain more at risk than men. There is also a large gap between adult and pediatric anti-retroviral treatment coverage, a lack of age-disaggregated data to understand the situation regarding coverage of HIV, and sexual and reproductive health services among adolescents⁵.

1.1.3.1 HIV and youth in Tanzania.

The concept of youth varies from one community to another depending on socioeconomic circumstances, culture, and history. In general, a youth is a boy or girl who is in the transition period from childhood to adulthood. While the international definition considers youth as persons aged between 15 and 24 years, in Tanzania, youth refers to persons aged 15 to 35 years¹⁸. According to the 2012 population census data, the young population aged 15-24 years was found to constitute 19.1% of the total population of Tanzania⁷. For this thesis, we define youth slightly differently, as 18-25 years old, because people aged 18 years and above

are legally and ethically allowed to sign informed consent forms. In this thesis, the term 'young adults' has been interchangeably used with 'youth' when it comes to literature citations. In most cases, the term 'young adults' refers to both adolescents and youth because there is no term equivalent to 'adolescent' or 'youth' in many African languages¹⁹.

The Tanzania HIV/AIDS and Malaria Indicator Survey 2011-12 indicated that age at first sexual intercourse marks the time at which most young people risk exposure to sexually transmitted infections including HIV since the main route of HIV transmission is through heterosexual contact¹⁷. In addition, HIV infection among young people aged 14-25 is an important proxy gauge for determining trends in HIV incidence and prevalence¹⁴. A survey conducted in Tanzania in 2016/17 showed general HIV prevalence to be 1.4% among young adults aged 15 and 24 years (2.1% and 0.6% in young women and men respectively). This was slightly more than a quarter of the overall national HIV burden among the adult population¹⁶. Furthermore, the previous two surveys of HIV indicators compared and found estimates of HIV prevalence between 2007-08 and the 2011-12 in the 15-19 age group unchanged, at 1%¹⁷. The HIV indicator survey of 2011-12 revealed that 9% and 10% of women and men respectively aged 15-24 had sex before they were 15 years old. Fifty percent of women and 43% of men reported having sex before reaching 18 years¹⁷. In the same survey, among all sexually active young people age 15-24, 4% and 14% of women and men respectively reported having sexual intercourse with two or more partners in the past 12 months prior to the survey¹⁷. Overall, the surveys have shown that young women are at higher risk of HIV infection than their counterpart males in the same age group. Some of the predominant HIV drivers in this age group were risky sexual behaviors, such as having multiple concurrent partners, living in urban areas, early sexual debut, inadequately low condom use and low knowledge of HIV¹⁷.

1.2 HIV VACCINE DEVELOPMENT AND ITS INITIATIVES

1.2.1 Global initiatives

Use of anti-retroviral drugs for therapy and prevention, male circumcision, microbicides and other behavior interventions have had a significant but limited effect on the number of new HIV infections. The available prevention methods do not offer long-lasting protection against the acquisition of HIV infection. The prospects for strengthening prevention efforts have never been more promising, as a series of highly effective biomedical prevention tools have emerged in recent years to buttress the prevention benefits of behavioral and structural factors²⁰. Just like many other infectious viral diseases, a safe, effective and affordable preventive HIV vaccine is ultimately needed to complement and enhance the effectiveness of existing prevention strategies to control the HIV/AIDS pandemic, particularly in low-income countries²¹.

The scientific community has been working tirelessly and endlessly to explore different technologies for developing an effective HIV vaccine from as early as 1984. Initial efforts involved exploration of envelope-based vaccines, virus subunits, synthetic peptides, vaccinia-

vectored vaccines, neutralizing antibodies along with the development of non-human primate models for HIV infection. The first HIV vaccine trial took place in the United States in 1988²². Thereafter, a number of early phase I/II HIV clinical trials have been recorded in the International AIDS Vaccine Initiative (IAVI) database²³. The trials took place mostly in the US and other high-income countries and a few in low- and middle-income countries like Uganda, Kenya, Tanzania and South Africa²³. Favorable outcomes to develop an effective HIV vaccine in clinical trials have, however, been hampered by genetic variability of HIV, lack of natural immunity to HIV, variability of HIV types, lack of correlates of protective immunity and lack of an animal model that reliably predicts vaccine efficacy in humans²⁴.

After studying safety and immunogenicity outcomes of vaccines in phase I/II, initial efficacy clinical trials were conducted but yielded disheartening conclusions. One of the first trials, STEP, involved the immunization of almost 3 000 healthy uninfected volunteers with three adenovirus vectors, each expressing an HIV gene of a vaccine. The STEP trial was designed to elicit strong cellular immunity but, nonetheless, it showed no protection against infection. More alarmingly, the vaccine appeared to increase the rate of HIV infection in individuals with prior immunity against the adenovirus vector used in the vaccine. In addition, the same vaccine was being administered in South Africa to 3 000 individuals in the Phambili trial when the initial results of the STEP trial were made public. Since no one could have predicted the correlation between preexisting vector-specific immunity and an increase in susceptibility to HIV infection, the results lead to the immediate halting of both the STEP and Phambili trials²⁵.

Nevertheless, in 2009, results of HIV clinical trials involving 16 402 Thai men and women at mostly heterosexual community risk of HIV-1 provided the first breakthrough and demonstration in humans that a vaccine can prevent HIV infection. Two HIV vaccine candidates showed a vaccine efficacy in preventing HIV infection among the volunteers, 60% and 31% efficacy at 12 months and 3.5 years respectively. The vaccine efficacy was higher among those whose initial self-reported risk was low and did not change during the trial. It was lower among those whose risk was not low at baseline and/or increased during the trial²⁶. That breakthrough gave researchers a platform to improve research activities to further study immune response, methodology and administrative approaches of RV144 in order to improve the design of future trials²⁴.

Based on RV 144 trial results, in November 2016, a large phase IIb/III HIV vaccine clinical trial, HVTN 702, was launched among 5 400 seronegative South African adults over 24 months and potentially up to 36 months from enrollment²⁷. The HVTN 702 study is the largest, phase IIb/III advanced stage clinical trial to take place in South Africa that aims to determine if an investigational HIV vaccine regimen is safe, tolerable and effective at preventing HIV infection among South African adults. The experimental vaccine regimen is based on the one tested in the RV144 clinical trial in Thailand. The HVTN 702 vaccine regimen has been adapted to the HIV subtype that predominates in southern Africa, where the pandemic is most pervasive²⁸.

1.2.2 Tanzanian initiatives

In the 1990s, Tanzania started to prepare its sites for early-phase HIV vaccine trials by conducting incidence and prevalence studies to assess the suitability of police officers for trials^{29,30}. The researchers trained laboratory and clinical personnel; and developed and established virological and immunological methods for vaccine immunogenicity assays in collaborating laboratories in Sweden and Tanzania³¹. The preparations paved way for a phase I/II clinical trial (HIVIS03) with 60 healthy HIV negative volunteers in Dar es Salaam, Tanzania. The aim was to continue evaluating the safety and immunogenicity of multiclade HIV-1 plasmid DNA vaccine followed by MVA boost with heterologous HIV-1 inserts. The vaccine demonstrated excellent safety and immunogenicity by eliciting cell-mediated and antibody responses to Env-antibody responses³¹. Following the success of the HIVIS 03 trial, between 2010 and 2012, a phase IIa randomized clinical trial, TaMoVac 01, recruited 120 healthy, low-risk, HIV-negative participants from two centers in the Dar es Salaam and Mbeya regions. In Dar es Salaam, these participants were police officers and prison service officers, as well as young people from a youth friendly IDC and in Mbeya, they were from the general population³². In this trial, investigators found that a simplified intradermal vaccination regimen with 2 injections of combined HIV-DNA plasmids primed cellular responses was as efficient as the standard regimen of 5 injections of separated plasmid pools after boosting twice with HIV MVA. In the aftermath, the TaMoVac II phase II clinical trial was carried out between 2012 and 2015 to assess the safety and immunogenicity of DNA priming administered by electroporation, as it was hypothesized that electroporation would increase immune responses and thereby the efficiency of DNA priming and lead to a dose-sparing DNA vaccine regimen. This would in turn reduce the number of shots necessary to deliver the full dose and induce comparable immune responses as is the case with lower DNA vaccine concentrations³³.

1.3 RATIONALE

Generally, young people are disproportionately affected by the burden of HIV/AIDS and AIDS-related death, thus they need to be included in HIV vaccine trials. AIDS is the leading cause of death among young people in Africa³⁴. Young women are twice as likely to acquire HIV infection than young men because of early sexual debut, poor condom use, sexual violence and have less comprehensive knowledge of HIV³⁵. Furthermore adolescent girls and young women are often prevented from seeking services and making decisions about their own health due to gender inequalities³⁴. The vulnerability is further fueled by laws and discrimination of young people in key populations such as female sex workers, young men having sex with men, and intravenous drug users³⁵. The inclusion of youth in HIV prevention clinical research has the potential to improve the current understanding of the safety and efficacy of biomedical prevention technologies in younger populations that are at increasing risk of HIV infection. However, there are significant individual, operational, and community-level barriers to engaging youth in clinical prevention trials. Such barriers include insufficient understanding of clinic prevention research, self-presentation bias, access to clinical trials, mistrust of research, and stigma associated with participation in clinical trials³⁶.

Moreover, HIV vaccine trials are shrouded in negative attitudes and personal fears from significant others³⁷, misconceptions such as that the vaccine will cause HIV infection, or, conversely, that the vaccine in a trial will protect from HIV infection³⁸ leading some participants to see participation in a vaccine trial as an opportunity to stop using HIV prevention strategies such as condoms and partner reduction³⁹. Another possible barrier to youth participation in HIV vaccine trials emerged in a study on men who have sex with men, where participants worried that vaccine-induced seropositivity, VISP, would be interpreted by society as actual HIV infection and entail the same level of stigma⁴⁰.

Whereas involving youth in multistage HIV vaccine trials with many follow-up visits is crucial, very little has been investigated as regards the challenges pertaining to recruitment and participation in Tanzanian settings. In light of this, we studied issues surrounding the willingness of young people to be recruited, experiences of young volunteers in an early-phase HIV clinical trial, as well as tried to elucidate the role and opinions of significant others towards youth participation in HIV vaccine studies in order to add some knowledge to the existing literature. The findings from this project may contribute to shaping a national HIV vaccine framework, strategies and policy and help to address challenges pertaining to recruitment, participation as well as the implementation of future HIV vaccine studies among young people in Tanzanian settings.

2 AIM AND OBJECTIVES

General aim:

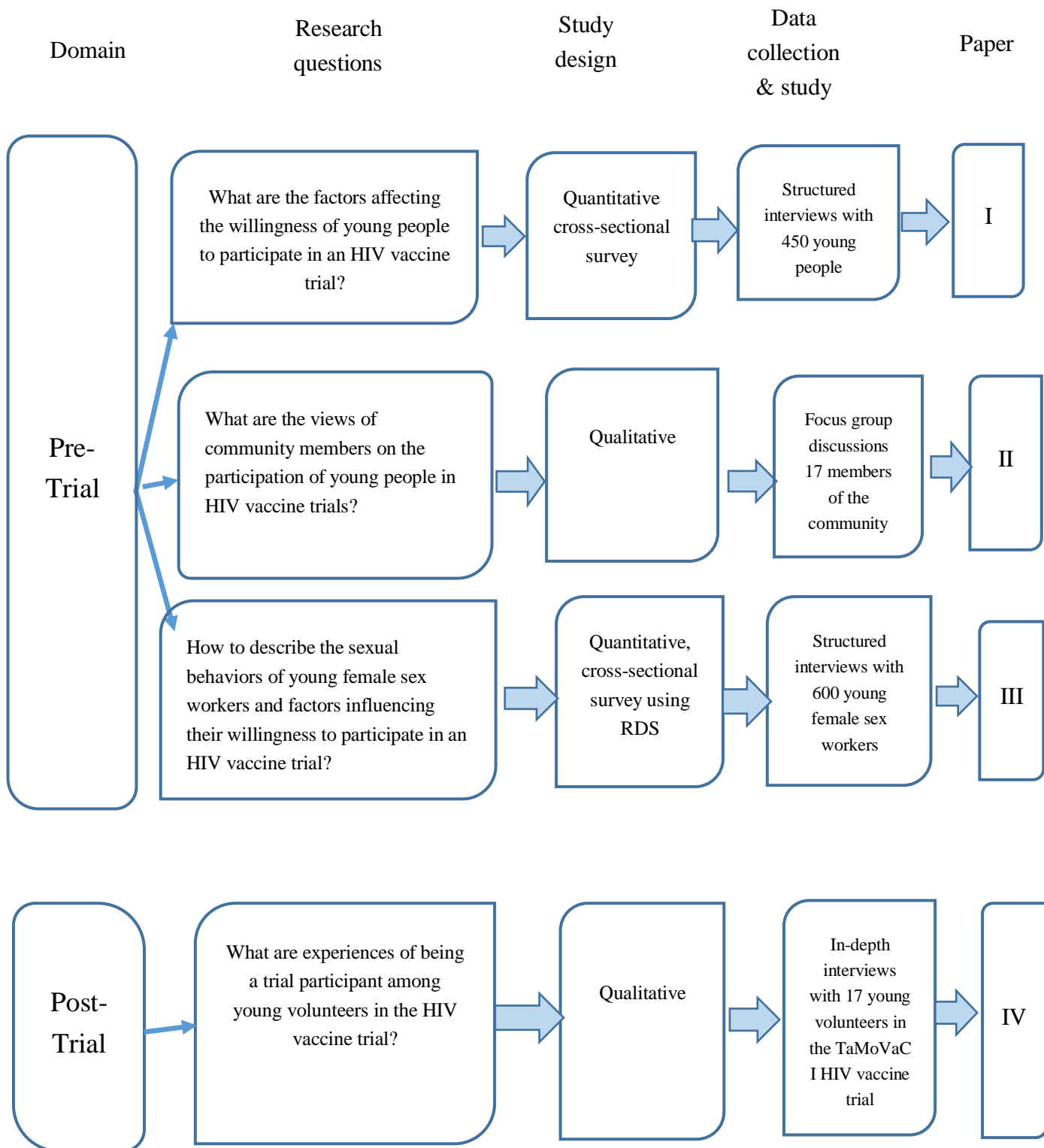
To increase knowledge of factors contributing to recruitment and participation of young people in preventive HIV vaccine trials.

Specific objectives:

- I. To characterize the willingness of young adults in Tanzania to participate in a phase I and II HIV vaccine trial and identify the factors that influence this willingness.
- II. To explore the views of members of the community on participation of youth in an HIV vaccination trial.
- III. To describe the recruitment approaches, risk behaviors and practices and willingness of young female sex workers to participate in efficacy HIV vaccine trials.
- IV. To investigate experiences among young adult volunteers who participated in a phase I and II HIV vaccine trial.

3 METHODS

3.1 SUMMARY OF STUDIES IN THESIS



This thesis included our sub-studies that used both quantitative and qualitative methods to answer research questions surrounding the factors influencing participation of youth in preventive HIV vaccine trials in Dar es Salaam, Tanzania. Quantitative research is research that places emphasis on numbers in the collection and analysis of data⁴¹. In this thesis, it was used to quantify, describe and characterize the youth willing to be recruited to HIV vaccine trials, whereas a qualitative method was employed to seek in-depth understanding of the research gaps in cultural issues and the social support contextual settings of HIV vaccine trial participation among young people⁴². Both methods complemented each other to generate deeper understanding and a contextual explanation of outcomes of interest in the thesis.

3.2 SETTING

The Dar es Salaam region is found along the coast of Tanzania (see Figure 1). According to the 2012 national census, this region was inhabited by a total of 4.3 million people, of whom 51.3% were female. Its population growth rate per annum was 5.6. The literacy rate of people aged 5 years and above was 93.6%. It is one of the biggest business cities in Tanzania that is involved in tourism, business, fish farming, livestock and poultry⁴³. The region has been divided into five administrative municipalities: Kinondoni, Ilala, Kigamboni, Ubungo and Temeke. There is one national referral hospital, Muhimbili National Hospital, in Ilala, with five referral hospitals in all 5 municipalities. For years, Muhimbili National Hospital has served as one of the major teaching hospitals, and recently a new teaching hospital, the Muhimbili University of Allied Health and Sciences Academic Medical Centre, has been opened in Ubungo district. Apart from that, Dar es Salaam has a number of government-owned district hospitals, health centers, dispensaries, as well as health facilities run by faith-based, private and non-government organizations.

3.3 STUDY PARTICIPANTS

All study participants were recruited from all districts of Dar es Salaam region, mostly females aged 25 years or less. Most of them had completed seven years of basic primary school education and were single. In study I, the young adults visiting the youth friendly IDC for medical consultation, health education, family planning services, HIV counselling and testing consented to participate. In study II, the participants were community members, such as parents, guardians, friends, peers and siblings, whom were identified by the young people who took part in study I. The community members participating in study II were close to the young people and played important roles in providing social support. In study III, young female sex workers who had provided sex in exchange for money, drugs or gifts in the past 6 months were recruited. Study IV included the young volunteers who received the first three doses of HIV 1 DNA vaccines or placebo injections in the HIV vaccine trial, TaMoVac 01.

3.4 STUDY DESIGNS

3.4.1 Cross-sectional studies

3.4.1.1 *Study I*

Study I was a cross-sectional study using a self-administered questionnaire, written in Kiswahili, among 450 youth at an Infectious Disease Clinic (IDC). This IDC is a government facility located in Ilala Municipality that provides youth-friendly health care services such as screening and treatment of sexually transmitted infections, contraceptives, counselling, testing, care and treatment for HIV. In 2012, a total of 4,379 individuals, 28% of whom were young people, aged 12-25 years, visited the IDC. Most of the newly registered attendees sought HIV counselling and testing followed by treatment of other STIs. The participants of the study were all individuals aged 18-25 years who visited the IDC from February to September 2012. Of the 548 youths approached, 98 (18%) did not accept this invitation, primarily because of time constraints. The participants were then systematically selected by including every other patient. For those who declined, their replacements were selected in the same manner until we reached the required sample size. Each participant filled out a written consent form, then answered research questions in the questionnaire with minimal supervision from research assistants.

3.4.1.2 *Study III*

Study III was a cross-sectional study using a self-administered questionnaire among 600 young female sex workers recruited using the respondent-driven sampling (RDS) strategy. The study examined recruitment approaches, risk behaviors and willingness of young female sex workers to participate in an efficacious HIV vaccine trial. The RDS strategy was used in order to facilitate recruitment of hard-to-reach participants by using a dual incentives system that compensated a participant both for being interviewed and for recruiting others to the study⁴⁴. The study was based on the findings of a formative study conducted among 15 participants between November and December 2016 using in-depth interviews. The formative session was conducted so as to establish hot spots, the scheduling of visits at trial centers, perceived stigma and barriers to health-seeking behaviors. Initially, 10 of 15 key participants were identified as seeds/initial recruiters, eventually the number of seeds increased to 20 because some initial recruitment chains ceased early by not referring their peers to the study site. The seeds recruited the first wave of study participants. Each of the seeds and subsequent recruiters received three coupons with unique serial numbers. The following instructions were given to the recruiters: to recruit female peers and friends aged between 18 and 25 years, the peers/friends who exchanged sex for goods, gifts or money within their circle and recruit the girls the recruiters had an idea about where they lived. The recruiters were further asked to observe a deadline for the date of return of valid coupons given to recruited participants. Finally, the research assistants discussed with them about the nature of compensation, i.e. compensation of transport allowance and time as a recruiter after bringing eligible participants for enrolment in the research. Thereafter, each referred

respondent received three coupons, and recruited their peers until the sample size was met. At the clinic, each referred respondent voluntarily presented herself with a valid coupon, signed a consent form and filled in a questionnaire. The participants were provided with counseling on STI risk reduction such as HIV and contraceptive use. They were offered HIV counselling and testing at the clinic. Those who were HIV-positive were referred to care and treatment at the IDC or other center of their choice.

3.4.2 Qualitative studies

3.4.2.1 Study II

Study II was a qualitative study focused on perceptions and roles of members of community regarding the participation of youth in HIV vaccine trials based on the findings of study I. Some participants in study I were asked to refer one person who played a key supportive role in their life. The participants for study II included peers, friends, siblings, parents and guardians, collectively referred to as members of the community. They formed a group with different socio-demographic information and backgrounds. Study participants were recruited using purposeful sampling to obtain participants with the wealth of information required to answer research questions⁴⁵. The study participants were initially contacted about the study by the respective young person, thereafter, a research team made formal contact. All potential study participants were informed about the aim of the study, venue, form and nature of meeting.

3.4.2.2 Study IV

Study IV was a nested, qualitative study exploring positive and negative experiences among all young adults who had completed three HIV 1 DNA/placebo vaccinations in an HIV vaccine trial. The study participants were among the volunteers in the main HIV vaccine trial named TaMoVaC 01³². For the purpose of Study IV, out of 25 young volunteers in TaMoVac 01, only 17 volunteers were reached and consented to participate in the study. We were not able to recruit another 8 volunteers because some were not in Dar es Salaam at the time of interview, others were sick and others could not be reached by mobile phone. Data collection was done through in-depth interviews using semi-structured interview guide because interviews give detailed information about a person's thoughts and behaviors and can also lead to in depth exploration of new issues. The interviews furthermore provide context to other data, offering a more complete picture of what happened in the program and why⁴⁶.

3.4.2.3 Steps of recruitment of young adults in the phase I/II HIV vaccine trial, TaMoVac 01

For the larger HIV clinical trial, the TaMoVac 01 trial, the potential young volunteers were informed of it at different youth NGOs such as KIWOHEDE, UMATI and SALVATION ARMY so as to sensitize youth, their teachers, trainers and guardians to HIV prevention lessons. Young people who showed interest in HIV prevention sessions were invited to the youth friendly IDC. At the IDC, the potential volunteers were given a health education

information package focusing on HIV prevention messages, contraception use, STI management, HIV counselling and testing, adolescence and reproductive health and HIV vaccine trial participation among youth. After the first session, the participants were asked to fill in forms to obtain their demographic and contact information. Further, the participants were asked to indicate if they would want to come to a second educational session which focused on HIV vaccine trial participation among youth. During the second session, usually a week after the first session, interested participants came to the IDC specifically to receive information on HIV vaccine trials. Among the things discussed were history of vaccines, stages of vaccine production, inclusion and exclusion criteria in clinical trials, benefits and expected adverse events, clinical trial schedule, need for contraceptive use during the trial period and inclusion of significant others during the trial. At the end of the second session, participants who were interested to join in the clinical trial were registered and asked to come to the third session with people whom they regarded as significant in their decision making and who played other key roles in the provision of social support. During the same session, more detailed information on the HIV vaccine clinical trials was provided including type of investigations, amount of blood drawn per visit and HIV risk assessment. In these sessions, potential trial participants had the opportunity to obtain accurate information about trial processes and answers to myths about HIV vaccine trials. After the educational sessions, those who were willing to participate in and thought to be eligible for trials were given informed consent forms. The potential volunteers were asked to take the consent forms, read and share the information with their significant others and to return with the forms at the following scheduled meeting. Finally, the potential volunteers presented themselves at the trial center in Muhimbili National Hospital to start formal recruitment procedures, including the review and signing of consent forms to ensure the potential participants understood what it entailed to be trial participant, review of individual inclusion and exclusion criteria, risk assessment and to take samples for investigation. In sum, the TaMoVac I trial in Dar es Salaam recruited 60 healthy HIV-negative volunteers, of which 25 were young volunteers aged 18-24 at the time of recruitment³².

3.5 DATA COLLECTION TOOLS

3.5.1 Structured interviews

Structured interviews were employed to conform to a standardized list of questions, sequence of questioning and systematized ratings of the responses of the study participants. Structured interviews improve validity, reliability and coverage of interviewees and reduce variability⁴⁷. In studies I and IV, the standardized structured interviews using questionnaires had both open- and closed-ended questions. The open-ended questions were used as follow up questions to the closed-ended questions. The open-ended questions were used to get more information and meaningful explanation of the responses to some key closed-ended questions. In study I, the questionnaires comprised of questions on sociodemographic information of the study participants, sexual risk assessment, contraceptive use, knowledge about and perception of HIV vaccine studies, presence and type of social support that young

people would need or have when they decided to join HIV vaccine trials and willingness to participate in HIV vaccine trials.

In study III, firstly, participants filled in the questionnaires for assessing social network size, tracking of recruiter-recruit relationship and reasons for accepting the coupons. That was followed by a standardized behavioral assessment questionnaire for assessing the sociodemographic information of the study participants, risk behaviors, willing to participate in efficacious HIV vaccine trials, people within sexual networks who might influence their participation in the vaccine trials and other practices of using HIV prevention methods.

In both studies, participants filled questionnaires by themselves in order to give them the opportunity to answer truthfully some of the sensitive information, hence minimizing the negative impact of social desirability. However, the completed questionnaires were immediately reviewed by trained research assistants, who were trained and registered nurses. The research assistants helped to provide guidance to participants on questions that were unclear, counsel participants in case of discomfort, or guide them on completion of the questionnaires.

3.5.2 Focus group discussions

A focus group is a technique involving the use of in-depth group interviews in which participants are selected because they are a purposive, although not necessarily representative, sampling of a specific population, this group being ‘focused’ on a given topic⁴⁸. Participants in this type of research are selected on the criteria that they would have something to say on the topic, are within the age-range, have similar socio-characteristics and would be comfortable talking to the interviewer and each other⁴⁹. In study II, to preserve homogeneity, the groups were separated by gender so as to ensure freedom of discussion among members⁴⁹. The participants were divided into a total of seven male and female only groups; comprising of three and four groups of women and men respectively. Each group had between five and eight participants. The FGD guide was used to ensure consistent flow of thoughts hence enabling meaningful flow of discussions. During sessions the PhD candidate TM and co-author EAMT moderated the sessions interchangeably to keep discussions within topic and ensure every member had equal opportunity to express their view. The guide included socio-demographic information and three leading questions: 1. What impedes young people from participating in clinical trials? 2. How would you support such participation? and 3. What other facilitating factors might promote participation? A total of seven group discussions were conducted, to reach saturation⁵⁰. All discussions took place at IDC. The duration of each session was approximately 30 to 67 minutes, and each was audio-recorded after obtaining permission from the participants.

3.5.3 In-depth interviews

In depth interviews were conducted for Study IV using a semi-structured interview guide. They give detailed information about the interviewee’s thoughts and behaviors and can also lead to an exploration of new issues in depth. The interviews furthermore provide a context to

other data, offering a more complete picture of what happened in the program and why⁴⁶. For this study, a semi-structured interview guide was used to bring an interviewee into discussion, thereafter letting them describe their positive and negative experiences as an HIV trial participant in the *Kiswahili* language. The interview guide probed about the meaning of being a trial participant, reasons for volunteering, coping with follow-up visits, phlebotomy (injections & taking blood samples), and views on fertility, contraceptive uses, risk perception, sex practices during and after trial, benefits and challenges of trial participation, and the role of social support. All 17 interviews were conducted in a room with a door and windows covered by curtains to maintain privacy so as to provide the most comfortable environment possible. The interviews lasted about 45 minutes each, they were all audio-recorded after permission had been sought from the interviewees beforehand.

3.6 DATA ANALYSIS

3.6.1 Quantitative analysis

3.6.1.1 Logistic regression (Study I)

Double data entry for 450 questionnaires was carried out in an EpiInfo database. Two data sets were merged, compared, and cleaned. The frequency distributions of all socio-demographic and independent variables were determined. The proportion of young people who were willing to participate in an HIV vaccine trial was determined. Assessment of perceptions of HIV vaccine studies was conducted by 8 Likert like statements with 4 responses: strongly agree, agree, disagree and strongly disagree, which were scored as 4, 3, 2, and 1 respectively for positively phrased statements. In negatively phrased statements, the order of scores was reversed to reflect the scores above. The Cronbach alpha coefficient was 0.64, reflecting relatively low internal reliability of the statement in measuring perception⁵¹. However, we included this analysis because at individual level these questions collected information that was critical to understating how participants felt about HIV vaccine studies. The median total score for each statement for all participants was 22. This categorized perception of HIV vaccine studies as positive for any score of 22 and above and negative for any score less than 22. The assessment of knowledge concerning HIV vaccine studies was done by asking six questions. The questions investigated the concept of placebo versus vaccine, infectivity, safety, and protection afforded by the HIV vaccines. They were not standardized questions, but we formulated them based on needs that arose after a literature review of the knowledge of HIV vaccine studies among young people revealed limited awareness of the subject. The internal reliability of 0.6 was determined using Cronbach alpha coefficient. Despite the fact that it was low, the aggregate variable of “knowledge concerning HIV vaccine” was included in the analysis. Responses to questions were scored as 1 when answered correctly and 0 for incorrect answer or ‘I don’t know’. The mean total possible score out of 6 was 2.1. Therefore, this variable was categorized as having some knowledge for all participants with scores at or above the mean, and low knowledge for those with less than the mean score.

Using Chi square tests, bivariate analyses were performed to examine the associations between gender and sexual behavior, then willingness to participate with socio-

demographic characteristics, sexual behavior, social support, perceptions and knowledge concerning HIV vaccine studies. Logistic regression models were employed to control for cofounders as follows: all bivariate analyses of willingness to participate with a p-value of less than 0.2 were included in multivariate logistic regression analyses and were considered to be statistically significant if the resulting p-value was less than 0.05⁵². The Hosmer-Lemeshow goodness of fit test was applied to assess the logistic regression model, and a final p-value of less than 0.05 was taken as indicating good fit. The frequency of missing data was 3.3%. All statistical analyses were two-sided and performed using Stata Version 12.1 for Windows.

3.6.1.2 RDS and Logistic regression (Study III)

We conducted double data entry to minimize data entry errors. Two data sets were compared to identify errors, which were corrected using the unique RDS and registration numbers in source documents. Preparation of data for analysis was done by coding variables such as age groups into categorical variables, and aggregating some variables into one category e.g. widow and divorced. Moreover, other categorical and binary variables whose responses were in word format were changed into numeric values⁵³. The data analysis started by using the RDS-SS Analytical package⁵⁴ because in RDS, the sample is used to make estimates about social network connecting the population, then, using information about social network size, estimates are generated about characteristics of the population⁵⁵.

Weighted frequencies of the population proportions of selected variables of interest were compared with unweighted ones. Furthermore, 95% confidence intervals of weighted population proportions were calculated using the RDS-SS Analytical package⁵⁴. Using the STATA 13/SE package, and considering the weighting and clustering, the bivariate associations of willingness to participate in HIV vaccine trials using selected independent variables such as sociodemographic characteristics, risk behaviors and power dynamics in sexual networks, were determined by computing weighted data in regression models⁵⁶. All those associations of the willingness to participate and variables with P value of ≤ 0.25 were entered into the final model to look for factors associated with willingness to participate in trials⁵⁷. The results of logistic regression models were presented as odds ratios with 95% confidence intervals. Thereafter, all variables that had P value of ≤ 0.05 were regarded as statistically significant in the final model.

3.6.2 Qualitative analysis

3.6.2.1 Content analysis (Study II)

The purpose of content analysis is to organize and elicit meaning from the data collected and to draw realistic conclusions from it. The researcher must choose whether the analysis should be of a broad surface structure (a manifest analysis) or of a deep structure (a latent analysis)⁵⁸. During the analysis, each transcript from seven focus group discussions constituted a unit of analysis⁵⁸. During analysis, recordings were transcribed verbatim, with final Swahili transcripts translated to English. Using content analysis, the results were expressed primarily

as manifest and latent content. The views of members of community were abstracted from sentences having similar meanings in the transcripts to form meaning units. Here, a meaning unit refers to words, sentences or paragraphs containing aspects related to each other through their content and context⁵⁹. The meaning units were then coded using different colored codes within the transcripts. The codes having similar thoughts and meaning were further organized and abstracted into categories. A category refers mainly to a descriptive level of content and can thus be seen as an expression of the manifest content of the text⁵⁹. Finally, three themes emerged from summarized categories that contained the same concepts. In this analysis, a theme was considered as a thread of an underlying meaning through condensed meaning units, codes and categories, on an interpretative level, seen as an expression of the latent content of the text⁵⁹.

3.6.2.2 *Interpretive descriptive analysis (Study IV)*

Data analysis was conducted using the interpretive description approach as this is an inductive analytic approach designed to create ways of understanding clinical phenomena that yield applications implication⁶⁰. The foundation of interpretive description is the smaller scale qualitative investigation of a clinical phenomenon of interest to the discipline for the purpose of capturing themes and patterns within subjective perceptions and generating an interpretive description capable of informing clinical understanding. Interpretive description departs from traditional qualitative descriptive approaches in that it assumes investigators are rarely satisfied with description alone and are always exploring meanings and explanations that may be adapted in clinical settings. Simply stated, interpretive description provides direction in the creation of an interpretive account that is generated on the basis of informed questioning, using techniques of reflective, critical examination, and which will ultimately guide and inform disciplinary thought in some manner⁶¹. Using this approach in Study IV, data was transcribed from all the verbatim audio-recorded data, with the transcripts translated from Kiswahili to English. PhD candidate TM familiarized herself with data by reading all transcripts in both languages to ensure transcribed and translated texts had captured all the information as described by the participants. All transcripts were broken into small paragraphs that described similar concepts to obtain meaning units, which described the core meaning of each paragraph. The meaning units were then examined and assigned to groups of similar patterns or codes. Different colored papers were used to identify different codes within the transcripts. This was a descriptive part of analysis whereby the transcripts were naturally labelled as they were initially explained. Similar codes were then discussed, contextualized and grouped into categories. Finally, after examination, rearrangement and sorting of similar categories, two themes emerged inductively based on data, and not on a pre-existing analytical framework. Throughout this process, raw data was conferred to ensure that researchers' interpretations were coming from the data. The emerged themes portrayed the living experiences of being a young trial participant. The member check was done by holding a debriefing meeting with some participants. During the meeting, PhD candidate TM presented the findings and their meaning as per researcher's perspectives. The participants were given opportunity to discuss and interpret findings in their own words. At the end, all

participants agreed that the findings of this investigation echoed the experiences of the young people participating in the trial.

3.7 ETHICAL CONSIDERATIONS

The studies were granted ethical approval by the Institutional Review Board at Muhimbili University of Health and Allied Sciences (MUHAS) as follows: studies I&II MU/DRP/AEC//Vol.XIV/33 dated 31st October 2012, study III 2017-04-12/AEC/Vol.XII/78 dated 12th April 2017 and, study IV MU/DRP/AEC/Vol.XVI/100 dated 28th February 2013. Permission to use IDC as a venue for data collection was granted by the relevant authorities. Study participants were informed of the aim of the studies, the need for participation, their right to withdraw at any time and the benefits and risks of participating. The researchers and research assistants were available to clarify additional questions before the participants decided to sign the consent forms. All potential participants signed the consent forms before taking part in the respective studies.

4 RESULTS

In general, the findings will be discussed in a modified socio-ecological model to explain the intertwining of factors at different level that positively and negatively affect the participation of young people in preventive HIV vaccine trials in Tanzanian settings.

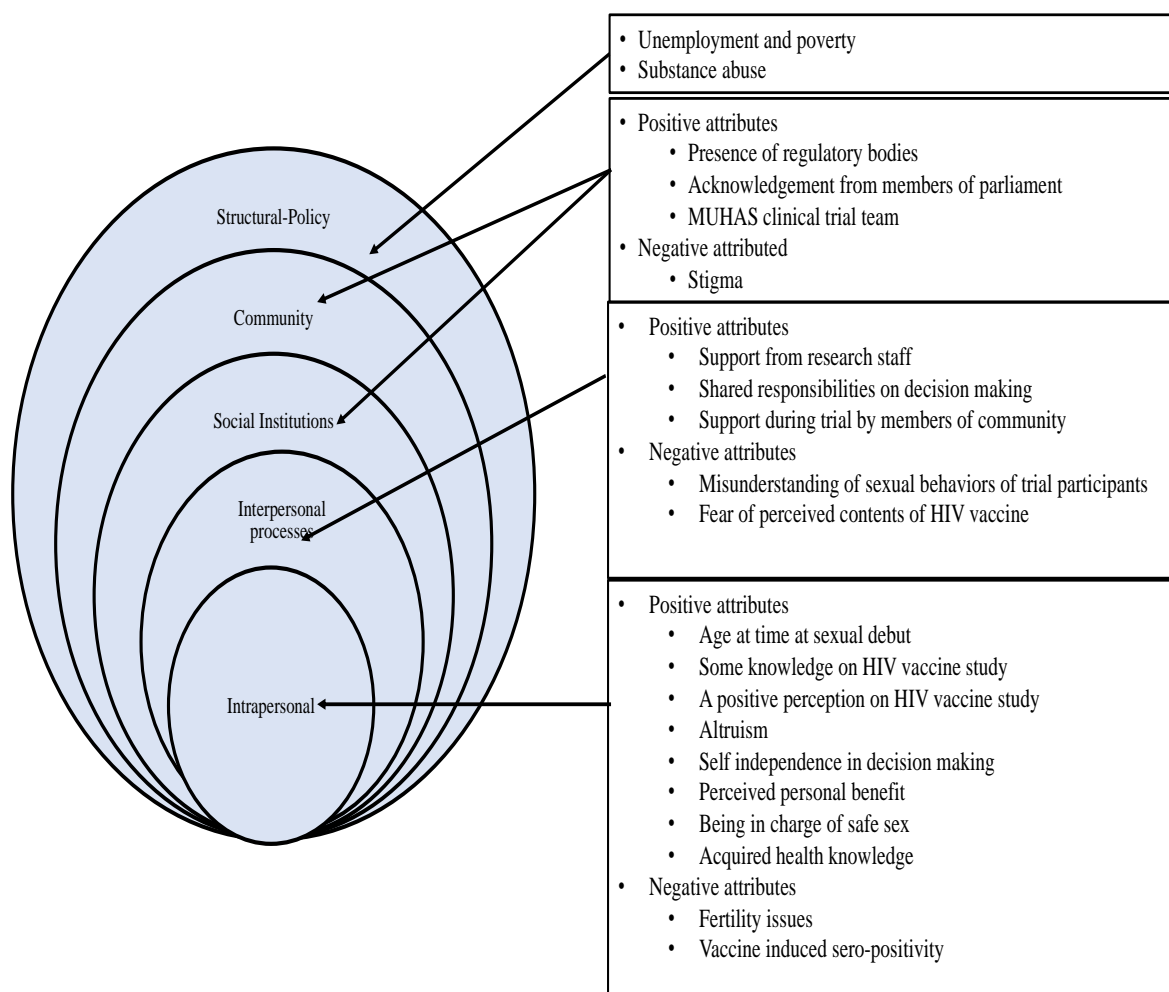
The socio-ecological model, SEM, was proposed by McLeroy et al⁶², who describe it as a model for health promotion and disease prevention. For this project, the model explains HIV vaccine trial participation among youth as a health promotion entity to prevent the acquisition of new HIV/AIDS infection. The model looks at both individual and environmental factors as targets for health promotion interventions to address changes in intrapersonal, interpersonal, organizational, community and public policy in order to maintain health behaviors.

Furthermore, the model assumes that changes in social environment will bring changes in individuals, and that support of individuals in population is necessary for implementing environmental changes as detailed below:

- Intrapersonal factors describe characteristics of individuals such as knowledge, attitudes, behavior, self-concept and skills, including the developmental history of the individual.
- Interpersonal processes and primary groups refer to formal and informal social networks and social support systems, including family, work groups and friendship networks.
- Institutional factors include social institutions with organizational characteristics and formal rules and regulations for operation.
- Community factors refer to relationships among organizations, institutions and informal networks within defined boundaries.
- Public policy describes local, state and national laws and policies.

In this thesis, our results have been organized and discussed in terms of intrapersonal factors, interpersonal processes, institutional/community and structural/policy factors as illustrated in figure 4 below.

Figure 4: Modified socio-ecological model illustrating factors for the participation of the young people in the HIV vaccine trials, adapted from McLeroy et al.



4.1 CONTRIBUTORY FACTORS IN THE RECRUITMENT AND PARTICIPATION OF YOUTH IN PREVENTIVE HIV VACCINE TRIALS

4.1.1 Intrapersonal factors

In study I, intrapersonal elements associated with the recruitment of youth in HIV vaccine trials included: being 15 or older at the time of sexual debut (AOR for age groups 15-19 years and older participants 2.6 (95% CI 1.0-6.7) and 2.7 (95% CI 1.0-7.1) respectively; having some knowledge about HIV vaccine studies (AOR 2.1, (95% CI 1.5-3.4); and a positive perception of such studies (AOR 2.3, (95% CI 1.5-3.6). In study III, almost all respondents, 545 (91%), responded positively to a question on willingness to participate in a hypothetical HIV vaccine trial. Some of the reasons given for wanting to participate in an HIV vaccine trial were altruism (20%), wanting to contribute to a cure for HIV and wanting to learn about vaccine trials. Furthermore, the participants expressed some degree of autonomy in decision making, as 61% of the participants did not need permission from anyone to participate in a

trial. In Study IV, participants reported that during educational sessions they were told about regular checkups during the trial period. This, coupled with the fact that the services would be provided on a regular basis, attracted them to join the HIV vaccine trial, TaMoVac 01, as illustrated below:

“I wanted to know my overall health status as one would be checked every now and again, (Female participants, TMV 2)”, others cited *“I just wanted to have regular HIV and pregnancy tests during trial”*, TMV 9.

Furthermore, participants in Study IV reported being eager to know how vaccine trials were conducted as a reason for joining the trial. One explained as follows:

“To know whether or not the vaccine would have ill-effects, how effective it would be in the human body as well as understand what the research was all about”, TMV 10.

In Study IV, positive attributes leading to participation and staying in the HIV vaccine trials included gained health knowledge during trials. Here, the participants stated that they acquired knowledge, which helped them to dispel myths and suspicion about the trial. Knowledge made the participants confident and resilient, two qualities needed not only to stay but also to complete the trial as illustrated below:

“I got the chance to understand a great deal about HIV and family planning. The participation turned me into a different young person. I am young and there are many temptations that we, youth, come across. I am afraid I might have been swept off my feet and keep bad company if I had no help in the form of advice from staff”
(Informant 8, unmarried female, 23 years old).

Participants reported that having regular feedback from the results of different clinical investigations during trial made them aware of how the body worked. This lessened their initial fears of receiving test results, and assured them that they were in good health as expressed below:

“I got a lot of self-confidence as opposed to the time before trial when it came to testing for HIV, but now I am full of confidence” (Informant 16, unmarried female, 22 years old).

Participants in study IV stated that the availability of condoms at the trial center made them feel they were in charge of safe sex. The use of condoms was regarded as safer sex behavior because of its dual protection from both sexually transmitted infections, including HIV, and unplanned pregnancy. The latter conditions, if they had occurred during the trial period, would have led to discontinuation of the vaccination schedule. Participants felt that the trial provided them a good excuse not to get into parenthood because some of them were not ready for it. At the same time, they were able to negotiate safe sex with their partners as conveyed by the following statement:

“We used condoms for both purposes - protecting ourselves against STIs and avoiding the possibility of her getting pregnant” (Informant 5, unmarried male, 24 years old).

For those with no children, condom use was a means of delaying parenthood and for those who had children, they described condom use as a means of spacing children. This was expressed as:

“I found pregnancy prevention was a good thing. To begin with, I already have a child. What do I need another one for? In fact, the father himself is a problem - so why get another child?” (Informant 16, unmarried female, 22 years old).

In addition, male participants saw condom use as a more reliable family planning method than other methods because other methods were under the control of their partners. This was expressed as follows:

“I believe in condoms because women forget to take the pill, but also in today’s world, girls want to use pregnancy as a means of trapping men” (Informant 3, unmarried male, 25 years old).

In contrast to the above, negative attributes such as fertility issues and false HIV positivity post vaccination were mentioned as barriers that may have contributed to not participating and hence poor retention in vaccine trials. In Study IV, participants struggled to maintain the balance of, on the one hand, fulfilling expectations from their community to reproduce and, on the other hand, as the trial participants, not conceiving during the trial period. For some married participants, disclosing avoidance of pregnancy to spouses during the trial period was difficult because some spouses were not aware of participants’ involvement in the trial. Other participants felt their spouses would suspect them of having extra-marital affairs if condoms were to be used, as expressed in the following statement:

As a vaccine participant, I decided not to get pregnant; but I got pregnant because I was not using any family planning method and my husband did not know I was a trial participant. The pregnancy left me perplexed; I stopped visiting clinic because we were told very clearly that we should not get pregnant (Informant 4, married female, 26 years old).

Another participant added:

“Unfortunately, I made my girl pregnant during the trial because using condom in a steady relationship appears as being unfaithful” (Informant 12, married male, 23 years old).

Apart from the above, fear of being falsely ‘HIV-positive’ due to vaccination came up as a concern during participation in the HIV vaccine trial. The participants admitted to

understanding the meaning of being falsely HIV-positive post vaccination, but even with that understanding, their fear of being seen as ‘HIV-positive’ after vaccination was genuine, as narrated below:

“I am afraid of testing for HIV after trial because a percentage of participants have been found to be HIV-positive after the completion of the research. I do not know whether or not showing that vaccine trial participation card would make them take another type of test after the first one has come out positive” (Informant 9, unmarried female, 22 years old).

4.1.2 Interpersonal factors

Interconnection of positive social networking among young people, parents, clinical team, peers, friends, guardians and friends was shown to be imperative to participation of youth in HIV vaccine trials. In the Tanzanian context, having social supportive system was one of the important components in the recruitment of youth in HIV vaccine trials. In all studies, it was clearly illustrated that members of the community played a critical role in assuring young people that taking part in a vaccine trial was virtuous. This, in return, boosted the self-confidence of the participants, as illustrated in Study IV:

“I am thankful to our teacher [at school] because she was very supportive and encouraged us to join in the vaccine trial. Without her we wouldn’t have joined the program in the first place. In addition, my mother was very understanding and supportive as well” (Informant 8, unmarried female, 23 years old).

In addition, participants reported that the trial team was available to settle qualms, doubts and myths surrounding HIV vaccine clinical trials, expressed by one participant as follows:

“The trial staff taught us very well, made us understand the whole issue, helped me to overcome my fear” (Informant 9, unmarried female, 22 years old).

In study I, most respondents (86.4%) reported having a significant other who might influence their decision. This availability of social support in connection with decision making was significantly associated with willingness to participate in the HIV vaccine trials among youth (AOR 2.5 (95% CI 1.3-4.9)). Whereas, in study III of young girls at high risk for HIV infection, only 39% reported having significant others, such as parents or guardians, as key people to seek permission from for recruitment and subsequent participation in HIV vaccine trials.

Study II demonstrated the presence of the covert power of community members to influence decision making as regards participation in HIV vaccine trials by youth. Traditionally, decision making in any major socially and health-related event is viewed as a responsibility of elders rather than of young people in a Tanzanian setting. Elders are expected to guide young people into making ‘right’ and ‘appropriate’ decisions because of their perceived wisdom and years of experience. Likewise, regarding the participation of young people in HIV vaccine trials, study participants, including younger community

members themselves, felt that young people lacked authority when it came to decision making. This observation was expressed as:

“There is a strong relationship between decisions made by a youth to participate in a trial and her/his parents’ support or lack thereof. We would be lying if we said a young person can decide independently of his/her parents since our young people have not been brought up that way” (FGD 1, participant 3, male, age 28).

Most participants agreed preservation of the habit of involving members of community in decision making was an important matter for the successful involvement of youth in HIV vaccine trials. Participants reasoned that youth needed harmonious and balanced social relations from different key players including spouses and parents in order for them to stay focused, maintain psychological well-being and complete the trial schedule.

Additionally, the impact of community support on participation of youth in vaccine trials was a common theme in the narratives of the participants. The study participants said that community members would support youth because of the ‘novelty’ of HIV vaccine trials in the Tanzanian setting. Participants believed it was the role of community members as parents, guardians, friends and peers to help young people facing perceived uncertainties, fears and unpleasant effects of participating in an HIV vaccine trial, as stated below:

“I will encourage young people to join and stay in the trial. I will look for information about participants in previous HIV vaccine trials, this information will help me to ease their fear that they were the first ones to participate in a vaccine trial.” (FGD 7, participant 5, male, age 26).

In addition, there was strong support extended to participants in the HIV vaccine trial from the trial staff, who played a substantial role in informing participants about the process of trial participation. Participants reported that the trial team was available to settle qualms, doubts and myths about HIV vaccine clinical trials, expressed as follows:

“The trial staff taught us very well, made us understand the whole issue, helped me to overcome my fear” (Informant 9, unmarried female, 22 years old).

Nevertheless, participants in study II mentioned some attributes that may negatively impact the participation of youth in HIV vaccine trials. One was a misunderstanding of the sexual behavior of trial participants by members of the community. Study participants wrongly perceived and believed that young people participating in HIV vaccine trials would be asked to have unprotected sexual intercourse with HIV-infected individuals as part of trial to see if the vaccine was working properly or not. One participant expressed this erroneous observation as:

“People are afraid of a trial because the participants need to have unprotected sexual intercourse with an HIV-infected individual to see whether or not the vaccine works” (FGD 6, participant 3, male, age 24).

Other participants mistakenly thought that, as a part of the HIV prevention program, young volunteers would be required to abstain from sex during the trial period (Study II). Participants were worried that abstinence from sex by young people in adolescence and young adulthood was nearly impossible as this was the time they were very sexually active. Therefore, instructions like abstaining from sex would make young people less willing to volunteer for the trial.

“It will be difficult for youth to participate if they are told not to have sex because most youth like sex” (FGD 7, participant 5, male, age 26)”.

Another impediment to participation was a fear of the perceived contents of the HIV vaccine since study participants had no prior knowledge of HIV vaccine trials (Study II). During discussions, it was shown that participants believed that young people might experience fear that the vaccine would actually contain HIV, which could infect young volunteers:

“We used to take our children for vaccination, whereby care providers used to inject them with medication [vaccine]. The same procedure, getting vaccine injection with HIV would be done for young people in the HIV vaccine trials; therefore, young people would be afraid to join the trial” (FGD 4, participant 5, female, age 45).

Since the ability to have children is seen as vital in Tanzanian settings, other participants alleged that the HIV vaccine contained things [chemicals] that would purposely interfere with the fertility of the young volunteers, thus reducing population growth (Study II). A young participant expressed this as follows:

“Most youth in my community do not trust people from the west because the westerners want to get hold of our wealth. The westerners introduce things like vaccines with an aim of reducing the native population’s ability to have children” (FGD 7, participant 3, male, age 23).

4.1.3 Community/institutional factors

Examining the interplay of community factors that may facilitate or hinder participation and retention of youth in HIV vaccine trials was one of the important outcomes of this thesis. Study IV found that study participants were encouraged to continue being volunteers in the HIV vaccine trial, TaMoVac 01, until the end because of the endorsement and management of the trial by regulatory bodies such as the Tanzanian Food and Drugs Authority (TFDA) and the National Parliament. Such bodies implement laws and guidelines governing the

deployment of HIV vaccine trials in order to protect the well-being of trial participants, as commented below:

“I thank our Members of Parliament, who ascertained that vaccine trials conducted in Tanzania, neighboring and First World countries were safe. So, the significance of the trial among community members has been highlighted and understood to be a serious issue” (Informant 12, married male, 23 years old).

In addition, the support provided by the clinical trial team to participants in Study IV, who volunteered for the TaMoVac 01 HIV vaccine trial, played a key role in ensuring that the young volunteers finished the trial. The clinical staff centered their work on providing standardized information on the processes of each step of the trial. The clinical team provided counselling to participants at each clinic visit during the trial in order to settle qualms and provided correct answers to myths about HIV vaccine clinical trials among participants, expressed as follows:

“The trial staff taught us very well, made us understand the whole issue, helped me to overcome my fear” (Informant 9, unmarried female, 22 years old).

On the other hand, some participants in study II mentioned stigma as a negative factor for participation and retention in HIV vaccine trials. Perceived high-risk behaviors by youth coupled with HIV infection and its preventive activities are highly stigmatized matters that have adversely affected the uptake of HIV preventive programs in Tanzanian settings. In study II, participants thought that, if young people decided to volunteer in any HIV vaccine trial, their communities would judge them as promiscuous or, worse, think they were infected with HIV. As a result, this sense of perceived stigma led to fearful thoughts of isolation from the community should a young person become a trial participant, as expressed below:

“Young people may desire to participate in a trial but they think people would judge them as promiscuous since they volunteered for the trial” (FGD 3, participant 2, female, age 25).

“Once people from the community know a young person has been vaccinated [become a trial participant], they will think that that person lives with HIV. As a result, s/he may be isolated by the community” (FGD 1, participant 3, male, age 28).

4.1.4 Structural factors

In addition, unemployment and poverty among youth was identified as a hindrance to the participation and retention of youth in HIV vaccine trials. Participants in study II observed that most Tanzanian youth have poor and tough lives, with low socioeconomic status. They stated that despite being of age (18 years and above), young people still depended socially

and economically on their parents as a result of unemployment. They might therefore be too busy looking for jobs to participate in vaccine trials:

“Most of the time, youth are busy, looking for means to earn a living. It would be difficult for them to leave their daily activities to attend meetings to discuss vaccine issues” (FGD 5, participant 7, male, age 23).

Notably, participants in study II were concerned that most youth were victims of drug abuse, making them hostile and violent as well as likely to acquire risky sexual behaviors.

Participants thought that substance abuse by some young people would not only impede the trial but also expose them to HIV. Due to such behaviors, participants felt that such young people would be unfit to join the vaccine trials, as expressed below:

“Most youth are involved in risky sexual activities influenced by injectable drugs, peer pressure, alcoholism, and smoking weed. For example, if a young woman receives [a vaccine], then drinks excessively, then ends up having unprotected sex, such a volunteer would not be able to follow the vaccine trial through to the end because of such behavior” (FGD 1, participant 3, male, age 28).

5 DISCUSSION

Once vaccines have been tested for safety in laboratory settings, clinical trials in human beings are needed to test their safety, immunogenicity and ultimate efficacy. Having a preventive, affordable and effective HIV vaccine would benefit the young people who need it the most, particularly in sub-Saharan Africa. This thesis looked at the interaction of different actors at the intrapersonal, interpersonal, community and structural level and how this interaction influences positively or negatively the recruitment and participation of young people in preventive HIV trials.

Participation of young people in HIV vaccine trials

5.1 INTRAPERSONAL FACTORS

5.1.1 Altruism

Altruistic sentiments were among the factors influencing youth's recruitment and participation in HIV vaccine trials. Young people felt they could sacrifice their body, time and effort in order to achieve the greater good, i.e. helping to develop an effective HIV vaccine. Their feeling of altruism could have been promoted by knowing the burden of the disease in society or by having relatives, friends, family members or peers who had either died from or were living with HIV in their community. A study in Kenya revealed that the majority of volunteers in HIV vaccine trials were motivated by social benefits, suggesting that altruism was one of the major contributing factors in decisions to participate in HIV vaccine studies. Respondents' primary motivator was the desire to contribute to the advancement of research which in turn led to improvement in societal well-being, in order to help their family, society or the world, This was particularly the case among volunteers who often knew of someone infected with HIV/AIDS⁶³. Similarly, in the United States, a study among low- and high-risk individuals of African-American origin concurred with our finding that altruism was the most prominent factor related to willingness to participate (WTP), suggesting that helping one's community improve the health of its residents was the strongest motivator for trial participation⁶⁴. In addition to the above, the majority of young women (29%) in a Microbicide trial in the US and Puerto Rico were motivated to join the study for altruistic reasons including "helping other women," "making a difference," and "contributing to a product that could be life-changing for everybody." The young volunteers thought that helping to empower other women was among the greatest motivators, and most emphasized the importance of doing something for others. Some enjoyed being part of a project they considered important; for example, it made some women feel that they were teaming up with research staff to advance science⁶⁵.

For the young female sex workers in the present study, though altruism was mentioned as one of the reasons for volunteering in the clinical trial, the nature of their life conditions rather than altruistic sentiment could have been an underlying reason for wanting to participate. In this group, the participants might have mistakenly thought that the HIV vaccine would have protective effects that would prevent them from getting HIV from their sex clients. This view

was supported by African-American participants in the study mentioned above, whose WTP was highly correlated to perceptions of decreased risk if enrolled in a trial and perceived behavioral risk of HIV infection⁶⁴. It is important for the clinical trial team to have a comprehensive and detailed process of informed consent. This process should aim to educate participants, in the simplest language, about important aspects and concepts of vaccine trials. This will help potential volunteers to decide to join a trial after being made aware of the risks and benefits as well as without having false hopes of the vaccine protecting them from HIV infection.

5.1.2 Perceived personal benefit

5.1.2.1 Regular medical check-up

In the existing study, some young people joined and completed the HIV vaccine trial because they perceived personal benefits such as free, regular medical reviews including HIV tests, appointments to see specialists during scheduled visits, provision of contraceptive methods, health education to themselves and their spouses/partners and coverage of health insurance during trial. Such services were rarely available as part of normal healthcare services. Our findings were similar to low- and high-risk participants in the United States, in that those who had less healthcare access reported more WTP due to the perceived health benefit of trial participation⁶⁴. In India, financial incentive, life insurance and free medical treatment for trial-related illness or injury all had a significant impact on WTP. The promise of access to the vaccine for free, if found to be efficacious in the trial, was one of the highest motivators among participants. It is important to keep in mind that the concerns among Indian men who have sex with men (MSM) might have reflected larger structural factors like poverty and lack of access to healthcare rather than logistical challenges or vaccine-specific concerns⁶⁶.

Moreover, among urban American women at high risk of HIV infection, the likelihood of willingness to participate in trials was strongly associated with perceived personal benefit from an HIV vaccine, suggesting that personal gain would be a strong motivator for participation in an HIV vaccine trial that might outweigh general concerns regarding safety or possible discrimination. It was pointed out, however, that the decision to enroll in an HIV vaccine trial involves complex decision making and consequently the perceived benefits of participation must be weighed against realistic consequences⁶⁷.

5.1.2.2 Gained confidence

The young volunteers in the TaMoVac 01 trial became empowered and gained confidence as result of participation in the trial. They developed a deeper understanding of health status and matured from being fearful of receiving HIV test results to being advocates of spreading HIV prevention messages to other young people. The young volunteers were empowered to decide safer ways of expressing sexual intimacy that shielded them from HIV infection. Similar findings in a social behavioral follow-up study conducted among the adult HIVIS 03 volunteers between 2 and 3 years after the second HIV MVA boost revealed only 6.1% of the

individuals reported extra partners compared to 58.2% of the same cohort interviewed before. This suggested that prolonged follow-up counselling was played a useful role in significantly reducing the number of extra sexual partners^{68,69}.

Overall empowerment and transformation of young volunteers in the present study was vital to their participation in the HIV vaccine clinical trial because it made them confident about their health, about choices of family planning and protection from STIs. Furthermore, this transformation may signify the translation of abstract scientific concepts and procedures into the practical aspects of real life whereby the procedures that started as part of the clinical trial became part of the participants' practices in life outside the clinical trial setting. This was made possible partly because participants received information about such procedures through trustworthy and appropriate people at the trial center as seen in South Africa and Tanzania^{70,71}.

Our findings should however be interpreted with caution due to social desirability bias whereby participants may underreport actual sexual behaviors and contraceptive practices in favor of what the researcher wants to hear. In the course of participation in TaMoVac 01 trial, some of the young volunteers did not finish the whole vaccination schedule due to pregnancy and some male volunteers became fathers. This reflected the dilemma the young people had to face in terms of keeping a balance of being trial participant and a parent at the same time.

5.1.3 Vaccine-induced seroreactivity

Vaccine-induced seroreactivity, VISR, post vaccination posed a challenge in this project i.e. routine HIV serological testing could falsely be interpreted as HIV infection rather than an effect of the HIV vaccine. Concerns about VISR among those who received HIV vaccines emerged notwithstanding several steps to mitigate the impact beforehand. Trial staff explained to volunteers what it meant to have VISR, what to expect after it occurred, and volunteers were given special identification cards in case they were found to be HIV-positive if checked in routine care. In addition, volunteers were offered access to advanced HIV confirmatory testing at the trial center. This points to a gap between factual acceptance of trial concepts during an informed consent process and the actual acceptance of an untoward outcome of the trial when it happens. After all the counselling sessions on the negative effects of HIV vaccine, it would be easy to think that volunteers were well equipped to face the weight of being falsely HIV-positive, or would be bold enough to convince significant others that VISR was nothing to be worried about. Clearly, this was not the case in the present study. Volunteers understood and probably accepted the circumstance of being falsely HIV-positive but when it finally happened, they found it difficult to articulate the concepts of VISR or assure spouses, parents, friends and probably care workers that they had VISR due to trial vaccine. Their hesitancy and confusion may partly be explained by personal fear of unknown effects since the vaccine was on trial, and not much had been documented about the reversal of positivity effects, or they were worried about stigma, discrimination and abandonment in case everything came out in the open.

Our findings of the importance of VISR are supported by results from a long-term follow-up study of 287 vaccine recipients in several African countries, where 14 recipients reported social harm as misconceptions expressed by parents, partners, neighbors, and clinic staff from non-study sites. Recipients cited positive HIV test results due to vaccine-induced antibodies indicating prevalent HIV-infection as the cause of this social harm. Clearly, VISR posed problems here leading to discrimination or stigmatization in healthcare institutions, during ante-natal care, in blood banks or in relation to organ donation⁷².

At the same time, a review conducted in the US on social harm associated with VISR included the following: disruption of personal relationships, difficulties in finding or keeping employment, difficulties in obtaining insurance, impediments to travel, inability to enlist in military, inability to donate blood and organs and inappropriate medical treatment⁷³. It is therefore an ethical obligation of trial teams to thoroughly inform and ensure that volunteers and people close to them understand and translate difficult trial concepts such as VISR throughout trial participation, and if necessary to link them with other medical establishments to assure availability of long-term alternative HIV testing to exclude true HIV infection even after completion of a clinical trial.

5.2 INTERPERSONAL FACTORS

5.2.1 Support from members of the community

5.2.1.1 Encouragement from members of the community during trial

Social support systems were a central phenomenon, cutting across recruitment and implementation of clinical trials among young people in Tanzanian settings. It was observed that having social support from family, peers, friends, guardians, teachers, colleagues and members of the community in general was essential for recruitment and full-length participation of potential young volunteers in clinical trials. In the Tanzanian settings, social support through the acceptance of new clinical interventions such as HIV trials by members of the community had a major impact on recruitment and ultimately the implementation of clinical trials among young people because of existing close kinship between young people and the community. Since young people are an integral part of the community, they enjoy a sense of belonging such that they still depend a lot on their elders for decision making in major life events such as marriage, enlisting in the military, attending schools and volunteering in HIV vaccine trials. Young people will seek opinions, blessings and permission of the significant others like parents, spouses and guardians before deciding to participate, and such opinions will have an influence on the decision to stay in the trial until the end. Our findings concur with those in a study performed in the US among African-American individuals, which showed that having social support for trial participation had a strong association with WTP in Phase- II vaccine trials⁶⁴. Likewise, in India, discussants in focus group discussions (FGDs) described consulting with and even getting ‘permission’ from parents and partners as essential to WTP. Interestingly, discussants who were financially dependent on parents feared being cut off; and those whose parents were financially dependent on them feared becoming ill or injured as a result

of the trial and not being able to provide for the family, proving that financial considerations link the centrality of family to WTP⁷⁴.

However, the majority of female sex workers (FSWs) in the present study were not shown to have such well-defined support systems. Participants seemed to be capable of making decisions on their own. This stance shown by FSWs in the present study could partly be explained by being self-reliant at an early age due to exposure to hard social living conditions or by a lack of long-term family or societal ties due to the nature of their work, perceived stigma and high mobility. Contrary to our findings, men who have sex with men (MSM) in India, who did not live with their parents and were unmarried, expressed reliance on the advice of community leaders and community-based organization (CBO) staff, a type of surrogate family and high WTP contingent on CBO endorsement⁷⁴.

5.2.1.2 Guidance on decision making

In the same light, members of the community clearly showed influence and interest in helping potential young volunteers to join trials. They felt it was their obligation and right to influence such decision of young people to participate in trials because they embraced the role of parenthood and guardianship in relation to youth. Members of the community saw themselves as pillars of support, a place of refuge for youth, and even people to nurse, care and pick up the pieces in case some young people fell ill due to the side-effects of trial vaccines. In Tanzanian settings, elderly people are regarded as wise and looked upon by youth to provide clear direction on certain important life aspects. It is expected that young people will listen to and follow the advice provided. Failure to do so would be seen as disrespectful, and even in some communities, people believe that going against elders' advice attracts misfortune in life. In China, family support to attend HIV vaccine trials is critical. The role of the family in traditional Chinese culture was shown to be an important component for WTP in HIV vaccine trials among MSM such that participants who believed that their family would support their HIV vaccine trial participation had a significant higher WTP⁷⁵.

Conversely, the literature shows that members of the community may be not supportive of HIV preventive vaccine trials at all times. During the HIVIS 03 study in Tanzania, relatives and colleagues at police posts stigmatized, uttered discriminatory comments and showed mistrust towards the HIV trial vaccine⁶⁸. This suggests that social harm following participation in HIV vaccine trials may no longer be an uncommon phenomenon hence assessing the frequencies of occurrence, the magnitude, and seriousness of the harm is important in order to protect future participants in HIV vaccine trials⁷⁶.

More than a third of the 150 women who participated in the Microbicide Development Program trial using vaginal gel in South Africa reported cases of intimate partner violence; half of which were related to involvement in the trial. Participants described their partners as authoritarian, controlling and suspicious of women's infidelity due to excessive vaginal wetness after gel application before sex. Additionally, they reported verbal abuse, abandonment, and in some cases, beatings. These findings raised questions as to whether trialists conceptualized, understood and addressed everyday domestic violence towards

women due to HIV trial participation. This finding further underscores efforts to address existing social and gender inequities in communities while empowering women to protect themselves from HIV infection at the individual level⁷⁷.

Working with communities is one the most principal strategies for the effective implementation of any biomedical intervention. Communities motivate governments to prioritize HIV vaccine development as part of their comprehensive response. Investing in community work would cultivate a sense of community ownership, building trust and deepening knowledge of local realities. It could improve the quality of the data collected by ensuring that trial protocols, procedures, and strategies are acceptable to trial participants and build on locally understood languages and customs⁷⁶.

Our findings on WTP among youth from general population and FSWs were slightly different in the sense that a higher proportion of FSWs were WTP compared to their counterparts (50.6% in study I). Similarly, a study done in China showed that 76.7% of MSM were willing to participate in HIV vaccine trials⁷⁵. However, the likelihood of MSM participating in HIV vaccine trials was related to having family support and a desire for economic incentives contrary to the majority of FSWs in the current study who wanted to participate because of altruism. This high level of WTP shown by our study participants could partly be explained by fact that FSWs might have felt they were at a higher risk of acquiring HIV infection as compared to other group of youth. Probably, the FSWs erroneously thought the vaccine on trial would have a protective effect. Since the efficacy of the vaccine is not known at the moment, FSWs would still benefit from other HIV preventive packages offered during trial, and this may serve as one of the motivators for trial participation. All in all, it is important and an ethical obligation for trialists to inform all potential volunteers that it was not known whether the vaccine could protect them or not. Therefore, it is extremely important for the volunteers to protect themselves from contracting STIs including HIV.

5.2.2 Mischaracterization of sexual conduct

5.2.2.1 A lack of sexual inhibition

Mischaracterization of the reasons for advice on sexual conduct during trial was seen as barrier to the uptake of clinical trial interventions by youth. It emerged that many concepts of trial procedure were at risk of misinterpretation by both participants and perhaps members of the community as well. In the present study, some participants wrongly thought a lack of sexual inhibition was a prerequisite for testing efficacy of the vaccine product. FGDs on post-trial HIV vaccine acceptability among South African youth revealed the most common fear expressed by the discussants was that people would have more unsafe sex when they thought they were protected by the vaccine. They thought vaccines would discourage condom use, increase multiple partnerships, teenage pregnancy and the amount of sexual activity occurring. An increase in partner cheating as a behavioral consequence of HIV vaccination was raised only in women's groups. These women appreciated the advances in HIV

prevention that a potential HIV vaccine might bring, but they were suspicious of the greater relationship insecurity that might accompany such vaccine programs⁷⁸. Some participants in India expressed concerns that an HIV vaccine may actually increase unprotected sexual practices and sexual activity more generally but particularly amongst young people who, it was implied, would take advantage of availability of such vaccines⁷⁹.

5.2.2.2 *Fertility issues*

The idea of abstinence from sex during trial as way of preventing HIV and as a means of contraception was reported in current study. Having children is an important, almost sacred affair in Tanzanian settings, where young people are expected to fulfill their parental roles in perpetuating lineage. Therefore, misunderstanding trial procedures and requirements would unduly weaken efforts to recruit to and implement HIV clinical trials. Police officers in Tanzania voiced concerns over pregnancy restrictions imposed while participating in the trial. More often they were concerned about the views of others on the effects of taking part in the HIV vaccine trial on their reproductive ability. Both men and women in that study expressed a fear of postponing pregnancy and described how they had been subject to negative views from others. In addition, young unmarried men without children expressed a loss of confidence in the vaccine trial. Although the pregnancy restriction during the trial was temporary, the participants in that study expressed fear that the vaccine would affect their childbearing ability⁸⁰.

Such mischaracterization of trial requirements reported in this study may partly be explained by less availability of information about trial procedures in common news platforms such as newspapers, televisions, radio and social media. Typically, information about trial procedures is provided during the trial period, using physical meetings between potential volunteers and clinical staff or found on websites dealing with trials, places not commonly visited by many people. In a society like Tanzania, where sexual matters are still considered taboo, i.e. not something to be discussed openly, it is imperative to design ways of delivering such information in permitted cultural contexts that would not be offensive to anyone or any group of people. Since the involvement of the community is important in the uptake of HIV preventive interventions, age- and gender-sensitive messages on sexual matters would greatly contribute to correcting the mischaracterization of sexual conduct during trials.

5.3 COMMUNITY/INSTITUTIONAL FACTORS

5.3.1 Support from research team

Health care workers and other staff at clinical trial centers formed another essential part of the observed support system. The staff in clinical trials were regarded as a bridge between scientific interventions and layman's knowledge of such interventions. The clinical trial staff were regarded as key to bringing light and deeper understanding to hard, scientific concepts used in clinical trials, to dispel myths and misconceptions about HIV vaccine trials, to counsel on anxieties and worries raised by young people and their significant

others. The staff constantly monitored trial participants via mobile phones or by paying physical visits to the areas where participants lived. Kenya observed a high retention rate ranging from 90% to 96% in HIV trials in four Phase I/II clinical trials among healthy, adult, HIV uninfected volunteers. The research team attributed the high retention rate in four trials to the informed consent process whereby individuals' questions were answered comprehensively and recurrent volunteer education on the trial procedures was carried out during follow-up visits. Further, many contacts between potential volunteers and the study team prior to enrolment facilitated good rapport and trust between the two, hence enhancing volunteers' retention in the study. Also, it was possible that the medical care given to volunteers for all the adverse events might have contributed to the good follow-up rate⁸¹.

Interestingly, frontline health service providers (FHSPs) working with MSM and FSWs in India felt that the relationships they developed through close interactions with FSWs and MSM placed them in an ideal position to take part in vaccine trials and rollout programs as an extension of their responsibility as FHSPs. Further they thought their long-term rapport with community members would enable them to maintain communication channels during clinical trials so as to ensure the ethical conduct of clinical trials and the implementation of future HIV vaccine delivery programs⁷⁹.

In contrast to our findings, a higher proportion of FHSPs working with key populations in India reported a lack of belief in vaccines and a preference to promote other HIV prevention strategies. This reflected health service providers' familiarity with on-the-ground realities that pose obstacles to vaccine uptakes or acceptability among key populations. In the same study, 7.5% of third line health service providers, HSPs, expected difficulties in convincing members of key populations to receive a future HIV vaccine, suggesting poor communication between HSPs and key populations, so that HSPs did not feel that it was worth their while to convince community members to accept an HIV vaccine⁸².

A follow-up study among HIVIS 03 volunteers in Tanzania showed a decrease in mistrust towards HIV vaccine trials over time. The implication of the findings was that the community increasingly understood the logic behind HIV vaccine trials⁶⁸. But an alternate explanation would be that volunteers might have demonstrated confidence and assertiveness while dealing with the mistrust as revealed in a previous study of their experiences as volunteers in HIV vaccine trials⁸³.

5.3.2 Support from regulatory institutions

The role of regulatory institutions like Food and Drug Authorities in Tanzania⁸⁴ was critical for gaining the trust of potential and actual young volunteers in clinical trials and hence make it easy to recruit and retain volunteers in HIV vaccine trials. It is worth noting that the regulation of clinical trials in many lower- and middle-income countries like Tanzania, where some HIV vaccine clinical trials are taking place, is still new and evolving. In some countries, regulators are primarily pharmacists and often they have more of a pharmaceutical background and are less experienced with vaccines or biologicals⁸⁵. Likewise, HIV preventive clinical trials in Tanzanian settings are a relatively new undertaking that is viewed

suspiciously since its origins are mostly in Western countries. Young people and the community in general can mistakenly perceive such interventions to have bad intentions, i.e. cause detrimental health outcomes such as the impaired ability of young people to reproduce. In conjunction with that, WHO recognizes and acknowledges scientific challenges posed by the clinical development of prophylactic HIV/AIDS vaccines due to many unknowns in the field, such as diversity of legal and ethical frameworks, lack of human survivors, and considerable viral genetic or strain variability⁸⁵. Therefore, having international harmonization and standardization of regulatory practices will help to ensure that HIV vaccines are evaluated and licensed based on internationally accepted scientific criteria and standards⁸⁵. This will not only send a message to the community that protecting the health of Tanzanian young people is the utmost priority but also will ensure that the government adheres to standard guidelines of ethical, regulatory requirements when conducting any clinical research using human subjects.

5.3.3 Stigma

The presence of perceived stigma associated with HIV and its preventive activities in Tanzanian settings is one of the social risks posed to young people participating in HIV vaccine trials. Despite current HIV prevention programs in Tanzanian settings, stigma exists because the main mode of HIV transmission is sexual, which is associated with promiscuity. Promiscuity is also linked with flawed thoughts of increased sexual activities happening in adolescence and young adulthood as young people experiment sexuality. In our study, members of the community said that HIV infection and its preventive activities had been stigmatized because HIV infection is seen as a disease with no cure, a shameful condition associated with promiscuity, as a source of unrelenting suffering and death. Our findings showed that young people would have a hard time deciding to join HIV preventive trials in order to avoid unnecessary consequences of discrimination. In support of our findings is a study in Kenya among peer leaders, community advisory board members, former and current volunteers in clinical research, study staff, community leaders and community members. This study found that opinions about and willingness to participate in HIV-vaccine research of potential volunteers were negatively shaped by stigma and discrimination in families and the community. The respondents feared experiencing stigma or discrimination given the strong perception among all respondents that being a HIV vaccine study volunteer was widely equated with being HIV-positive. Gossip, finger-pointing and casting accusations about moral character were a salient concern among respondents and women were more vulnerable to accusations of infidelity, violence and abandonment⁸⁶. Likewise, a study among MSM in India revealed that there was stigma operating at the community level. This was expressed as fears of being looked down upon by one's peers as one who engages in sexual risk behaviors or is HIV-positive. As a result, potential volunteers who were motivated by altruism and wanting to give back to their community changed such motivations into liabilities⁷⁴. This level of stigma in the present study shows poor knowledge of HIV and its preventive methods, further demonstrates deep-seated fears of contracting HIV due to a lack of permanent cure for the disease. Tackling stigma using tailored, gender- and age-specific educational messages about HIV, its transmission, prevention methods and antiretroviral therapy (ART) would help to

improve the situation at family and societal levels. This would hopefully result in acceptance, without prejudice, of new HIV preventive interventions, including HIV vaccine trials in Tanzanian settings.

5.4 STRUCTURAL FACTORS

5.4.1 Poverty and unemployment

Poverty and unemployment among youth were factors hindering trial implementation because young people would not be able to adhere to trial schedules. Looking for employment would be their primary interest over making scheduled clinic visits to receive HIV vaccine. It would therefore be difficult for them to concentrate on trial procedures. Most unemployed young people would be at risk of joining street gangs or selling drugs in order to make living. This would jeopardize their personal safety, would cost clinical teams in time invested, diminish derived health benefits and lead to an inconclusive outcome as regards vaccine testing. Young people could be advised to pursue vocational training programs that enable them to become self-employed as part of solving unemployment and poverty. In future trials, the trialists could liaise with different stakeholders who provide life skills interventions to marginalized youth not only to get young people off the streets but also to inspire some youth to become potential volunteers in future HIV vaccine trials.

5.4.2 Substance abuse

Concerns about substance abuse among young people were expressed by members of the community. Use of illicit drugs among young people had been rampant in peri-urban and urban areas in Dar es Salaam because of idleness, peer pressure, fashionable trends and other youth considered it as a way of earning living. This lifestyle exposed young people to the dangers of drug addiction leading to mental illnesses, inability to keep jobs or work normally, exposure to criminal prosecution, and acquisition of STIs including HIV infection. According to 2011 and 2012 National Survey on Drug Use and Health data in the US, nearly 27 and 12 million young adults aged 18 to 25 drank alcohol and used an illicit drug in 2012 respectively. Of those using illicit drugs, 3.2 million used marijuana, 57 304 used heroin and 51 319 used cocaine⁸⁷. In Germany, a review of data on the prevalence of addictive behaviors from ten national surveys and one regional survey conducted between 2002 and 2012 among adolescents (11-17 years) and young adults (18-25 years) revealed some strong associations still existed between social inequalities and the prevalence of substance use. Low socioeconomic status (school type, employment status) was consistently associated with more cigarette smoking and problematic patterns of alcohol consumption were significantly more prevalent among young unemployed males compared to secondary high school/grammar school students of the same age. In terms of the consumption of cannabis, the unemployed and students with a low educational level emerged as high-risk groups⁸⁸. In phase I and II clinical trials, potential volunteers need to be healthy, HIV-negative individuals, with low a risk of exposure to HIV infection. Therefore, recruitment and follow-up of young people who abuse drugs would pose a challenge due to the likelihood of exposure to HIV, leading to false

conclusions about the vaccine on trial. Surprisingly, an assessment of the patterns of substance use and its impact on retention of volunteers in phase 1 preventive HIV vaccine clinical trials among enrolled participants from 10 HIV Vaccine Trials Network phase 1 preventive HIV vaccine clinical trials, conducted between February 2009 and September 2014 in the Americas and Switzerland, found neither frequency of alcohol use, binge drinking, marijuana, nor other drug use negatively impacted retention and adherence rates in those clinical HIV prevention trials. It is worth noting that evidence pointed to trial participants engaged in binge drinking behavior being associated with higher rates of unprotected sex, which might have been an indicator of an increased risk for acquiring HIV⁸⁹. Age- and gender-specific risk reduction counselling should be part and parcel of all participant preparation in any HIV vaccine trial.

On the other hand, in phase III efficacy HIV vaccine trials, young people who inject drugs would be ideal participants as such trials would recruit participants with high-risk behaviors that would continually expose them to HIV infection. The literature suggests that injecting drug users (IDUs) should and could be recruited for HIV vaccine trials because HIV prevention is their human right to health and a public health imperative. To ensure that prevention methods are safe, efficacious, and accessible to this population, novel prevention strategies and approaches must be assessed from this community's standpoint, hence IDUs must participate in HIV preventive research⁹⁰.

There is well-documented evidence of the challenges of having IDUs as trial participants, such as stigma, discrimination, criminalization, harsh policing practices, inaccessibility of sterile injecting equipment, the prevalence of comorbidities such as viral hepatitis and mental health illness, lack of access to basic services, high unemployment rates, an overall lack of respect for the basic human rights of people who inject drugs⁹⁰ as well as trial specific challenges such as cost, requirement for multiple doses, and limited time⁹¹. It therefore suffices to say the recruitment of such individuals to trials should vigilantly follow criteria stipulated in protocols to ensure maximum participation of potential volunteers in Tanzanian settings.

The trialists must fulfil an ethical obligation to ensure young people protect themselves from acquiring HIV at any cost, despite their drug use habits. Most of all, there is a need for a multi-sectoral approach to dealing with the use of unsafe illicit drugs so as ensure young people and nations are safe from drugs.

5.5 METHODOLOGICAL CONSIDERATION

5.5.1 Validity

Validity is ability of a measuring instrument to give a true measure, i.e. how well it measures what it purports to measure⁹². In study I, we ensured internal validity by designing questionnaires with questions that were borrowed from other research studies. We conducted pilot testing of the data collection tools in order to clear up ambiguities, to assess understanding of respondents of concepts/questions and to check the time taken to fill in the

questionnaires. We also ensured that our respondents were sampled systematically to remove sampling bias. The validity was not fully realized in assessing perception and knowledge of HIV vaccine studies among youth due to use of some unvalidated data collection tools. At the time of developing the research protocol, there was limited literature on assessing those concepts with reference to factors affecting willingness of youth to participate in HIV vaccine trials in Dar es Salaam. We therefore designed questions to address those concepts on our own and pilot-tested them. In the analysis, we conducted internal consistency analysis that found that questions designed to assess perception and knowledge had low internal reliability and our findings should therefore be interpreted with caution. Yet, we decided to include them in our results because of their importance with regard to adding information to the small amount of literature that was available on this topic.

External validity implies the ability to generalize beyond a set of observations to some universal statement⁹². Since the study was conducted among youth seeking care at IDC, the application of findings could be limited to young people in similar settings. On the other hand, the study provided insights into, e.g., the role of significant others in HIV vaccine participation, a theme which had been discussed in other HIV vaccine research studies among adults and youth in different contexts^{74,83}. Therefore, even if it has some limitation, it is worth considering some of the implications in a broader context.

5.5.2 Non-probability sampling

Usual census data do not include all information about key populations due to illegality and criminalization of their lifestyle. They are therefore not included in the population survey data. There is no sampling framework for FSWs in Tanzania that can be used to draw our sample. Therefore, the surveys are non-probability, which means that each member of population has an unknown probability of being sampled. Several sampling methods for key populations have been documented such as venue-based sampling, targeted sampling, time location sampling; referral-based methods such as convenience sampling of known, most at-risk populations, snowballing sampling along networks and respondent-driven sampling (RDS)⁹³. For our study, we used RDS because it is a probability-based sampling method that uses long-chain peer referral to penetrate sub-networks of hidden populations⁹³. We also used RDS so as to be able to infer our findings to the study population. In RDS, though recruitment starts as snowballing by giving coupons to seeds, it differs from snowballing in that the number of coupons given to seeds and subsequently referred participants is limited so as to minimize effect of over- or under-sampling of individuals. In our study, we limited coupons to three. Furthermore, RDS draws its statistical basis from First Order Markov theory whereby, if the recruitment has more waves of recruitment, it will have longer chains of recruitment so that the final sample of individuals recruited to the study will not have similar characteristics to the seeds or original recruiters, reflecting equilibrium. When the state of equilibrium is reached, the final sample can be inferred to the population from which the sample population was drawn⁹³. During analysis in the present study, the RDS analytic

tool considered weights from recruitment patterns and reported network sizes of respondents in order to adjust for under- or over-representation of individuals in the study.

5.5.3 Low rate of coupon transfers

Coupons were slow in being used, which resulted in the ‘death’ of some seeds early on during data collection leading to an increase in the number of seeds in order to reach 20. One of the reasons for the poor redemption of coupons in the present study was a fear among young FSWs to approach health facility where the study was being conducted because there was a general crackdown on key populations and their activities at the time of data collection. The respondents feared being captured by the local authorities and thrown into jail. They thought the authorities were using health facilities as a new strategy for identifying and capturing them. So, they failed to refer their peers in time, i.e. before the expiry date on the coupons. Therefore, in order to reach our sample size, we had to review recruitment data periodically and increase the number of seeds by calling those who had participated in formative research sessions.

5.5.4 Incentives

RDS employs a dual incentive system in which one is reimbursed for time and transport as a study participant. The same individual will be reimbursed as a recruiter after recruiting eligible peers within a stated timeline. It is possible that participants could be coerced into participating in the study or even bring ‘coached’ peers, meaning people who do not really belong in the same network or do same activity so as to receive double incentives. We minimized this risk by setting a reasonable amount of money that would not be source of coercion. A formative study was conducted prior to the current study. Among other things, it determined a range of reasonable amounts of money to compensate the study participants for time spent travelling to and from clinic and at the clinic during the research and for every peer referred. The proposed amount was further reviewed and discussed during ethical approval processes, and a final amount was approved by MUHAS Institutional Review Board and researchers. Further, at the clinic, recruitment manager conducted screening questionnaires for eligibility.

5.5.5 Social desirability

Social desirability is when a participant answers study questions in a way that s/he knows is what research wants to hear. This may lead to under- or over-reporting of outcomes of interest in the research. In studies I and III, we used self-administered questionnaires to give participants room for privacy and confidentiality in filling questionnaires. However, we asked the participants sensitive questions about sexual behaviors, and there was a chance that participants had under-reported in study I or over-reported in study III. In study I, young people were recruited from the general population, so they probably were not too comfortable about revealing their actual risk behaviors hence they under-reported them. In study III, the participants had already been “labelled” as female sex workers, as a result they might had exaggerated their responses with regards to risk behaviors. During the interviews, the

researchers addressed and interacted with the respondents respectfully, so as make them comfortable, then assured them complete confidentiality in the research process. Finally, the research team encouraged them to fill in questionnaires as best they could.

5.5.6 Trustworthiness/validity

Validity in qualitative research or trustworthiness is a concept that explains how sound and good quality the study is. Validity establishes truth, value and authenticity of the study⁹⁴. In this thesis, trustworthiness has been discussed in the following aspects:

5.5.6.1 Credibility

Credibility refers to the ability of research outcomes to really capture multiple realities of the study participants. It describes how well investigators managed to reconstruct the subjective realities of study participants, if the study participants would recognize those subjective realities in outcomes and finally, if other people in different contexts could relate to such realities in final reports⁹⁵.

5.5.6.2 Triangulation

Triangulation is the combination of multiple observers, theories and data sources (researchers) hopefully to overcome the intrinsic bias that comes from single methods, single observers, and single theory studies⁹⁶. The logic behind triangulation is based on the premise that no single method ever adequately solves the problem of rival explanation, since each method reveals different aspects of empirical reality⁹⁷.

In this thesis, triangulation was addressed by using both quantitative and qualitative research methods. Quantitative methods were used to quantify and provide a clear description of the problem and its possible determinants. Combining with qualitative inquiry, meanings and understanding of concepts and descriptions were realized. Triangulation of methods of data collection refers to the combination of different methods in studies while triangulation of data sources refers to different study participants and triangulation of investigators means using more than one investigator⁹⁵. For instance, we used questionnaires in study I which gave rise to insights into the role of significant others in HIV vaccine participation among youth. Detailed answers were provided by using focus group discussions in study II. We further used in-depth interviews that elicited experiences of young volunteers in trials that gave more insight into WTP in HIV vaccine trials. We also collected data using FGDs from young people with diverse characteristics and background, along with some adults. Further, the studies had been conducted by team of international researchers that have different backgrounds, experiences and disciplines in research methodologies; medical, nursing, global health, and the HIV vaccine clinical trials.

5.5.6.3 Peer debriefing

Peer debriefing means presentation of preliminary findings to colleagues, allowing researchers to evaluate their work, and receive input from those outside the research process⁹⁵. In this study, peer debriefing took place after data collection and analysis of

preliminary findings. We presented the initial findings to other investigators and staff at IDC for critical review, discussions and understanding of the preliminary results. Then the investigators provided feedback and comments that helped to shape final discussions and design research questions for the subsequent studies. For instance, preliminary findings in study I paved the way for an improved design of study II.

5.5.6.4 Member check

Member check entails feeding back the results to the members of the studied group. This process clarifies the information provided and confirms the researchers' interpretation⁹⁵. The results of study IV were presented to some participants so as to see if our interpretations of findings represented their original thoughts. Most of them agreed that the interpretations reflected their thoughts on the readiness of youth to be involved in HIV vaccine trials.

5.5.6.5 Reflexibility

Reflexibility describes a journey of discovering how the researchers shaped and how they were shaped by the research process. The researchers acknowledged the changes brought about in themselves as a result of the research process and how these changes have affected the research process⁹⁸. Reflexivity involves a process of on-going mutual shaping between researcher and research. Simply put, reflexivity concerns itself with the effect of the whole-person-researcher on the research as well as the effect of the research on the researcher. Reflexivity seeks to help researchers grow their capacity to understand the significance of the knowledge, feelings, and values that they brought into the field to the research questions that they came to formulate, to the analytical lenses that they chose to employ, and to their findings. The role of reflexivity involves raising awareness of processes of research with the dual aim first of enriching one's lived experience, and then articulating this awareness as a contribution to the deepening of understanding of the field⁹⁹.

Being a young optimistic researcher, parent, doctor and PhD candidate in research fieldwork has left me with a deeper understanding and appreciation of the complexities of looking for permanent cure for HIV. I was dealing with some young female volunteers in the trial who experienced marital discordance following participation in the trial. As a young parent and female, I was devastated to see what those young people went through. I was afraid for their future since it was uncertain if their marriages would work out or not. However, during counselling sessions with them, as a result of my training, I could show them empathy rather than sympathy in order to ensure I played my role as a counsellor in a professional and ethical manner. At times, I was frustrated to see young people in the trial got pregnant or become expectant fathers, in my mind I thought that they were not serious enough and could not see how important HIV vaccine research was. Over time, by listening and working with them, I came to appreciate the dilemmas, personal griefs, sacrifices, worries and choices the volunteers went through to reconcile their participation in the clinical trial with their lives in their communities. It taught me that there were multiple factors and realities in play for any clinical intervention to succeed or not. During data collection using in-depth interviews, I was worried that young volunteers would give

answers that I wanted to hear for fear of disappointing me or for fear that I would see them differently after all the years of interaction at the trial site. Through my PhD training, I was able to establish a good rapport, explaining my role as a researcher, assuring them of privacy and confidentiality. Then by using a semi-structured interview guide, I was able to probe, monitor and obtain fairly good answers to questions about their experiences of being young volunteers in the TaMoVac I trial. During data analysis, coding and creating categories and themes was wearying and draining. I used to worry that abstracted information from interview texts and discussions would not really reflect and represent the ideas and concepts of the participants. Under the guidance of qualitative experts, AK and EAMT, I learnt that data analysis was not mere coding and abstraction, but also entailed listening to audios, reading texts, ensuring translated texts had all the meaningful information, and at the same time being professional researcher by conducting analysis that followed scientific methods. The process taught me how to disengage my a priori ideas or interpretation and extract emergent themes from collected data. Having that experience enabled me to formulate themes and arrive at conclusions that not only answered research questions but also added knowledge to the research topic.

5.5.6.6 Transferability

Transferability refers to the application of research findings to other contexts⁹⁵. To allow transferability, the researchers must provide sufficient detail of the context of the fieldwork for a reader to be able to decide whether the prevailing environment is similar to another situation with which he or she is familiar, and whether the findings can justifiably be applied to this other setting. It is also important that a sufficiently detailed description of the phenomenon under investigation is provided to allow readers to have a proper understanding of it, thereby enabling them to compare the instances of the phenomenon described in the research report with those that they have seen emerge in their situations. In order to assess the extent to which findings may be true of people in other settings, similar projects employing the same methods but conducted in different environments could well be of great value¹⁰⁰.

In this thesis, we observed scientific methods from proposal development to data collection and analysis at the same time as adhering to the ethics of research work. Furthermore, final articles, abstracts and reports had to clearly describe background information, methodological steps, results and discussions in order to allow readers to make valid informed conclusion if our findings could be applicable in their settings. For instance, the young volunteers in HIV vaccine trials in this thesis had fears of vaccine-induced seroreactivity, and the same impressions were found in volunteers in HIV vaccine trials in the US, Belgium, Kenya, South Africa, Rwanda and elsewhere.

5.5.6.7 Dependability

In addressing the issue of dependability, researchers need to demonstrate techniques that show that, if the work were repeated, in the same context, with the same methods and with the same participants, similar results would be obtained. In order to address the dependability issue more directly, the processes within the study should be reported in

detail, thereby enabling a future researcher to repeat the work, if not necessarily to gain the same results¹⁰⁰. In this thesis, we clearly described research plans and ways of their implementation. After seeking permission from the participants, we used audio tapes to record the in-depth interviews and discussions in focus groups. In addition, during data collection, we took notes for impressions, for jogging memory on certain emphasized points during discussions, record-keeping and reference during write-ups.

6 CONCLUSION

Youth showed readiness to participate in phase IIa HIV vaccine trial. For most young people, the decision to participate in vaccine trials largely depend on support of members of the community. In contrast, for high-risk young women, this decision largely be their own. Some factors like altruism, support from members of the community and, perceived personal benefit served as positive attributes to participation. Despite such readiness, fertility issues, stigma, poverty were perceived as hurdles needed to be resolved by different stakeholders on individual, community and societal levels for successful participation.

7 RECOMMENDATIONS

Practical aspects

- Increase awareness of health professional such as nurses, laboratory technicians, phlebotomists and clinicians on the existence of clinical trials, their roles in supporting volunteers in health facilities.
- Increase understanding among members of the community such as parents, guardians, youth organizations and peers of the trial process, concepts and advocate for their support of HIV vaccine trials.
- Advocacy to develop guidelines on inclusion of significant others and other members of the community in clinical trials involving young people.
- Conduct scheduled meetings with volunteers and significant others for regular updates on the progress of clinical trials locally and globally as a retention strategy.

Research Aspects

- One of the studies in this thesis provided some background information about female sex workers and willingness to participate in HIV vaccine trials. This is information that could be used to design future efficacious HIV vaccine trials in key populations. Hence, the following research studies should be considered:
 - Studies of socioeconomic inequalities among young people in key populations in HIV vaccine research programs and how inequalities may impact their participation in trials
 - Perspectives of health care workers and policy makers on participation of high-risk youth in HIV vaccine research programs
 - Longitudinal cohort studies among youth in key populations to establish HIV incidence.

8 ACKNOWLEDGEMENTS

I praise and thank you Lord, my God for your love, blessings, mercy, and grace. Here when I thought You had done too much for me, Lord, you have done it again.

Although this thesis bears my name on its cover, its work has been contributed by many people, some of whom I would like to mention here by names. For those whom I would not be able to say their names, I want you to know I acknowledge your contribution and support that had made this journey a unique experience.

My most profound appreciation goes to Associate Professor Asli Kulane, (principal supervisor). Thank you for believing in me. I am particularly grateful for sharing your vast experience, guidance, and knowledge on matters of Public Health, without which I would not be able to finish my doctoral education. I thank you for developing and nurturing my research and analytical skills. I am grateful for guiding me in developing study plans and proposals, for reading and critiquing all “zero” drafts (and so many other drafts) of every research work I put on your desk. It was a tough job, but due to your steady commitment and professionalism, you made it possible and this journey to doctoral education worthwhile. I thank you for constructive and timely feedback, passion, patience, encouragement and always getting out of your way to ensure I had a safe and comfortable stay in Sweden.

I am indebted to my co-supervisor Professor Muhammad Bakari who brought me on board for doctoral education. I appreciate your encouragement and advice when I thought the journey was endless. Despite your busy schedule, you always dedicated time to provide constructive comments for my research work and for dealing with all administrative issues.

A special thank you goes to my co-supervisor, Professor Eric Sandström who saw ‘a young researcher’ in me many years ago at the youth-friendly clinic, IDC. Thank you for your wisdom, encouragement, and advice that helped me to join the doctoral education. Throughout the way, you provided critical reviews of every draft of my work and offered “out of the box” thinking that had shaped my thought processes and scientific writings.

My sincere gratitude to my co-supervisor Dr. Edith A. M Tarimo for being a reassuring presence when I had panicking moments. You used to tell me, “Theodora, relax, we are here to assist and guide you.” I specifically recognize your vast contribution in developing my qualitative skills and for shaping my thoughts to look at the research work in its totality.

Thanks to my co-supervisor, Professor Anna Thorson for guidance and comments on the research work.

To Professor Eligius Lyamula, my mentor, I am forever grateful for guiding me through tough and calm days of Ph.D. training. Your wisdom and experience made this journey possible.

I want to express my sincere gratitude to Professor Gunnel Biberfeld, Professor Said Aboud and Professor Anna Mia Ekström for coordinating all administrative work that enabled me to travel for conferences and courses in Tanzania, Sweden and elsewhere.

I want to thank the head of Department of Public Health Sciences, Professor Marie Hasselberg, and the former head, Professor Lucie Laflamme for good leadership and administrative work that made my stay as a Ph.D. student in this department meaningful and memorable. I want to extend my appreciation to the group leader of Equity and Health Policy Research group, Professor Bo Burström for smooth coordination of group and all members of this research group. I enjoyed the academic discussions we shared, and I value your critical inputs in manuscripts. My appreciation goes to Professor Anna Mia Ekström, the group leader of Global and Sexual Health Research group and all members of the group for academic and social support.

Many thanks go to Bo Planstedt for technical support with IT matters. To Gun-Britt, Malin, Kersti, Amanda, Marita and other members of the administration team at PHS for ensuring my LADOK and annual reports were in order throughout my training.

Many thanks are also due to Global Health Research School for giving me a rare opportunity to study Global Health in the broader perspective. I am very grateful for sponsoring courses, conferences and travels to Umea for the courses. My stay in school made me interact with experienced scholars, Ph.D. and Masters students from different background and disciplines, indeed those were among the best moments of my training.

I want to thank Dr. Candida Moshiro and Dr. Joel Francis for statistics lessons and comments on the manuscripts.

I am grateful to my colleagues who finished their Ph.D. training before me; Dr. Patricia Munseri, Dr. Agricola Joachim, Dr. Helga Naburi, Dr. Matilda Ngarina, and Dr. Tumaini Nagu and ongoing Ph.D. colleagues; Dr. Roseline Urio, Dr. Goodluck Lyatuu, Dr. Frank Msafiri, and Dr. Diana Faini in Tanzania. My fellow Ph.D. colleagues at Karolinska Institutet; Lisa Blom and Galit Zeluf. Thank you all for sharing news on Ph.D. courses, discussions, conference presentations, achievements and challenges of Ph.D. training. Importantly I appreciate the conversations and advice on ways of overcoming challenges along the path.

I want to express my heartfelt gratitude to Mr. Emilian Busara, CEO at Management and Development for Health, MDH. No words can show my appreciation for ensuring I finish Ph.D. training after the demise of our beloved CEO, Dr. Guerino Chalamilla. Your faith, kind heart, wisdom, and love for academic achievement for everyone have enabled me to finish my training without blemish. This training would have been almost impossible without your moral support and encouragement.

I am deeply grateful to all members of the Senior Management Team, my colleagues and friends at MDH for your support and care. I recognize every contribution each one of you made towards my training. It is my prayer that God continues to bless you abundantly.

I am particularly indebted to Dr. Lameck Machumi for constant supervision, guidance and shouldering my duties at MDH throughout this journey. Thank you for setting aside time for academic discussions and inputs on the conceptual framework that formed the basis of this thesis. Many thanks go to Dr. Ali Kaduma for the encouragement, advice and sharing my responsibilities. To Dr. Talumba Samatta and Dr. Sara Mdingi for excellent mentorship, and supervision. To my friends and office mates; Victor Mponzi, Irene Macha, Angelica Rugarabamu, Dr. Faida Emily, Nassir Kashmir, Daniel Sanga, Neema Mabuba and Malumbo Khamsini for shouldering my work and encouraging words.

I am forever thankful to all the participants who contributed their time and knowledge in my research topic. Without your participation, I would not be able to finish my doctoral education. Also, thank you Sr Beatrice Kiwelele and Sr Shida Mpangala for being great research assistants, for dedicating time and efforts for accurate data collection.

I wish to express my gratitude to IDC team, HIVIS 03/TaMoVac 01 and 02 research teams in Muhimbili, Mbeya and Mozambique. Thank you for sharing your expertise and knowledge on HIV vaccine clinical trials. As we worked together during recruitment and following up of the volunteers, I gained a lot of the experience and knowledge in pursuit of research work.

My studies were made possible by the generous financial support from The Swedish International Development Cooperation Agency, SIDA. Your help made my dream of pursuing Ph.D. training at a prestigious medical university, Karolinska Institutet a reality. I would also like to thank Dr. Bruno F. Sunguya, a director at Directorate of Research and Publication and administration of MUHAS for allowing me to undertake Ph.D. training under sandwich modality.

Many thanks go to my landlady Gunn Sandell for providing me with your hospitality, kindness, care and a safe home during my stay in Stockholm.

My sincere gratitude goes to my friends for prayers, advice, and support; Dr. Neema Minja Kileo, Geraldina Duwe, Dr. Rehema Msimbe, Dr. Shally Mwashemele, Dr. Joan Rugemalila, Dr. Stella Kasone, Dr. Milka Mathania, Dr Esther Steven, Dr. Albina Gelege, Dr. Amina Mgunya, Dr. Mariam Ngaeje, Dr. Annapendo Kweka, Dr. Berezy Makaranga, Kay Ngalomba, Dr. Joyce Wamsele, Dr. Hawa Mziray, Wema Kamuzora, and Lilian Itemba.

To Dr. Nyasule Neke-Kraus and Dr. Frida Ngalesoni for love, care, laughter and tears as we were pursuing Ph.D. training. Even if we were miles apart, you were always there to provide quick solutions to academic and social challenges in Europe.

I want to thank my niece, Happiness Kokushekya Mpesha, Mama Nyambura Mpesha and Abanya Mureithi for your unconditional love, and all members of Mpesha family for support.

My sincere appreciation goes to Abela Mpobela Agnarson, Annika Östman, Christina Östman and Hanna Atterling for opening your homes, embracing and sharing your lives with me. Thank you for enriching my “Swedish experiences.” There were no dull moments with you. I will forever cherish loving memories.

My heartfelt and the sincerest appreciation goes to my mother, Ndeana Grace Masawe Mbunda. Mama, you have been my rock and strength in my life. You had taken care of me, my daughters and family when I was not around. No amount of words I can write here will reflect my gratitude. Your love, prayers, and confidence in me made me feel special and protected always. I have always felt the presence of our late dad in you. Thank you for lifting me during rough times, it could have been worse without you.

Moreover, to my dearest sisters N’ana Daniel Mbunda, Zawadi Daniel Mbunda, and Donatha Daniel Mbunda. I would not ask God for other sisters but you. Your belief in me made a huge difference in my training. I comfortably travelled to Sweden and elsewhere in the world knowing my daughters and family would be well taken care of by you. Indeed, you had not disappointed me even once. Thank you for group prayers, care, love and support during my doctoral education. What would I have done without you?

The last but not the least to my beautiful daughters; Makena Nyambura and Ekisha Ndeana, you are my heroines. I thank you for every drop of tears you cried when I travelled for the training. Your tears were my sole source of energy, focus and a drive to finish my doctoral training. I thank you for your prayers, love, encouragement, good behaviour at school and home. By God’s grace, I believe I will make up for the "lost time" and all absences from home. I continue to praise God for His endless love and protection over you. To the father of my daughters, Muhanuzi Mpesha, I would like to express my gratitude for taking care of our daughters during my training. God bless you always.

9 REFERENCES

1. Merson MH, O'Malley J, Serwadda D, Apisuk C. HIV Prevention 1. The history and challenge of HIV prevention. *Lancet* 2008; 372: 475–88. August 6, 2007
DOI:10.1016/S0140- 6736(08)60884-3.
2. Joint United Nations Programme on HIV/AIDS (UNAIDS). Fact Sheet 2017 Global HIV statistics.
http://www.unaids.org/sites/default/files/media_asset/UNAIDS_FactSheet_en.pdf.
Accessed on 10/08/2018.
3. Joint United Nations Programme on HIV/AIDS (UNAIDS). UNAIDS data 2018.UNAIDS/JC2929E http://www.unaids.org/sites/default/files/media_asset/unaid-data-2018_en.pdf#page=4&zoom=auto,-62,843. Accessed on 12/08/2018.
4. Joint United Nations Programme on HIV/AIDS (UNAIDS). Global AIDS Updates. UNAIDS 2016. http://www.unaids.org/sites/default/files/media_asset/global-AIDS-update-2016_en.pdf. Accessed on 12/08/2018.
5. Ministry of Health and Social Welfare (MoHSW) [Tanzania Mainland], Ministry of Health (MoH) [Zanzibar], National Bureau of Statistics (NBS), Office of the Chief Government Statistician (OCGS), and ICF International 2015. Tanzania Service Provision Assessment Survey (TSPA) 2014-15. Dar es Salaam, Tanzania, and Rockville, Maryland, USA: MoHSW, MoH, NBS, OCGS, and ICF International.
6. National Bureau of Statistics (NBS), Dar es Salaam., Office of Chief Government Statistician (OCGS), Zanzibar. *The United Republic of Tanzania. 2012 Population and Housing Census. Population Distribution by Administrative Areas. March 2013.*
7. National Bureau of Statistics(NBS). *The United Republic of Tanzania. Proportion of Young Population 15-24 Years. National Bureau of Statistics.*<Http://Www.Nbs.Go.Tz/>. Accessed on 12/08/2018.
8. National Bureau of Statistics(NBS). *The United Republic of Tanzania. Total Fertility Rate by Region. National Bureau of Statistics.*<Http://Www.Nbs.Go.Tz/>. Accessed on 13/08/2017.
9. National Bureau of Statistics (NBS). *The United Republic of Tanzania. Distribution of the Male Population 15 Years and above by Literacy. National Bureau of Statistics.*<Http://Www.Nbs.Go.Tz/>. Accessed 12/08/2017.
10. National Bureau of Statistics (NBS). *The United Republic of Tanzania. Distribution of the Female Population 15 Years and above by Literacy. National Bureau of Statistics.* <Http://Www.Nbs.Go.Tz/>. Accessed 20/08/2017.
11. National Bureau of Statistics (NBS). *The United Republic of Tanzania. Highlights for the Third Quarter (July–September) Gross Domestic Product, 2017. January, 2018.* [Http://Www.Nbs.Go.Tz/Nbs/Takwimu/Na/Highlights_for_The_Third_Quarter_\(July_September\)_Gross_Domestic_Product_%202017.Pdf](Http://Www.Nbs.Go.Tz/Nbs/Takwimu/Na/Highlights_for_The_Third_Quarter_(July_September)_Gross_Domestic_Product_%202017.Pdf). Accessed on 06/06/2018.
12. Ministry of Health, Community Development, Gender, Elderly and Children (MoHCDCGEC). *The United Republic of Tanzania. Health Sector Strategic Plan July 2015 – June 2020, HSSP IV. Reaching All Households with Quality Health Care.* Http://Www.Tzdpd.or.Tz/Fileadmin/Documents/Dpdg_internal/Dpdg_working_groups_cl

usters/Cluster_2/Health/Key_Sector_Documents/Induction_Pack/Final_HSSP_IV_Vs1.0_260815.Pdf. Accessed 06/09/2017.

13. Ministry of Health and Social Welfare (MoHSW). *Surveillance of HIV and Syphilis Infections among Antenatal Clinic Attendees 2008*. Dar Es Salaam, Tanzania: MoHSW.
14. Joint United Nations Programme on HIV/AIDS (UNAIDS). *The United Republic of Tanzania. Global AIDS Response Country Progress Report 2014*. March 2014. [Http://www.unaids.org/sites/default/files/country/documents/TZA_narrative_report_2014.Pdf](http://www.unaids.org/sites/default/files/country/documents/TZA_narrative_report_2014.pdf). Accessed on 15/07/2018.
15. Population Council, Tanzania Commission for AIDS (TACAIDS), Zanzibar AIDS Commission (ZAC), and UNICEF Tanzania 2015. *The Adolescent Experience In-Depth: Using Data to Identify and Reach the Most Vulnerable Young People, Tanzania 2009-2012*. Dar Es Salaam: Population Council, TACAIDS, ZAC and UNICEF Tanzania.
16. Ministry of Health, Community Development, Gender, Elderly and Children (MoHCDGEC), the Ministry of Health (MoH) Zanzibar, National Bureau of Statistics (NBS) and the Office of Chief Government Statistician (OCGS). *Summary Sheet: Preliminary Findings. Tanzania HIV Impact Survey (THIS) 2016-2017*. December 2017. https://phia.icap.columbia.edu/wp-content/uploads/2017/11/Tanzania_SummarySheet_A4.English.V19.Pdf.
17. TACAIDS, ZAC, NBS, OCGS and ICF International. *Tanzania HIV and Malaria Indicator Survey 2011-2012*. Dar Es Salaam, Tanzania.
18. National Bureau of Statistics (NBS) and the Office of Chief Government Statistician (OCGS). *The United Republic of Tanzania. Economic Activity Monograph, June 2015*. National Bureau of Statistics (NBS) and the Office of Chief Government Statistician (OCGS).
19. Airhihenbuwa C. *Healing Our Differences: The Crisis of Global Health and The Politics of Identity*. New York, NY: Rowman & Littlefield Publishers, INC; 2007:17.
20. Joint United Nations Programme on HIV/AIDS (UNAIDS). *Global Report: UNAIDS Report on the Global AIDS Epidemic 2013*. UNAIDS / JC2502/1/E, November 2013. [Http://files.unaids.org/en/media/unaids/contentassets/documents/epidemiology/2013/Gr2013/UNAIDS_Global_Report_2013_en.Pdf](http://files.unaids.org/en/media/unaids/contentassets/documents/epidemiology/2013/Gr2013/UNAIDS_Global_Report_2013_en.pdf). Accessed on 12/08/2017.
21. World Health Organization (WHO). *UNAIDS HIV Vaccine Initiative*. [Http://www.who.int/immunization/research/forums_and_initiatives/hiv_vaccine_initiative/En/](http://www.who.int/immunization/research/forums_and_initiatives/hiv_vaccine_initiative/en/). Accessed 5th Dec 2016.
22. Esparza J. A brief history of the global effort to develop a preventive HIV vaccine. *Vaccine* 2013. Volume 31 Issue 35 Pages 3502-3518 <https://doi.org/10.1016/j.vaccine.2013.05.018>.
23. International AIDS Vaccine Initiative (IAVI). *Database of Preventative HIV Vaccine Candidates*. International AIDS Vaccine Initiative. www.iavi.org/trials-database. Accessed on 14.10.2016.
24. College of Physicians of Philadelphia. *The History of Vaccines. An Education Resource by College of Physicians of Philadelphia. The Development of HIV Vaccines*.

Www.Historyofvaccines.Org/Content/Articles/Development-Hiv-Vaccines. Accessed on 04/09/2018.

25. Sekaly R-P. The failed HIV Merck vaccine study: a step back or a launching point for future vaccine development? *J Exp Med.*205(1); 2008.
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2234358/>.
26. Kim JH, Exceler J-L, Michael NL. Lessons from the RV144 Thai Phase III HIV-1 Vaccine Trial and the Search for Correlates of Protection. *Annual Review of Medicine*, January 2015. Vol. 66:423-437. <https://doi.org/10.1146/annurev-med-052912-123749>.
27. National Institute of Allergy and Infectious Diseases (NIAID). Pivotal Phase 2b/3 ALVAC/Bivalent gp120/MF59 HIV Vaccine Prevention Safety and Efficacy Study in South Africa (HVTN702). <https://clinicaltrials.gov/show/NCT02968849>. Accessed on 13/08/2018.
28. National Institute of Allergy and Infectious Diseases. *First New HIV Vaccine Efficacy Study In Seven Years Has Begun. South Africa Hosts Historic NIH-Supported Clinical Trial. Accessed from <https://www.niaid.nih.gov/news-events/first-new-hiv-vaccine-efficacy-study-seven-years-has-begun>. Accessed on 7th February 2017.*
29. Bakari M, Lyamuya E, Mugusi F, et al. The prevalence and incidence of HIV-1 infection and syphilis in a cohort of police officers in Dar es Salaam, Tanzania: a potential population for HIV vaccine trials. *AIDS* 2000 Feb 18;14(3):313-20.
30. Munseri PJ, Bakari M, Janabi M, et al. Declining HIV-1 prevalence and incidence among Police Officers – a potential cohort for HIV vaccine trials, in Dar es Salaam, Tanzania. *BMC Public Health* 2013, 13:722. <http://www.biomedcentral.com/1471-2458/13/722>.
31. Bakari M, Said Aboud, Buma D, et al. Broad and potent immune responses to a low dose intradermal HIV-1 DNA boosted with HIV-1 recombinant MVA among healthy adults in Tanzania. *Vaccine* 2011, 29(46):8417–28. doi:10.1016/j.vaccine.2011.08.001.
32. Munseri PJ, Kroidl A, Charlotta Nilsson, et al. Priming with a Simplified Intradermal HIV-1 DNA Vaccine Regimen followed by Boosting with Recombinant HIV-1 MVA Vaccine Is Safe and Immunogenic: A Phase IIa Randomized Clinical Trial. *PLoS ONE*, 2015; 10(4): e0119629. doi: 10.1371/journal.pone.0119629 PMID: 25875843.
33. *ClinicalTrials.gov. ClinicalTrials.Gov. A Phase II Trial to Assess the Safety and Immunogenicity of DNA Priming Administered by the ID Zetajet® With or Without ID Derma Vax™ Electroporation Followed by IM MVA Boosting in Healthy Volunteers in Tanzania and Mozambique (TaMoVac II). <https://Clinicaltrials.Gov/Ct2/Show/NCT01697007>. Accessed 09/08/2018.*
34. Joint United Nations Programme on HIV/AIDS (UNAIDS). Empower young women and adolescent girls: Fast-Track the end of the AIDS epidemic in Africa.UNAIDS / JC2746E; 2015.http://www.unaids.org/sites/default/files/media_asset/JC2746_en.pdf. Access 03/10/2018.
35. The Global Coalition on Women and AIDS. Advancing young women’s sexual and reproductive health and rights in the context of HIV.
https://www.aidsdatahub.org/sites/default/files/publication/Advancing_young_women_s

exual_and_reproductive_health_and_rights_in_the_context_of_HIV_2014.pdf.
Accessed 01/10/2018.

36. DiClemente RJ, Sales JM, Borek N. Barriers to Adolescents' Participation in HIV Biomedical Prevention Research. *Journal of Acquired Immune Deficiency Syndromes* 2010 July 1; 54(Suppl 1): S12–S17. doi:10.1097/QAI.0b013e3181e1e2c0.
37. Tarimo EA, Kohi T, Bakari M, Mhalu F, Kulane A. Reasons for declining to enrol in a phase I and II HIV vaccine trial after randomization among eligible volunteers in Dar es Salaam, Tanzania. *PLoS one* 2011.6(2): e14619. doi:10.1371/journal.pone.0014619.
38. Newman P, Naihua D, Roberts K, et al. HIV Vaccine Trial Participation Among Ethnic Minority Communities. Barriers, Motivators, and Implications for Recruitment. *J of Acquir Immune Defic Syndr* 2006;41:210–217.
39. Sayles JN, MacPhail CL, Newman PA, Cunningham WE. Future HIV Vaccine Acceptability Among Young Adults in South Africa. *Health Education Behaviour* 2010. Volume 37(2): 193–210. doi: 10.1177/1090198109335654.
40. Newman P, Rongprakhon S, Tejan S, Yim S. Preventive HIV Vaccine Acceptability and Behavioural Risk Compensation among High-Risk Men who have Sex with Men and Transgender in Thailand. *Vaccine* Volume 28, Issue 4, 2010, Pages 958-964. doi: 10.1016/j.vaccine.2009.10.142.
41. Bryman A. *Social Research Methods*. New York, NY: Oxford University Press; 2001.
42. Daniel E. The Usefulness of Qualitative and Quantitative Approaches and Methods in Researching Problem-Solving Ability in Science Education Curriculum *Journal of Education and Practice*. Vol.7, No.15, 2016. <https://files.eric.ed.gov/fulltext/EJ1103224.pdf>. Accessed on 01/09/2018.
43. National Bureau of Statistics (NBS) and Office of Chief Government Statistician, Zanzibar 2016. *The United Republic of Tanzania. Basic Demographic and Socio-Economic Profile. Dar Es Salaam Region 2016*. Http://Tanzania.Countrystat.Org/Fileadmin/User_upload/Countrystat_fenix/Congo/Docs/2012%20Tanzania%20Population%20and%20Housing%20Census-Basic%20Demographic%20and%20Socio-Economic%20Profile.Pdf. Accessed 03/07/2017.
44. Heckathorn D. Respondent Driven Sampling: A New Approach to the Study of Hidden Populations. *Social problems* 1997; 44(2): 174-199.
45. Patton M. *Qualitative Evaluation and Research methods* (pp. 169–186). Beverly Hills, CA: Sage 1990. <https://legacy.oise.utoronto.ca/research/field-centres/ross/ctl1014/Patton1990.pdf>. Accessed 16/05/2017.
46. Boyce C, Neale P. *Conducting in-depth Interviews: A Guide for Designing and Conducting In-Depth Interviews for Evaluation Input*. Pathfinder International ;2006.
47. Segal DL, Coolidge FL, O'Riley A, Heinz BA. *Clinical Handbook of Adult Behavioral Assessment. Structured and Semi-structured Interviews*. University of Colorado: Elsevier, INC; 2006.

48. Thomas L, MacMillan J, McColl E, Hale C. Comparison of focus group and individual interview methodology in examining patient satisfaction with nursing care. *Social Sciences in Health*. 1995;1:206–219.
49. Richardson CA, Rabiee F. ‘A Question of Access’ – an exploration of the factors influencing the health of young males aged 15–19 living in Corby and their use of health care services. *Health Educ J* 2001; 60, 3–6.
<http://journals.sagepub.com/doi/pdf/10.1177/001789690106000102>. Accessed 07/04/2016.
50. Rabiee F. Focus group interview and data analysis. *Proc Nutr Soc*. 2004 Nov;63(4):655–60.
51. Tavakol M, Dennick R. Making sense of Cronbach’s alpha. *Int J Med Educ*. 2011; 2: 53–55. doi: 10.5116/ijme.4dfb.8dfd.
52. Maldonado G, Greenland S. Simulation study of confounder- selection strategies. *Am J Epidemiol* 1993; 138: 923–36.
53. Imperial College London. *Stata Introduction and Data Management.doc workshops*.
<https://www.imperial.ac.uk/.../SIDM2%20Preparing>. Accessed on 13/08/2018.
54. Gile KJ. *Improved Inference for Respondent-Driven Sampling Data with Application to HIV Prevalence Estimation*. Nuffield College 2010.
55. Salganik MJ, Heckathorn DD. Sampling and Estimation in Hidden Populations Using Respondent-Driven Sampling. *Sociological Methodology*. 2004;34:193–239.
<https://doi.org/10.1111/j.0081-1750.2004.00152.x>.
56. STATA. *STATA 13.0. Statistics/Data Analysis*. Copyright 1985–2013 StataCorp LP.
<http://www.stata.com>.
57. Bursac Z, Gauss CH, William DK, Hosmer DW. Purposeful selection of variables in logistic regression. *Source Code Biol Med*. 2008 Dec 16;3:17. doi: 10.1186/1751-0473-3-17.
58. Bengtsson M. How to plan and perform a qualitative study using content analysis. *NursingPlus Open* 2. 2016:8–14 <http://dx.doi.org/10.1016/j.npls.2016.01.001>.
59. Graneheim U., Lundman B. Qualitative content analysis in nursing research: concepts, procedures and measures to achieve trustworthiness. *Nurse Educ Today*. 2004;24:105–112. <https://www.ncbi.nlm.nih.gov/pubmed/14769454>. Accessed on 06/07/2018.
60. Thorne S, Kirkham SR, MacDonald-Emes J. Focus on Qualitative Methods: Interpretive Description: A Non categorical Qualitative Alternative for Developing Nursing Knowledge. *Res Nurs Health* 20: 169–177, 1997.
<https://onlinelibrary.wiley.com/doi/epdf/10.1002/%28SICI%291098-240X%28199704%2920%3A2%3C169%3A%3AAID-NUR9%3E3.0.CO%3B2-I>
Accessed on 04/02/2017.
61. Thorne S. The Analytic Challenge in Interpretive Description Sally Thorne. *International Journal of Qualitative Methods*.2004;3:1 http://www.ualberta.ca/~iiqm/backissues/3_1/pdf/thorneetal.pdf. Accessed 02/03/2017.

62. McLeroy K, McLeroy KR, Bibeau D, Steckler A, Glanz K. An ecological perspective on health promotion programs. *Health Educ Q.* 1988;15(4):351–377.
63. Nyaoke BA, Mutua GN, Sajabi R, Nyasani D, Mureithi MW, Anzala OA. Volunteer motivators for participating in HIV vaccine clinical trials in Nairobi, Kenya. *PLoS ONE.* 2017; 12(9): e0183788. <https://doi.org/10.1371/journal.pone.0183788>.
64. Ma M, Young A T, Durham M, et al. Predictors of Willingness of Participate in HIV Vaccine Trials among African Americans. *J AIDS Clin Res.* 2014; 5: 361. doi:10.4172/2155-6113.1000361.
65. Giguere R, Zimet GD, Kahn JA, et al. The Motivations and Experiences of Young Women in a Microbicide Trial in the USA and Puerto Rico. *World J AIDS.* 2013; 3(3): doi:10.4236/wja.2013.33023.
66. Newman PA, Chakrapani V, Weaver J, Shunmugam M, Rubincam C. Willingness to participate in HIV vaccine trials among men who have sex with men in Chennai and Mumbai, India. *Vaccine.* 2014; 32: 5854–5861.
67. Metch B, Frank I, Novak R, et al. Recruitment of Urban US Women at Risk for HIV Infection and Willingness to Participate in Future HIV Vaccine Trials. *AIDS Behav.* 2013; 17(2): 760–772. doi:10.1007/s10461-012-0351-6.
68. Tarimo EA, Munseri P, Aboud S, Bakari M, Mhalu F, Sandstrom E. Experiences of Social Harm and Changes in Sexual Practices among Volunteers Who Had Completed a Phase I/II HIV Vaccine Trial Employing HIV-1 DNA Priming and HIV-1 MVA Boosting in Dar es Salaam, Tanzania. *PLoS ONE.* 2014; 9(3): e90938. doi:10.1371/journal.pone.009093800.
69. Tarimo EA, Thorson A, Bakari M, Mwami J, Sandstrom E, Kulane A. Willingness to volunteer in a Phase I/II HIV vaccine trial: a study among police officers in Dar es Salaam, Tanzania. *Glob Health Action.* 2009; 7;2. doi: 10.3402/gha.v2i0.1953.
70. Bakari M, Munseri P, Francis J, et al. Experiences on recruitment and retention of volunteers in the first HIV vaccine trial in Dar es Salam, Tanzania - the phase I/II HIVIS 03 trial. *BMC Public Health* 2013, 13:1149. <http://www.biomedcentral.com/1471-2458/13/1149>. Accessed 05/08/2018.
71. Adler DH. Inclusion of South African adolescents in HIV vaccine trials. *J AIDS HIV Res.* 2012; 4(2): 30–35.
72. Schmidt C, Jaoko W, Omosa-Manyonyi G, et al. Long-term follow-up of study participants from prophylactic HIV vaccine clinical trials in Africa. *Human Vaccines & Immunotherapeutics.* 2013;10:3, 714-723. DOI: 10.4161/hv.27559.
73. Voronin Y, Zinszner H, Karg C, et al. HIV vaccine-induced sero-reactivity: A challenge for trial participants, researchers, and physicians. *Vaccine.* 2015; 33(10): 1243–1249. doi: 10.1016/j.vaccine.2014.10.040.
74. Chakrapani V, Newman PA, Singhal N, Jerajani J, Shunmugam M. Willingness to Participate in HIV Vaccine Trials among Men Who Have Sex with Men in Chennai and Mumbai, India: A Social Ecological Approach. *PLoS ONE.* 2012; 7(12): e51080. doi:10.1371/journal.pone.0051080.

75. Chu Z, Xu J, Reilly KH, et al. HIV Related High Risk Behaviors and Willingness to Participate in HIV Vaccine Trials among China MSM by Computer Assisted Self-Interviewing Survey. *Biomed Res Int.* 2013;2013:493128. doi: 10.1155/2013/493128.
76. Inungu JN, Bender B, Gieber L. Socio-Behavioral Challenges to HIV Vaccine Trials: Literature Review. *Clin Res HIV/AIDS.* 2017; 4(1): 1034.
77. Stadler J, Delany-Moretlwe S, Palanee T, Rees H. Hidden harms: women's narratives of intimate partner violence in a microbicide trial, South Africa. *Soc Sci Med.* 2014;110:49-55. doi: 10.1016/j.socscimed.2014.03.021.
78. MacPhail CL, Sayles JN, Cunningham W, Newman P. Perceptions of Sexual Risk Compensation Following Post trial HIV Vaccine Uptake Among Young South Africans. *Qual Health Res.* 2012; 22(5): 668–678. doi:10.1177/1049732311431944.
79. Ramanaik S, McClarty LM, Khan S, et al. Frontline Health Service Providers' Perspectives on HIV Vaccine Trials among Female Sex Workers and Men Who Have Sex with Men in Karnataka, South India. *PLoS ONE.* 2015;10(10): e0141822. doi:10.1371/journal.pone.0141822.
80. Tarimo EA, Thorson A, Kohi TW, et al. Balancing collective responsibility, individual opportunities and risks: a qualitative study on how police officers' reason around volunteering in an HIV vaccine trial in Dar es Salaam, Tanzania. *BMC Public Health.* 2010; 10: 292. doi: 10.1186/1471-2458-10-292.
81. Omosa-Manyonyi GS, Jaoko W, Anzala O, et al. Reasons for Ineligibility in Phase 1 and 2A HIV Vaccine Clinical Trials at Kenya Aids Vaccine Initiative (KAVI), Kenya. *PLoS ONE.* 2011;6(1): e14580. doi:10.1371/journal.pone.0014580.
82. McClarty LM, Lorway R, Ramanaik S, Wylie J, Bekker M. Factors influencing frontline health service providers' likelihood to recommend future preventive HIV vaccine to key populations in Karnataka, South India. *Vaccine.* 2015 Jan 29;33(5):656-63. doi: 10.1016/j.vaccine.2014.12.009.
83. Tarimo EA, Thorson A, Kohi TW, Sandstrom E, Mhalu F, Kulane A. A qualitative evaluation of volunteers' experiences in a phase I/II HIV vaccine trial in Tanzania. *BMC Infect Dis.* 2011 Oct 24;11:283. doi: 10.1186/1471-2334-11-283.
84. Tanzania Food And Drugs Authority. Guidelines For Application To Conduct Clinical Trials In Tanzania. 2ed 2009. TFDA/DMC/CT/001.
85. Sheets RL, Zhou T, Knezevic I. Scientific and regulatory challenges in evaluating clinical trial protocols for HIV-1/AIDS vaccines e A review from a regulatory perspective. *Biologicals.* 2016;44(2):90-110. doi: 10.1016/j.biologicals.2015.11.003.
86. Nyblade L, Singh S, Ashburn K, Brady L, Olenja J. "Once I begin to participate, people will run away from me": Understanding stigma as a barrier to HIV vaccine research participation in Kenya. *Vaccine;* 2011: 29; 8924–8928. <https://doi.org/10.1016/j.vaccine.2011.09.067>.
87. CBHSQ. Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality. The CBHSQ Report: A Day in the Life of Young Adults: Substance Use Facts. Rockville, MD 2014.

88. Henkel D, Zemlin U. Social Inequality and Substance Use and Problematic Gambling Among Adolescents and Young Adults: A Review of Epidemiological Surveys in Germany. *Current Drug Abuse Reviews*. 2016;9: 26-48.
89. The HIV Vaccine Trials Network (HVTN). Investigators assess relationship between substance use and retention in 10 phase 1 preventive HIV vaccine clinical trials 24th May 2018. <https://www.hvtn.org/en/media-room/news-releases/investigators-assess-relationship-between-substance-use-and-retention.html>. Accessed 18th September 2018.
90. The World Health Organization and the Joint United Nations Programme on HIV/AIDS. The World Health Organization and the Joint United Nations Programme on HIV/AIDS. Ethical engagement of people who inject drugs in HIV preventive trials 2011. http://www.unaids.org/sites/default/files/media_asset/20110429-Ethical-engagement-people-inject-drugs-HIV-prevention-trials_en_0.pdf. Accessed 04/05/2018.
91. Young AM, DiClemente RJ, Halgin DS, Sterk CE, Havens JR. HIV vaccine acceptability among high-risk drug users in Appalachia: a cross-sectional study. *BMC Public Health*. 2014 May 30;14:537. doi: 10.1186/1471-2458-14-537.
92. Friis RH, Sellers TA. *Epidemiology for Public Health Practice 5th Ed. Burlington, MA: Jones & Bartlett Learning, LLC, an Ascend Learning Company; 2014.*
93. World Health Organization. Introduction to HIV/AIDS and sexually transmitted infection surveillance: Module 4: Introduction to respondent- driven sampling / World Health Organization. Regional Office for the Eastern Mediterranean WHO-EM/STD/134/E.
94. Holloway I. *A-Z of Qualitative Research in Healthcare 2nd Edition. United Kingdom: Blackwell Publishing; 2008.*
95. Dahlgren L, Emmelin M, Winkvist A. *Designing Qualitative Research 2nd Ed. Print Och Media, Umea University: Umea Sweden; 2007.*
96. Denzin NK. *The Research Act: A Theoretical Introduction to Sociological Methods. 3d Ed. Englewood Cliffs, NJ: Prentice Hall; 2001.*
97. Patton MQ. *Qualitative Research and Evaluation Methods. 3rd Ed. Thousand Oaks, California: Sage Publication, Inc; 2002.*
98. Palaganas EC, Sanchez MC, Molintas MVP, Caricativo RD. Reflexivity in Qualitative Research: A Journey of Learning. *The Qualitative Report*. 2017; 22(2), 426-438. <https://nsuworks.nova.edu/tqr/vol22/iss2/5>. Accessed 03/06/2018.
99. Attia M, Edge J. Be(com)ing a reflexive researcher: a developmental approach to research methodology. *Open Review of Educational Research*. 2017; 4:1, 33-45, DOI: 10.1080/23265507.2017.1300068.
100. Shenton A. Strategies for ensuring trustworthiness in qualitative research projects. *Educ for Inform* 22 (2004) 63–75. IOS Press.