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Socio-Behavioral aspects regarding participation to HIV Vaccine Clinical Trials among young people in Maputo, Mozambique

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ABSTRACT

Background: Research to discover an effective and safe vaccine is crucial to decrease HIV burden. However, it is paramount to understand social-behavioral aspects, such as underlying perceptions about HIV, misconceptions about HIV vaccine research and its volunteers, and the effects of experimental vaccines on trial participants, that can impede trial conduct and eventual vaccine uptake.

Methods:This research project is divided into 2 studies conducted in Maputo, Mozambique, using both quantitative and qualitative methods and the health belief model. As part of a 2-year follow-up incidence study, a willingness to participate questionnaire was administered to a cohort of 577 HIV-negative young adult participants, at screening and at the exit visit (***study I***). Research subjects who participated in a phase II HIV vaccine preventative clinical trial, answered to the same semi-structured questionnaire (31 participants) before and after unblinding (1-year interval) and participated in 12 in-depth interviews and 3 focus group discussion (***study II***).

Results: A total of 577 participants were screened, including 275 (48%) women. At screening 529 (92%) expressed willingness to participate and the proportion remained stable at 378 (88%) of the 430 participants retained through the exit visit (p=0.209). Helping the country (n=556) and fear of needles (n=26) were the top motive and barrier for willingness to participate, respectively. The health belief model was used to explain the decision-making progress to participate in a HIV vaccine study. HIV susceptibility, infection severity and benefits of participating in a HIV vaccine trial must outweigh barriers for trial participation in order to promote the switch from intention to action (actual participation in HIV vaccine trials). Participants also suffered negative social harm driven mainly by HIV stigma from family and peers regarding their participation in HIV vaccine trials.

Conclusion*:* The present research reports a continuous high intention to participate in HIV vaccine trial among young adults in Maputo city and identified the factors associated with it. It also describes how actual participants of a phase II HIV clinical trial reason their participation and the factors associated with their retention participation in the HIV vaccine trial.

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ABBREVIATIONS

AIDS	Acquired Immunodeficiency Syndrome
ART	Antiretroviral treatment
CISPOC	Polana Caniço Health Research and Training Center
FGD	Focus Group Discussion
GEE	Generalized Estimating Equation
HIV	Human Immunodeficiency Virus
HVTN	HIV Vaccine Trials Network
ID	Intradermal
IDI	In-depth Interviews (IDI)
IMASIDA	Inquérito de Indicadores de Imunização, Malária e HIV/SIDA
MUHAS	The Muhimbili University of Health and Allied Sciences in Dar es Salaam, Tanzania
NIMR-MMRC	The National Institute for Medical Research-Mbeya Medical Research Center in Mbeya, Tanzania,
PrEP	Pre-exposure prophylaxis
STAR Initiative	Unitaid Self-Testing Africa Initiative
STI	Sexual Transmitted Infections
U=U	Undetectable = Untransmittable movement
UNAIDS	Joint United Nations Programme on HIV/AIDS
VIR	Vaccine-Induced Reactogenicity
VISP	Vaccine-Induced Seropositivity
WHO	World Health Organization

1 Introduction

Human Immunodeficiency Virus (HIV) is one of the serious global health public problems, with a global prevalence of 0.7% (0.6%-0.9%) among adult people [1]. Notwithstanding worldwide attempts to eradicate the HIV pandemic, it still remains as one of the main causes of mortality in the world [2]. Since the beginning of the global epidemic in 1981, around 34 million people have died of Acquired Immunodeficiency Syndrome (AIDS)-related causes, with the peak being 1.7 million [1.2 million–2.4 million] in 2004 [1].

Antiretrovirals improve the survival, health, and virulence of HIV-positive individuals, and people with suppressed or undetectable HIV viral loads, are less likely to transmit HIV than untreated persons [3]. In the current context where there is no cure for HIV/AIDS, much of the attention has been focused on ensuring that people who are infected can have a long and healthy life, decreasing the number of AIDS-related deaths and preventing new HIV infections. These 3 objectives can be achieved by increasing the coverage of HIV infected people taking antiretroviral treatment [4].

Efforts, as part of an unprecedented worldwide commitments and collaborations, have led to significant progress in the fight against HIV [5], resulting in an increase in the number of people living with HIV who are receiving antiretroviral treatment . As of the end of 2019, 25.4 million [24.4 million-25.6 million] people were accessing antiretroviral therapy, up from 1.5 million [1.5 million-1.5 million] in 2004, and the number of AIDS-related deaths decreased 60%, from 1.7 million [1.2 million-2.4 million] in 2004 to 690.000 [500.000-970.000] in 2019. Unfortunately, this progress has not been the same in regard to the reduction of new HIV infections, were from 2004 to 2019, we only observed a 29% reduction of HIV new infections [1, 6].

Low and middle income countries are the most affected by the burden of HIV [2], and their governments have been leading the implementation of national HIV control programs, by providing health care facility-based HIV prevention strategies. However, these countries have fragile health systems that make it impossible for them to provide all the necessary HIV prevention services to the populations in need [7]. In order to overcome this obstacle, there is a general consensus that it is necessary to conduct research in order to optimize the implementation of current HIV prevention strategies and to develop new contextualized strategies [8, 9].

Different strategies that promote active involvement of communities and enable communities to take the lead in HIV prevention have been implemented, and proved to be a great success,

evidenced by the increase in the number of HIV-infected people who are diagnosed and are on antiretroviral treatment [10, 11]. Community-based test and treat strategies, emphasise communication to address persuasive stigma and discriminatory attitudes towards the most-at risk for HIV infection, in order to attract different hard to reach populations [12, 13], especially young people and men [14]. It also includes interventions that move from the traditional health care facility-based approaches to more convenient, private and flexibly approaches, such as mobile, home and self-testing conducted by trusted community members [15] and the use of antiretroviral treatment for prevention [16].

HIV diagnosis is the first step in ensuring that people living with HIV have access to HIV treatment [17]. The first HIV test was available in 1985, and since then, simpler and more accurate tests have become available. That prompted the adoption of various testing strategies that resulted in an increase in the number of people who knew their HIV status [18]. HIV self-testing[1] which is strongly endorsed by WHO, has been offered as a discrete option for HIV testing services. From 2015 to 2018, as part of the Unitaid Self-Testing Africa (STAR) Initiative initial implemented in Malawi, Zambia and Zimbabwe, and then Eswatini (Swaziland), Lesotho, South Africa, more than 2.3 million kits of HIV self-tests were distributed. Preliminary results in the first 3 countries where the initiative started, showed that HIV self-tests reached a high proportion of men, young people and first-time testers [18].

Proven to be effective in reducing the risk of HIV infection by 60% [19], male circumcision is recognized as a powerful and important HIV prevention method, especially in low and middle income countries [20, 21]. Targeting particularly young men living in countries with high HIV prevalence, voluntary male medical circumcision was introduced in 14 priority countries in Eastern and Southern Africa, (Botswana, Ethiopia, Kenya, Lesotho, Malawi, Mozambique, Namibia, Rwanda, South Africa, Eswatini, Tanzania, Uganda, Zambia and Zimbabwe) in 2007. The goal was to reach 20.8 million (80% coverage) of circumcised men by 2016, which would prevent about 3.4 million new HIV infections in the same period [22].

Pre-exposure prophylaxis (PrEP) can be an outstanding prevention method in reducing HIV infection [23, 24]. In 2015, the World Health Organization (WHO) recommended the use of oral

[1]HIV self-testing is a process in which a person collects their own specimen (oral fluid or blood) using a simple rapid HIV test and then performs the test and interprets their result, when and where they want.

antiretroviral drugs to all people at substantial risk of HIV[2], as part of an HIV prevention combination package [17]. A recent projected analysis using a combination of three modelling tools: 1) the AIDS Impact Model and; 2) the Goals model; and 3) the Incidence Patterns Model, applied to 13 countries (Eswatini, Ethiopia, Haiti, Kenya, Lesotho, Mozambique, Namibia, Nigeria, Tanzania, Uganda, Zambia and Zimbabwe), which included three priority populations, female sex workers, serodiscordant couples and adolescent girls and young women estimated that 3% to 8% of new HIV infections could be prevented by PrEP [25]. This provides evidence to convince policy makers at national and international levels to scale-up pre-exposure prophylaxis use associated with other prevention approaches.

Human immunodeficiency virus can be transmitted from an HIV-positive mother to her child during pregnancy, childbirth or breastfeeding, with transmission rates ranging from 15% to 45% in the absence of other HIV prevention measures [26]. Providing lifelong antiretroviral treatment for HIV positive mothers, and short-term treatment for their child can reduce the transmission rate to less than 5% [17, 26]. Globally progress as a result of implementation and scale-up of large mother-to-child transmission prevention of HIV[3] programs, resulted in the prevention of about 1.4 million HIV infections among children between 2010 to 2018 [7].

Despite all the efforts to develop and implement preventive approaches, especially behavioral and biomedical strategies, still 7.1 million of all people living with HIV, about 19%, did not know that they were living with HIV, only 67% of all people living with HIV were accessing HIV treatment, 150.000 children became infected, and of the 3 million people at substantial risk of HIV infection, only 350.000 people have ever taken PrEP in 2019 [7, 27]. Social, behavioural and biomedical prevention interventions have shown to have limited effects across the various socio, cultural, and environmental context. There is a need to better integrate existing interventions, if the goals are to be met [28, 29]. We are still behind the desired goals concerning the reduction of new HIV infections and research is needed to discovery new interventions that would close the gap in our current context.

[2] People at substantial risk refers to people belonging to populations with HIV incidence greater than or equal to 3%.

[3] Prevention of mother-to-child transmission of HIV, also known as prevention of vertical transmission, refers to interventions to prevent transmission of HIV from a mother living with HIV to her infant during pregnancy, labor and delivery or during breastfeeding.

The development and discovery of an HIV preventive vaccine, which is effective and accepted across different genetic, physiological, behavioural, and environmental settings could provide the most effective preventive method to final uplift the elimination of HIV. Recognized as one of the greatest contemporary challenges of science, a safe, effective, accessible HIV vaccine is one of the major global health priorities in the fight against HIV [30, 31]. Albeit, the modest efficacy has been insufficient to warrant licensure, results of a phase III Thai HIV vaccine trial, the RV 144, suggest that a vaccine to prevent acquisition of HIV infection is possible [32]. A long-term strategy to ultimately end the AIDS pandemic, must include, scale-up of existing HIV combination prevention and treatment strategies, and, research and development of a preventive HIV vaccine.

Research to discover an effective and safe vaccine is crucial, however, it is paramount to analyze socio, behavioral and cultural factors, such as: knowledge and perceptions about HIV and HIV vaccine clinical trials; stigma and discrimination due to misrepresented concepts associated with research related to HIV vaccines, and their volunteers; the expectations and potential participation of the community, associated with the support or not of the communities in which the potential participants are inserted; and the experiences lived during participation in HIV vaccine trials and the effects resulting from participating in an experimental HIV vaccine studies among clinical trials participants; in order to identify facilitating factors and barriers that may prevent clinical trials and subsequent acceptability of a possible vaccine [33].

In recent years there has been an increase in the number of studies that aim to contextualize, adapt and improve the implementation of HIV preventive vaccine clinical trials in the sub-Saharan region. Studies carried out in the same and/or different places, with the same and/or different populations, have reported different results [34, 35]. This emphasizes the need to implement socio-behavioural studies in countries who intend to conduct or are implementing HIV preventive vaccine trials, including Mozambique.

Mozambique has been implementing HIV vaccine trials since 2011, however there is little information on the willingness of volunteers to participate in HIV vaccine trials in Mozambique, and the associated factors, which could improve current recruitment strategies. Understanding the experiences, either positive or negative, participants had during their participation in the HIV clinical trials conducted in Mozambique can inform retention strategies for future studies. This is of upmost importance, if we consider clinical trials in Mozambique would like to recruit and retain large sample sizes of research participants.

The objective of this research project is to identify which factors may influence the participation of potential volunteers in HIV vaccine trials and the effects on their sexual behaviour and social life, as a result of having participated in an experimental HIV preventive vaccine clinical trial in Maputo, Mozambique. This research project includes a group of socio-behavioural studies that aim to strengthen the implementation of HIV vaccine clinical trials and reinforce the development of research for the discovery of an HIV vaccine in Mozambique. Understanding what the perceptions regarding the HIV vaccine and the effects are of conducting clinical trials of HIV vaccines, could help to decrease the limitations associated with conducting them, and eliminate the potential negative results of future clinical trials of a vaccine against HIV in Mozambique.

2 Literature Review

2.1 HIV Epidemic

Human immunodeficiency virus remains has one of the most serious global health issues, with 75.7 million people infected since the start of the epidemic, of whom 32.7 million people have died from Acquired Immunodeficiency Syndrome-related illnesses. In 2019, there were 38.0 million people living with HIV, with 95% (36.2 million) being adults, of whom half were women (Figure 2.1) [6, 27].

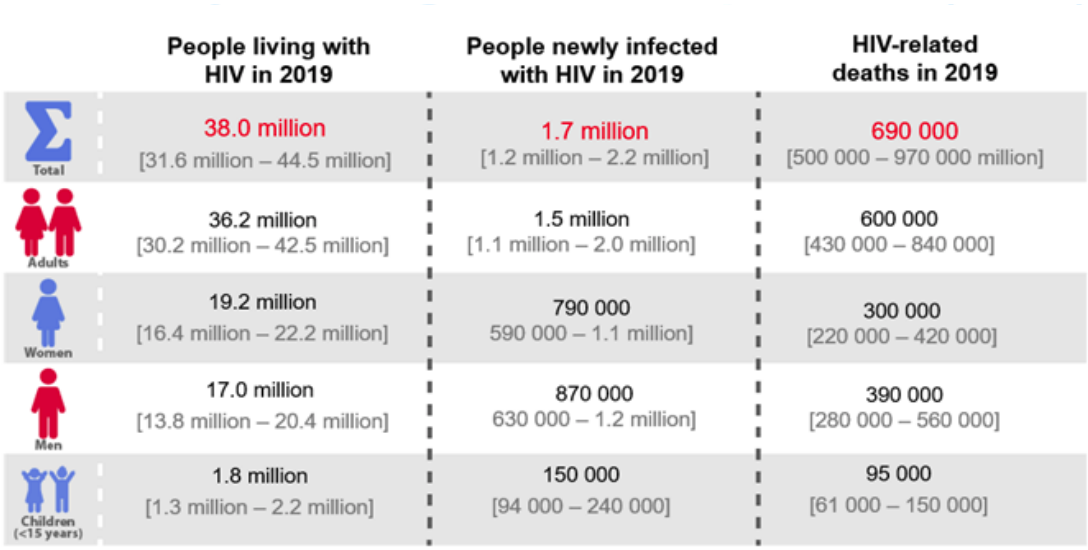


Figure 2.1 - **HIV globally summary**

Source: UNAIDS/WHO estimates [36]

Although we have witnessed a decrease in the number of new HIV infections[4], especially in Eastern and Southern Africa, they remain high. The World Health Organization estimates that in 2019, 1.7 million people acquired HIV, corresponding to a 23% decline in new HIV infections since 2010 [6, 29]. This reduction was less pronounced in the group of boys and men, which were responsible for 52% of the new infections (Figure 2.1). Worldwide, key populations[5] are responsible for the majority of new HIV infections (62%), ranging from 99% of new HIV infections in eastern Europe and Central Asia, to a low 28% in Eastern and Southern Africa. In

[4] New HIV infections, or "HIV incidence," refers to the estimated number of people who newly acquired HIV in a given period such as a year, in a specified population.

[5] Key populations are defined groups who, due to specific higher-risk behaviors, are at increased risk of HIV *irrespective of the epidemic type or local context.*

Eastern and Southern Africa of the total new infectious, 72% of the infections were among the non-key population, 15% among clients of sex workers and sex partners of all key populations, 6% among gay men and other men who have sex with men, 5% among sex workers and 2% among people who inject drugs [6].

Historically sub-Saharan Africa has been one the most affect region and continues to be [37]. Alone, it was responsible for 59% of all globally new HIV infections in 2019, were 59% of those infections occurred among girls and women (15-49 years old). Sub-Saharan young women aged 15-24 years are twice more likely to be living with HIV when compared to man of the same age (Figure 2.2) [6]. This reinforces the need to improve HIV control strategies in this particular vulnerable group[6]. Nearly 70% of all people living with HIV were in sub-Sahara Africa, and 40% of deaths occurred in the region.

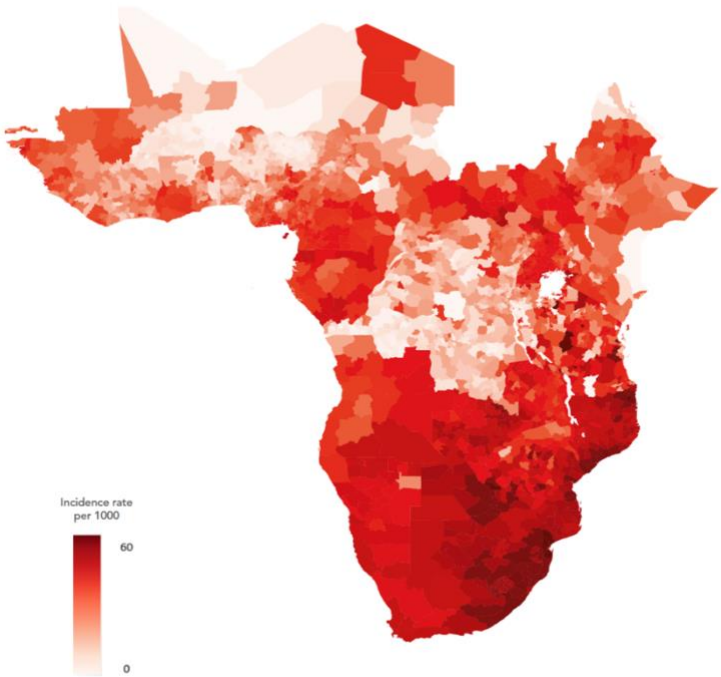


Figure 2.2 HIV incidence among adolescents and young girls age 15-24 years, Sub-Sahara Africa, 2019

Source: UNAIDS/WHO estimates [6]

[6] Vulnerable populations are groups of people who are particularly vulnerable to HIV infection in certain situations or contexts, such as adolescents (particularly adolescent girls in sub-Saharan Africa), orphans, street children, people with disabilities and migrant and mobile workers. These populations are not affected by HIV uniformly across all countries and epidemics.

Studies have shown that early and correct use of antiretroviral treatment (ART) is effective in guaranteeing and maintaining HIV viral suppression, which consequently improves the morbidity and mortality of HIV-infected people [3, 38]. This led countries to increase access to ART, which in turn, has prevented an estimated 12.1 million AIDS-related deaths between 2010 and 2019, corresponding to a 39% reduction of AIDS-related deaths. Reducing HIV viral load to undetectable levels, means that it is virtually impossible to transmit HIV from an infected person to an uninfected one [16]. Recognizing the important role of the antiretroviral treatment to control the HIV pandemic, the Joint United Nations Programme on HIV/AIDS (UNAIDS) launched the 90-90-90 ambitious treatment target to help end the AIDS epidemic, that aimed to achieve by 2020:

- 90% of all people living with HIV will know their HIV status;
- 90% of all people with diagnosed HIV infection will receive sustained antiretroviral therapy;
- 90% of all people receiving antiretroviral therapy will have viral suppression [4].

According to UNAIDS estimates for 2019, around 81% (30.8 million) of all people living with HIV knew their HIV status, of whom 82% (25.3 million) were on antiretroviral treatment, and 88% (22.3 million) of those who were receiving ART were viral suppressed. This means that, only 67% of the all people living with HIV were accessing ART, yet still 690.000 deaths occurred versus the target of less than 500.000 deaths, and more than 500.000 people became newly infected with HIV in 2019. Overall, we are still far from the (UNAIDS) 95-95-95 ambitions treatment target, that would enable the world to end the HIV epidemic by 2030 [9], which means that, it is necessary to accelerate and increase the implementation of existing efforts, and at the same time, develop new strategies to combat this pandemic.

Stigma and discrimination[7] towards people living with HIV and the most at-risk for HIV infection, are known stonewalls for obtaining and using the current HIV prevention and treatment programs [13, 39-42]. Surveys conducted in past years, report a variation in the trends of discriminatory attitudes associated with HIV infection, in which proportions that were decreasing (Figure 2.3) or were stable (Figure 2.4), recently showed a tendency to increase [6].

[7] HIV-related stigma and discrimination refers to prejudice, negative attitudes and abuse directed at people living with HIV and AIDS.

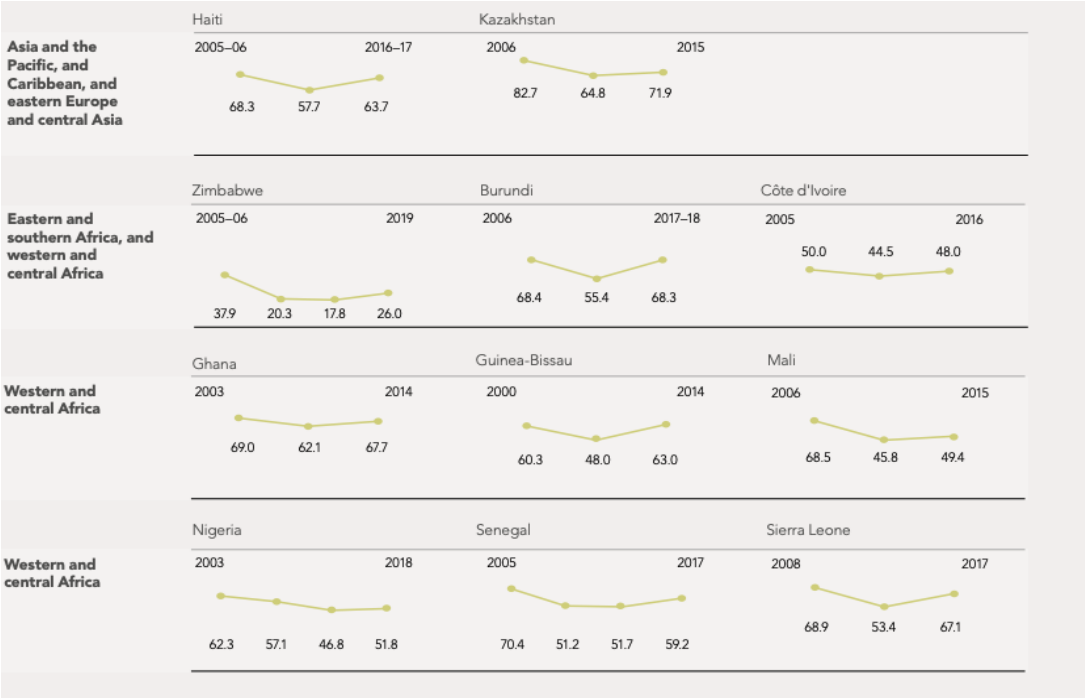


Figure 2.3 - Trends in HIV discriminatory attitudes (increase after declining)

Source: UNAIDS/WHO estimates [6]

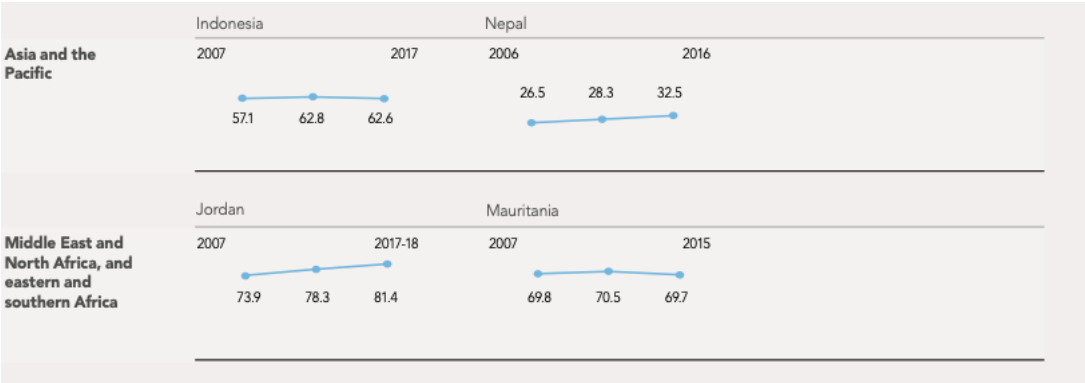


Figure 2.4 - Trends in HIV discriminatory attitudes (stable or increasing)

Source: UNAIDS/WHO estimates [6]

Disturbing, are the recent reports that stigma and discrimination at the health-care facilities, in the form of denial of service, contemptuous attitudes, coerced procedures or violation of confidentiality (Figure 2.5), are frequent [6]. As the entry door for HIV care continuum[8], health-

[8] HIV care continuum refers to the sequence (and assessment of the number of people who have reached that stage) of stages a person with HIV takes from diagnosis through receiving treatment until his or her viral load is suppressed to undetectable levels. The stages are: being diagnosed with HIV; being linked to medical care; starting ART; adhering to the treatment regimen; and, finally, having HIV suppressed to undetectable levels in the blood.

care facilities must be an attractive and pleasant place for people at risk of becoming infected and for people living with HIV, and the opposite scenario is a worrisome barrier.

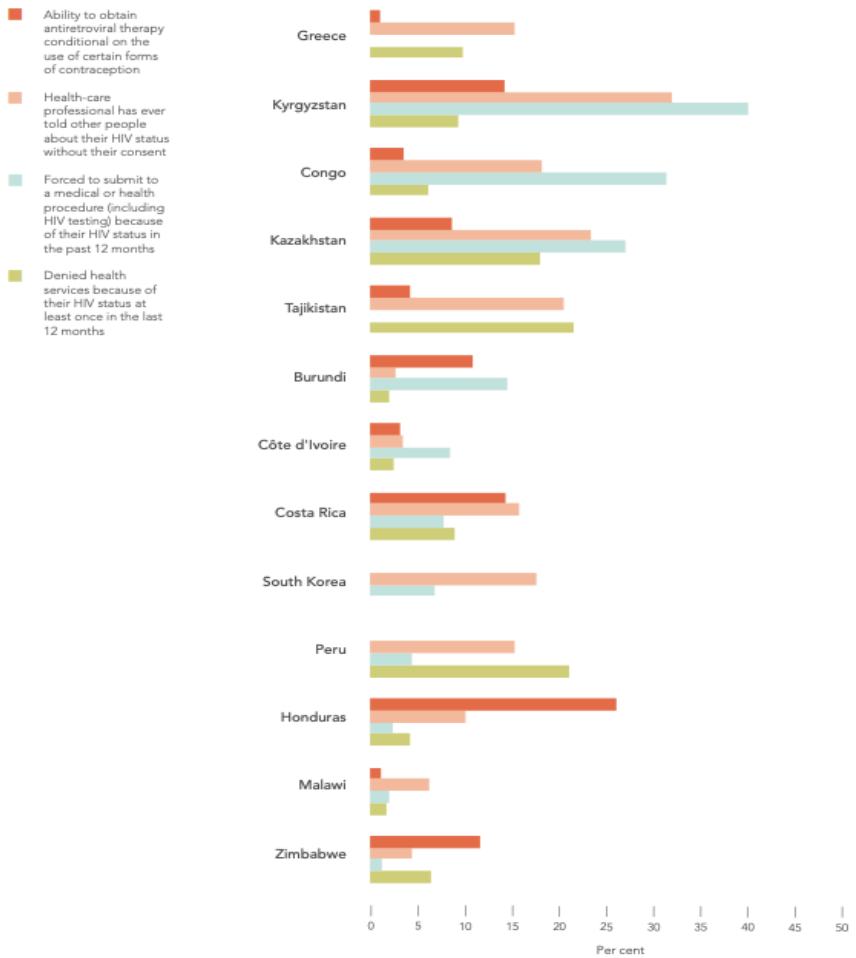


Figure 2.5 - Percentage of different forms of discrimination at health-care settings: Data from 2013–2018
Source: UNAIDS/WHO estimates [6]

Tackling stigma and discrimination, both at the individual and social levels, considering the cultural and legal context of different countries, must be a priority if we want to eliminate the HIV pandemic.

2.2 HIV Scenario in Mozambique

Located in the Southern region of the African continent, and with an estimated population of more than 28 million people in 2018 , of whom almost half is under 15 years old [43], Mozambique is one of the less-developed countries in the world and one of the most severe affected countries by HIV in the whole world (Figure 2.6) [6, 44]. Almost two thirds of the population leaves in the rural area, 48.4% of the total population lives under the poverty line with income less than US $ 1.90

per day, with 8 out 10 poor people living in rural areas [43, 44]. Life expectancy at birth is 58 years for males and 62 years for females [45] and 8.9 % of the country's gross domestic product[9] is invested in health, with much of the investment coming from international donors [46]. In 2016, only 0.8 healthcare professionals (doctors, nursing, maternal and child health) were available per 1,000 inhabitants, and only 1 health unit per 16,855 inhabitants in 2018 [47].

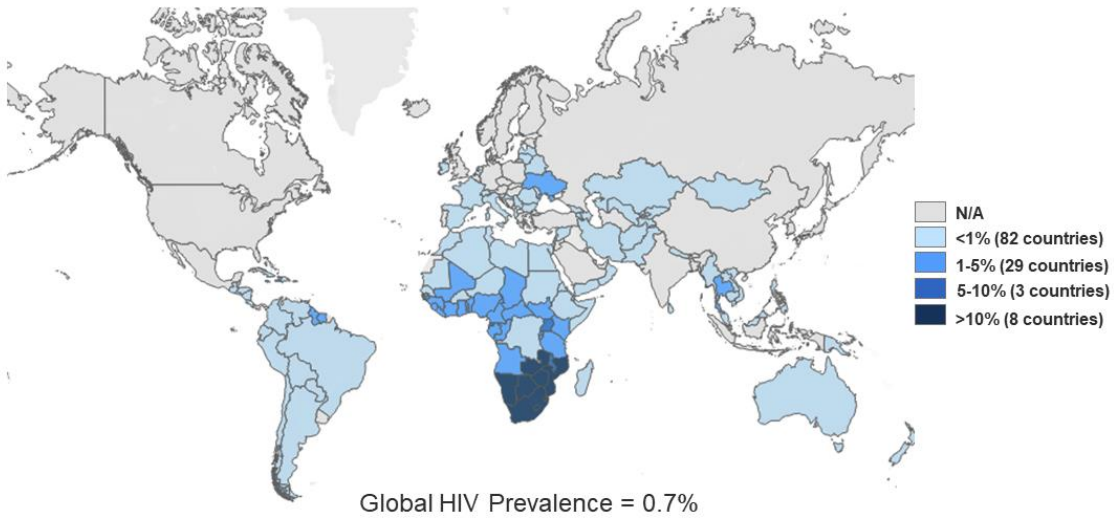


Figure 2.6 – Global estimates of HIV Prevalence in people aged 15-49 years, 2019
Source: KFF, based on 2020 UNAIDS data[48]

Globally, in 2018, Mozambique had the second highest number of people living with HIV (2.2 million) and was the third country in which the most deaths related to HIV/AIDS (54.000 deaths) occurred. Also, approximately 144.000 new HIV infections were reported in the country corresponding to both 8% and 14 % of HIV new infections in the world and in the African continent, respectively [1, 6, 49].

A national population-based survey - *Inquérito de Indicadores de Imunização, Malária e HIV/SIDA* (IMASIDA) - conducted in 2015, reported an HIV prevalence of 13.2 % (CI: 11,9 – 14,4) from people aged 15-49 years old, with the highest prevalence (21.2%) registered among the 35-39 age group. HIV prevalence varies significant depending on the area of residence (urban vs rural) and province. HIV prevalence in urban area was 16.8% vs 11% in the rural area, with 24.4% in Gaza province (southern part of the country) the highest and 5.2% in Tete province the lowest (central part of the country) (Figure 2.7). This prompts to classify the HIV epidemic in

[9] Gross domestic product (GDP) is the total monetary or market value of all the finished goods and services produced within a country's borders in a specific time period.

Mozambique has generalized[10]. Women are more affected then men (15.4 % versus 10.1%), in all age groups. HIV prevalence among people aged 15-24 years is 6.9%, with women (9.8%) roughly three time more vulnerable than men of the same age (3.2%) [50].

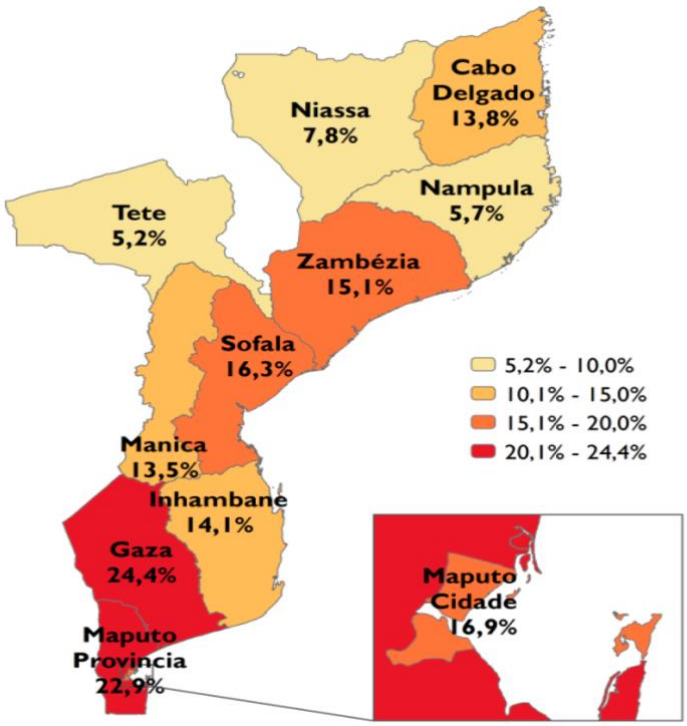


Figure 2.7 - HIV prevalence of women and man aged 15-49 years by Province, 2015
Source: IMASIDA [50]

The main form of HIV transmission is heterosexual [51]. Data from IMASIDA 2015, estimates that 9.6% of all cohabiting couples were serodiscordant and 7.1% of all couples were both HIV positive. HIV prevalence in the most-at risk people for acquiring the HIV infection is also high. Among female sex workers the highest prevalence observed was 31.2% in Maputo City [52], and for men who have sex with men, the highest prevalence was 9.1% in Beira City (Sofala Province) [53].

In order to address the HIV epidemic, the Mozambican Ministry of Health adopted and implemented different prevention strategies, including the scale-up of male circumcision and condom use [54, 55], and the introduction of the prevention of mother-to-child transmission

[10] Generalized HIV epidemic: HIV is firmly established in the general population, with national HIV prevalence consistently exceeding 1%.

programme in 2002, with the adoption of the B+ option in 2013 [54, 56]. As a result, from 2009 to 2015, there was an increase in male circumcision coverage from 47% to 63% [50], and the number of HIV positive pregnant women receiving antiretroviral treatment increased from 83% in 2013 to 101% in 2018 [47, 49]. Free antiretroviral treatment become publicly available for HIV infected individuals with CD4<200 cells/μL [57-59] in 2004, and in 2016 phased implementation of the test and treat strategy initiated [60]. This resulted in an increased number of people on ART, and a decrease of both numbers of deaths related to HIV/AIDS (Figure 2.8) and new infections (Figure 2.9).

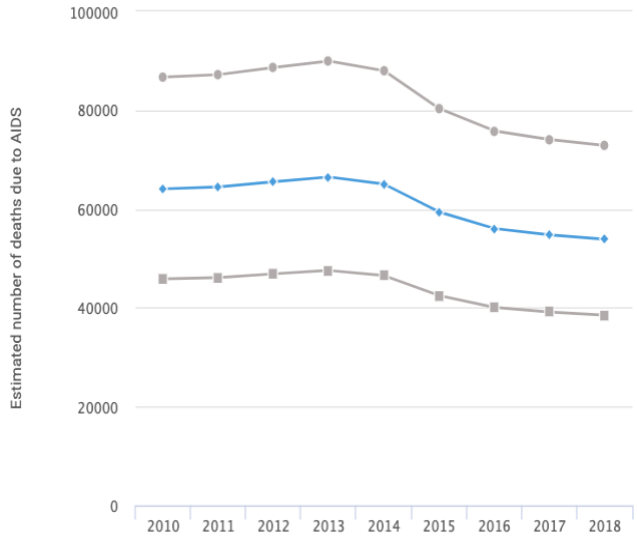


Figure 2.8 Number of HIV/AIDS deaths in Mozambique 2010-2018

Source: UNAIDS/WHO estimates [1]

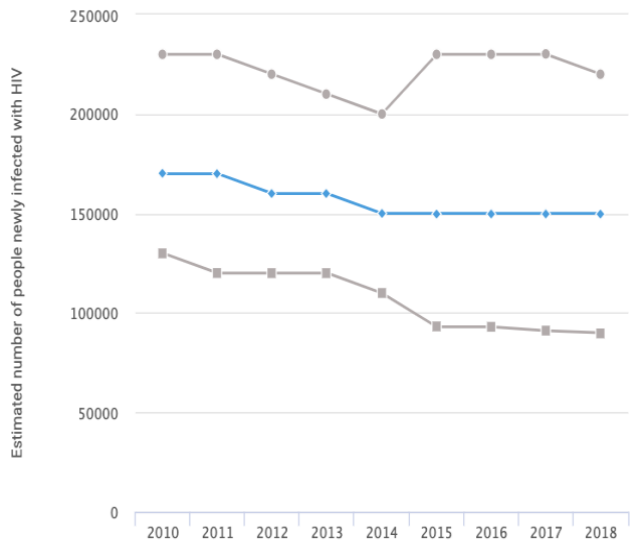


Figure 2.9 Figure 2.8 Number of HIV/AIDS new infections in Mozambique 2010-2018

Source: UNAIDS/WHO estimates [1]

2.3 HIV Prevention

Since the beginning of the HIV pandemic, considerable endeavors and progress towards the end of HIV were made in the sub-Saharan Africa region, in response to the fact that this region remains has one of the most heavily affected [61]. The Joint United Nations Programme on HIV/AIDS has led the universal fight against HIV, by establishing ambitious, but achievable goals, guiding the use of HIV control strategies informed by evidence, monitoring and reporting in real time their progress, and identifying areas that need more attention, at both national and international level [5, 7]. In 2017, it launched the HIV Prevention 2020 Road Map guideline, which served as a wake-up call to step-up current efforts for HIV prevention. The guideline considered 10 action points, to help frame, implement and evaluate HIV national prevention responses (Figure 2.10) to achieve zero new HIV infections, zero AIDS related deaths and zero discrimination towards HIV infection.

These led to unprecedent and encouraging achievements in countries with different geographically, economical, legal and socio-cultural contexts, including some of the most affected countries in sub-Sahara Africa. Twelve countries have achieved the first 90 and second 90, and 14 countries achieved the third 90. Eswatini it's an example to follow, since it has even passed the 2020 90-90-90 goal, and reached the 2030 95-95-95 goal:

- 95% of people living with HIV who know their status;
- 95% of people living with HIV who know about their status on antiretroviral treatment;
- and 95% of people on antiretroviral treatment being viral suppressed [28].

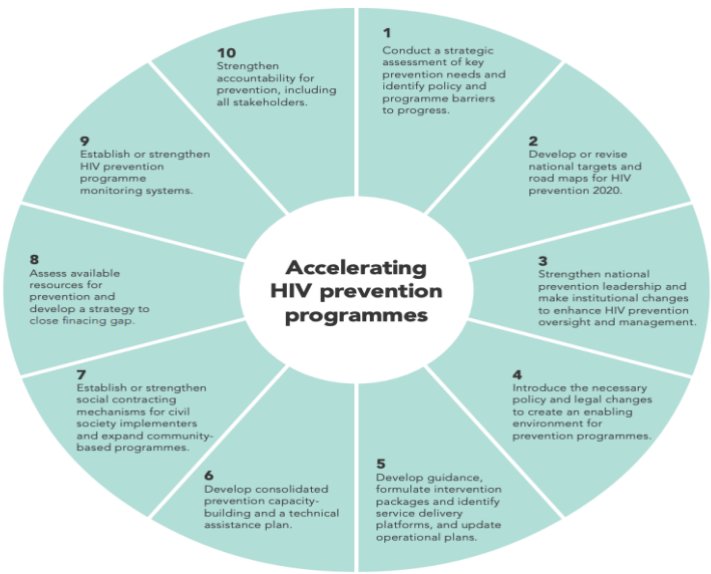


Figure 2.10 UNAIDS, Ten-point plan for accelerating HIV prevention at the country leveL, 2017

Source: UNAIDS, HIV Prevention 2020 Road Map guideline, 2017 [62]

Countries that have not yet achieved all 2020 90-90-90 goals, are committed to ending the HIV pandemic. Vietnam, a country in the Southeast Asia region, where HIV-related stigma and discrimination in healthcare settings presents itself as a strong barrier to its HIV prevention programs [12], has adopted a community-led communication strategy, that promotes the use of antiretroviral treatment as a proven strategy for protection against HIV - Undetectable = Untransmittable (U=U) movement - and incorporated it into its national HIV control program [63]. Vietnam become one of the 14 countries that already achieved the third 90 [28].

Targeting the most-at risk and vulnerable population for HIV acquisition is primordial to curb HIV infections rates. [17]. Results of a study conducted with women aged 16 to 35 years in 4 African countries (Eswatini, Kenya, South Africa and Zambia), showed a reduction of 50% in HIV infection rates, even with a 25% uptake rate [64]. A community-based study with man and women at risk for HIV infection conducted in Kenya and Uganda, showed a 74% reduction of HIV infection rates among people at high risk of HIV infection who had pre-exposure prophylaxis. It is important to highlight that, when compared to men, women were the ones who most adhered to the use of PrEP, although they did not use it on a regular basis. On the contrary, they used PrEP when they thought they were at risk, and even then, a significant reduction in the number of new infections was observed [65]. This demonstrates that pre-exposure prophylaxis must be considered as an important strategy for reducing infection transmission.

An important milestone in the fight against HIV was achieved by Malaysia. In 2018, the World Health Organization, certified that this country in the Western Pacific region eliminated the vertical transmission of HIV and syphilis. This is a result of two decades of work which resulted in this country attaining:

Impact Indicators that must be met for at least 1 year:

- Fewer than 50 new paediatric HIV infections due mother-to-child transmission of HIV per 100 000 live births;
- HIV mother-to-child transmission rate of less than 5% in breastfeeding populations, less than 2% in non-breastfeeding populations; and
- Fewer than 50 new cases of mother-to-child transmission syphilis per 100 000 live births, and:

Process Indicators that must be met for at least 2 years:

- ≥95% of pregnant women receive at least one antenatal visit;
- ≥95% of pregnant women are tested for HIV and syphilis; and
- ≥95% of infected pregnant women receive adequate treatment [66].

Once again, it demonstrates that a strong commitment to the implementation of integrated strategies can lead to the achievement of the agreed results.

In the past decades, we have observed an increase in the innovation and application of new and different behavioral and biomedical preventive approaches. Strategies that addressed HIV testing approaches and HIV preventing methods demonstrated to be functional and effective, when the topic is the reduction in the number of new HIV infections [7]. Despite this success, only one country has managed to achieve all the desired goals so far, with most of the affected countries needing to step up their efforts [6, 28, 29]. The lack of integration between existing interventions is one of the factors to be taken into account [8]. Factors associated with different social dynamics, cultural challenges and aspects related to environmental contexts can also hinder the adoption of biomedical strategies, including antiretroviral treatment as prevention, the use of condoms, and if discovered, a potential preventive vaccine [6, 29, 33, 48, 67].

The not-so-well-known complex interaction between the virus and the human body, makes it difficult to find a cure [31, 68, 69]. To achieve the goal of zero infections, there is a consensus on the need to optimize and combine different prevention strategies, while at the same time, research and development of new approaches must continue. Although, and yet to be discovered, a preventive vaccine against HIV would have an enormous impact, if combined with existing prevention instruments, in the control of HIV transmission, thus becoming one of the main research priorities in the fight against HIV [31, 68, 70-73].

2.3.1 HIV Prevention in Mozambique

The government of Mozambique has implemented the 2013-2017 National Strategic Plan for Response to HIV/AIDS, implemented and monitored by the National Control Program of sexual transmitted Iinfections-HIV/AIDS (NCP STI-HIV/AIDS) in an effort to control the HIV epidemic in the country. This plan describes the policies and national strategies to control the epidemic, and has two main goals.

1. Promote the improvement of the quality of life of people living with HIV/AIDS and reduce the impact of AIDS on national development efforts;
2. Prioritize the strengthening of prevention in all areas of activity, with the aim of reducing the number of new HIV infections in Mozambique. This includes conducting research to find a preventive vaccine against HIV [74].

The adoption of any preventive measure depends on people at risk knowing how HIV can be transmitted and being aware of existing HIV prevention strategies and how to access them. Regarding HIV prevention knowledge, only 47% of women and 56% of men aged 15-49 years old, knew that the HIV transmission can be reduced through the use of correct and consistent use of condoms and limiting sexual intercourse to an uninfected single partner. IMASIDA 2015 reported that merely 30% of adolescents and young people aged 15-24 years old had comprehensive knowledge about HIV prevention[11]. These are worrying figures, considering that in the group of women these knowledge have remained stable since 2011, and that in the group of men we observed a reduction of 22% since 2011 (52%), associated to the fact that 77 % of women and 72 % of man in these same age group, had their first sexual intercourse before the age of 18 years old [50].

Although we observed an increase between 2009 and 2015, in the proportion of circumcised men, it is important to highlight the 10-point percentual difference, in which the proportion of circumcised men in rural areas (59%) is lower than the proportion of circumcised men in urban areas (69%). HIV prevalence among all man aged 15-49 years old tested during the IMASIDA survey [50], was higher among non-circumcised (13,4%) vs the circumcised man (8.1%). In the 12 months before the survey, the percentage of men who had two or more sexual partners (21%) was 7 times higher than women, with 29% of women with two or more sexual partners using condoms in their last sexual relationship against 26% of men.

Paying for sex is an act of risk for HIV infection acquisition, which most of the time is associated with irregular condom use, and represents an unequal basis for negotiation for sexual relations [75]. When considering the 12 months prior to the survey, 19% of the men reported paying for

[11] Knowing that the correct and consistent use of condoms during sexual intercourse and having only one uninfected sexual partner can reduce the risk of contracting HIV, knowing that a healthy-looking person can have HIV and rejecting two most common misconceptions related to HIV prevention or transmission (contracting HIV through mosquito bites or eating together with an HIV-infected person).

sex, of whom 1 in 3 men reported not using condoms during paid sex. The percentage of men who paid for sex and who did not use a condom in the last 12 months prior to the survey, was higher in the rural area (77%) as oppose to the urban area (57%) [50].

Stigma and discrimination have a negative impact in the access to HIV preventive strategies. Around 90% of both men and women expressed willingness to care for an HIV infected family member, 75% reported both, that they would buy vegetables from a HIV infected vendor and agree that a teacher with HIV should continue to teach at the respective school, respectively. However, only 21% of women and 26% of men said that they would not want to hide that they have a family member with HIV, thus reducing the overall attitudes of acceptance towards HIV infection (11% for women and 14% for man) [50].

A recent evaluation of the 2013-2017 *National Strategic Plan for Response* to HIV/AIDS revealed that the percentage of people diagnosed with HIV who started ART has improved from 46% (2014) to 69% (2018), as a result of a significant increase in the number of HIV tests performed in the country in the same period, with a greater focus on provinces who registered an increase in HIV prevalence between 2009 and 2015. This is important, because it shows that the response to HIV control in the country is contemporary, since it is informed by research. Increasing the number of HIV tests performed does not guarantee an increase in the number of people diagnosed with HIV, which assess the HIV testing programs efficacy. During the evaluation period (2014-2018), the efficacy of HIV testing in Mozambique decreased, and the number of HIV diagnoses done varied between provinces, which means that some work is still needed [47].

The cascade of HIV care continuum implies a link between diagnosis and early treatment initiation - *new starts*, and retention to achieve viral suppression, it´s final and ultimate goal. Although, overall, the number of people who initiated antiretroviral treatment grew, this has not been accompanied by an increase in retention rates at 12 months among different populations (Table 2.1). In fact, these figures have varied slightly between years, however in general it remains stable [47].

Populations	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**
Adults	67%	66%	70%	70%	68%	66%
Pregnant women	48%	-	62%	67%	65%	68%
Children	69%	64%	69%	68%	70%	68%

Table 2.1 Evolution of retention rates of HIV infected people for ART at 12 months, Mozambique 2014-2019

Source: Annual NCP STI-HIV/AIDS Reports, 2014-2019

HIV positive pregnant women contributed significantly to the increase in the number of HIV diagnoses, and in 2017-2018 almost 100% of HIV positive pregnant women knew their HIV status, but only 56% started ART after the first prenatal care visit. HIV positive pregnant women played a great part in the reduction of the general retention rate at 12 months, since it is documented that many abandon ART after the birth of their child [76], associated with the fact that the number of prenatal consultations has reduced, particularly the final antenatal care visit. As a consequence, in 2019, Mozambique has one of the higher rates of vertical transmission in the world (15%) [49, 77], and 10% of the world new HIV infections in children younger than 15 years old, occurred in the country [6]. Of the 95.080 children younger than 15 years living with HIV, only 67% initiated ART in 2019.

Despite government efforts, circumcision rates varies significantly within the country, with the lowest in Tete Province (9%) and the highest in Niassa Province (95%), more than half of the people living with HIV are yet to initiate antiretroviral treatment, condom use amongst people with two or more partners is low and inconsistent (26% for men and 31% for women), and still high rates of HIV infection, mainly due to transgenerational sex, especially among adolescents and young females, it implies that more preventive strategies are needed to control HIV transmission [7, 60, 61, 78-81].

2.4 HIV Vaccine Research

Vaccines are considered one of the primary strategies to prevent infectious diseases [82], and an effective HIV vaccine would prove a turning point on the path to achieving zero new HIV infections [30, 83, 84]. HIV is an envelope RNA virus that primarily targets immune cells (CD4 + T cells, macrophages and dendritic cells), which leads to dysfunctional changes and consequent damage to the immune system. HIV genome consists of two copies of a single-stranded RNA which encodes the structural proteins (Gag, Pol, and Env), the regulatory proteins (Tat and Rev), and accessory proteins (Vpu, Vpr, Vif, and Nef) (Figure 2.11) [85]. HIV preventive vaccines aims

to induce the production of neutralizing antibodies[12] targeting HIV proteins in order to block the attachment of the virus to the cell as well as its entry into the cell [69, 85].

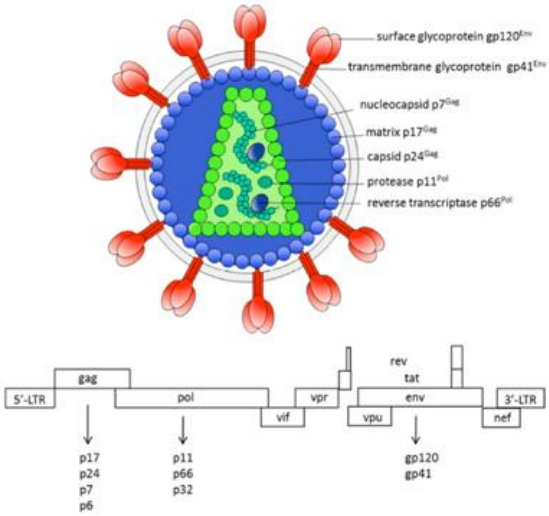


Figure 2.11 HIV type 1 genome and virion

Source: Trovato et al, HIV Vaccination: A roadmap among advancements and concerns [85]

In recent years there has been an increase in the number of HIV vaccine clinical trials conducted, which aim to find an effective preventive vaccine against HIV [32, 85]. The modest effectiveness, 30% over a 3.5-year period, of a Thai phase III clinical trial, RV144, has brought hope that this goal is achievable, especially in a context where other HIV vaccine efficacy trials reported negative results [85, 86]. From September 2003 through December 2005, a total of 16.402 HIV negative Thai man and women, aged 18-30 years with no specific HIV risk criteria (community risk) were enrolled in a randomized, multicenter, double-blind, placebo-controlled trial consisting of four "priming" injections of a recombinant canarypox vector (ALVAC-HIV expressing *gagpro* and *env* genes) followed by two "boosting" injections with vaccine AIDSVAX B/E Env protein given together with the last two injections of ALVAC in ALUM. This was the first time ALVAC and AIDSVAX were combined, although they have shown no efficacy when used individually [87].

Once again, highlighting the need to conduct research to combine different preventive methods, to obtain a comprehensive and effective HIV prevention strategy. Around the world, research has been carried out with the aim of improving the magnitude and durability of the RV144 vaccination scheme, by conducting improved HIV clinical trials [70, 73, 88]. Several African countries, mainly

[12] A neutralizing antibody is a type of antibody that is capable of keeping an infectious agent, from infecting a cell by neutralizing or inhibiting its biological effect.

in the sub-Saharan Africa region, are actively conducting HIV vaccine clinical trials, with Mozambique being one of them [89].

Successful execution of an HIV vaccine efficacy trial requires recruitment and retention of a large number of HIV-uninfected volunteers from a source population with a high incidence of disease [90]. This optimizes the efficiency of the trial by reducing the sample size needed to detect a significant reduction in HIV risk among vaccine recipients as compared to placebo [70]. Young adults tend to have a high incidence of new HIV infections [9, 91], and therefore, are a target group for both recruitment into HIV prevention trials and for a deployment of an efficacious preventive vaccine, once one is available [92-94].

Since the implementation of the first clinical trial of a vaccine against HIV in Uganda, implementation of preventive HIV vaccine clinical trials in Africa have always been surrounded by individual, cultural, social and legal issues that challenged their successfully implementation [95, 96].

It is important to understand potential clinical trial participants willingness to participate in clinical trials, and the factors that could influence willingness to participate in HIV vaccine clinical trials in order to establish strategies for recruiting and retaining participants, which is crucial for the development of future vaccines [97-99]. A considerable number of studies have been conducted with the aim of assessing the willingness to participate, and to understand the factors that influence willingness to participate in HIV vaccine trials in different key populations [35, 96, 100]. Recent reviews of the literature have observed that willingness to participate varies over time and within regions, thus emphasizing the need to assess willingness to participate in different and specific contexts [90, 96, 100, 101]. Identifying new factors and exploring underlying factors that can influence willingness to participate, can help to explain the differences observed in willingness to participate in different communities [33, 35, 90, 96].

Factors such as knowledge about HIV infection, practices and attitudes towards existing preventive methods for HIV infection prevention, sexual behavior and self-assessment of risk of HIV infection, have been explored and associated with willingness to participate as facilitators and/or barriers to the hypothetical and actual willingness to participate in clinical trials of the HIV vaccine. A complete analysis and understanding of such factors, will allow to determine the magnitude and type of association with willingness to participate [33, 35, 90, 96, 100].

Several studies have hypothesized and tested, that participation in HIV vaccine trials may lead to an increase in sexual risky behaviors for HIV infection, among volunteers who have received an HIV vaccine candidate during their participation in HIV vaccine trials. This is called *Risk Compensation* and it happens and occurs when, for example, participants in a preventive HIV vaccine clinical trial, who previously used condom regularly and/or had a single sexual partner, start to use condom irregularly or to have more than one sexual partner, thus increasing their risky behavior for HIV infection, as they feel more protected by the fact that they have received an experimental HIV preventive vaccine [102-104].

Expectations and experiences of participating in a HIV vaccine trial are also important and need to be evaluated, since it can influence WTP in a HIV vaccine trial. Participants of HIV vaccine clinical trials may also have negative experiences due to their participation in the trials. It is documented that family members, friends, and even health professionals, may have the perception that volunteers who participated in clinical trials are infected with HIV or at risk of HIV infection, regardless of the phase of the clinical trial [34, 105-108].

Many vaccine candidates intend to elicit broadly neutral and long-lasting antibody responses to HIV that can be detected by common serological tests [69], more commonly referred to as Vaccine-Induced Seropositivity (VISP) or Vaccine-Induced Reactogenicity (VIR). This is a challenge for researchers and volunteers [109], since many health facilities lack reliable means of diagnosis, that can distinguish a true HIV infection from vaccine-induced seropositivity and can also favor discrimination towards volunteers, for example, health professionals and the community.

A wide range of social and behavioral frameworks have been designed to improve the implementation of HIV vaccine studies, resulting in a consensus that more emphasis should be put on the socio-behavioral component [33, 90, 110, 111]. This understanding of the factors that could influence recruitment and retention, and consequent development of tailored strategies [33], can be achieved by conducting social-behavioral research, before, during and after the implementation of the clinical trial [112]. This knowledge is crucial, as it would allow researchers to discuss these issues with the community and, therefore, have a community that understands and supports the conduct of HIV vaccine trials [67, 106, 113].

2.5 Mozambique contribution to HIV vaccine research

As part of an international collaboration, Mozambique began its preparation for conducting HIV vaccine clinical trials with the conduct of an HIV incidence cohort study among young adults in 2009. From 2009 to 2011, 1.309 young adults aged 18-24 years old were enrolled and followed for 12 months to assess the suitability for future HIV vaccine trials by determining the prevalence and incidence of sexually transmitted viral infections. Participants were recruited from an outpatient youth clinic at Hospital Central de Maputo in Maputo City. HIV testing was done at screening and at 3 follow-up visits. Almost all participants enrolled were females (76%), with the majority being students (96%). At screening, 71 participants were diagnosed with HIV, translating into a HIV prevalence of 5.1% (95%CI: 3.97–6.31), which was higher in women than in men (5.8% vs 3.1%), correspondingly. During the study, a total of 14 seroconversions occurred, only among the female participants group. HIV incidence was 1.14/100 persons years (95% CI: 0.67 – 1.92). At the end of the study, 1.102 HIV negative participants finished study visits, corresponding to 84% retention rate [114]. The implementation of this study enabled the country to establish its capacity to conducted HIV vaccine clinical trials.

This laid the foundations to the conduct of the first HIV Vaccine trial in Mozambique, in collaboration with Tanzanian, Swedish, Italian and American institutions - the TaMoVac I. The study objective was to explored the safety, tolerability, and immunogenicity of delivering HIV-DNA at three priming doses, each of 600 μg (lower dose) or 1,200 μg (higher dose) intradermal (ID) using the needle-free Zetajet injection device that allowed up to 0.2 ml ID injections, followed by two HIV-MVA boosts. The DNA vaccine was based on seven plasmids carrying HIV-1 genes: Pool 1 encoding Env subtypes A, B, and C and Rev subtype B; and Pool 2 encoding Gag subtypes A and B and RTmut subtype and was manufactured by Vecura (Huddinge, Stockholm, Sweden). The HIV-MVA is a live recombinant nonreplicating poxvirus vector based vaccine that had been genetically engineered to express HIV-1 gp150 (subtype E, isolate CM235) and Gag and Pol (integrase deleted and reverse transcriptase nonfunctional, subtype A, isolate CM240), and was manufactured for the Walter Reed Army Institute of Research by ABL, Inc. (Rockville, MD). The Zetajet™ device (Bioject Medical Technologies, Inc., Tualatin, OR) is a needle free injection system with a disposable syring. Young adults aged 18-26 years old were recruited, from a HIV incidence cohort previously established for this purpose, to participate in a phase I randomized, placebo-controlled, double-blinded trial conducted at the Polana Caniço health research and training center in Maputo city, Mozambique. Seventy-seven healthy HIV negative participants

were screened, 24 participants were included in the study and followed from August 2011 to March 2013. More than half of the participants were female (n=14/24), and the median age at enrollment was 21.7 years (interquartile ranges 20.9–22.9). All participants had at least the secondary level of education. Study subjects were randomized to 2 treatments groups (group I and II):

- Group I received HIV-DNA/placebo prime in volumes of 0.1 ml per injection in both Left arm (pool 1, Env A, B, C RevB) and Right arm (pool 2, Gag A, B RTmut B) respectively,

or:

- Group II received HIV-DNA/placebo prime in volumes of 0.2 ml per injection, in both Left arm (pool 1, Env A, B, C RevB) and Right arm (pool 2, Gag A, B RTmut B) respectively.

HIV-DNA/placebo prime was administered at week 0, 4, 12 followed by Left arm (HIV-MVA) 1 i.m. injection of 108 pfu, 1ml at week 24 and 36. Participants were blinded to vaccine or placebo administration and were followed for 12 weeks after the last vaccination. At the end of the study 24 participants completed the final visit, with 97% of visit compliance rate (visits observed/visits expected). The results of this study showed that the vaccine regimen was safe, well tolerated and induced encouraging immunogenic cell-mediated responses, particularly after priming with a high dose (1,200 μg) of HIV-DNA injected with Zetajet [115].

Building on the success of the first phase I HIV vaccine clinical trial, a phase II HIV vaccine clinical trial was implemented in Mozambique and Tanzania – the TaMoVac II (Tanzania and Mozambique HIV vaccine trial). By employing and combining different strategies, this study aimed to enhance the efficiency of the DNA priming through the addition of adjuvants and methods that improve the delivery of the antigens contained in the vaccine using needle free devices and electroporation. Using a factorial design, TaMoVac II was a phase II, placebo-controlled, double-blinded, with two randomizations that aimed to assess a prophylactic HIV vaccine with the HIVIS DNA prime administered ID by the Zetajet® device with or without the Derma Vax™ electroporation device at a dose of 600μg in a concentration of 3mg/ml or in a concentration of 6mg/ml (first randomization), followed by IM MVA-CMDR 108pfu per ml either alone or given at the same time as IM 100 μg CN54 rgp140 adjuvanted with 5μg GLA-AF (second randomization) in order to determine the optimal prime boost regimen. HIVIS DNA and the MVA-CMDR vaccines and Zetajet device for vaccine administration were the same used in TaMoVac I.

The CN54rgp140 is a recombinant C-clade Env protein, manufactured (GMP) using a mammalian cell expression system by Polymun and purchased by Imperial College London and the GLA-AF is an adjuvant containing an aqueous formulation of glucopyranosyl lipid A, which is a complete synthetic monophosphoryl lipid A (MPL)-like molecule a ligand for toll-like receptor 4 (TLR4) and potent stimulator of the antigen presenting cells manufactured by IDRI. Electroporation[13] increases cell membranes permeability, thus increasing the uptake of DNA by applying external pulsed electric fields [116]. Five hundred and two participants were screened between November 2012 and November 2013, and 211 were included in the study. Nearly half of the participants were females (46%), and the median age was 22 years. Participants were primed with HIV-DNA/placebo at weeks 0, 4 and 12, followed by intradermal electroporation at the injection site. HIV-MVA/placebo boosts with or without subtype C rgp140/GLA-AF or placebo intramuscular were given at week 24 and 40. Separate injections were given in both deltoids for participants receiving two injections. All participants were followed for 12 weeks after the last injection and the lost to follow-up rate was 23.7% (n=50/211). The study results confirmed that the vaccine regimen was safe when delivered in a simplified approach.

The performance of these trials resulted in the strengthening of clinical and laboratory capacity in the country, with a view to the participation of Mozambique in future trials of HIV vaccines. Mozambique has recently become part of a global network that aims to discover a preventive HIV vaccine, HIV Vaccine Trials Network (HVTN). Since 2017, 95 people have been enrolled in 3 HVTNs clinical trials in Maputo city. The HVTN 107 it's a phase 1/2a partially double-blinded, randomized clinical trial that aims to characterize the safety and immunogenicity of clade C ALVAC-HIV (vCP2438) and Bivalent Subtype C gp120 alone, with MF59® adjuvant, and with alum adjuvant in 132 healthy man and women, HIV-uninfected adult participants. This study is being conducted in 5 research centers, and in Maputo it recruited 24 participants aged 18-40 years, 14 of whom were female [117]. At the same time a phase 2b study to evaluate the safety and efficacy of VRC01 broadly neutralizing monoclonal antibody in reducing acquisition of HIV-1 infection was also being implemented. About 1900 women aged 18-50 years old, HIV uninfected but at high-risk for HIV acquisition, participated in the study, with 26 women enrolled in Maputo – HVTN 703/HPTN081 [118]. Finally, the third clinical trial was a multicenter, randomized,

[13] Electroporation, or electropermeabilization, is a microbiology technique in which an electrical field is applied to cells in order to increase the permeability of the cell membrane, allowing chemicals, drugs, or DNA to be introduced into the cell (also called electrotransfer).

double-blind, placebo-controlled phase 2b efficacy study of a heterologous prime/boost vaccine regimen of Ad26.Mos4.HIV and aluminum phosphate-adjuvanted Clade C gp140 in preventing HIV-1 infection in women aged 18-35 years old in sub-Saharan Africa, the HVTN705/HPX 2008. This study target to enroll 2600 participants, with 45 being recruited in Maputo [119].

In preparation for conducting a phase IIb three-arm, two-stage HIV prophylactic vaccine trial with a second randomization to compare Tenofovir alafenamide/Emtricitabine to Tenofovir disoproxil fumarate/Emtricitabine as pre-exposure prophylaxis (PrEPVacc trial), a registration cohort for future participation in an HIV vaccine study has been carried out since 2019. The main goal of the registration study is to prepare a cohort of male and female HIV negative volunteers at high risk of HIV infection for future participation in the PrEPVacc trial, expected to start in 2021 [120].

Mozambique has successfully conducted two HIV vaccine clinical trials, a phase I and phase II trials [115, 121]. and is currently conducting more research [120, 122], in a global effort to develop a preventive HIV vaccine that's safe, affordable and efficacious for different populations [123].

3 Rationale and Objectives

Sub-Saharan Africa, especially the Southern Africa region, is one of the areas most affected by the HIV epidemic. Because of the high burden of the disease in sub-Saharan Africa, the volunteers from this region represent an important population for the development of HIV vaccine clinical trials. Understanding what can facilitate or obstruct participation in research related to the HIV vaccine is important for the successful implementation of HIV vaccine clinical trials [98, 106, 113]. UNAIDS has developed a framework to improve the acceptability and feasibility of biomedical HIV prevention trials, which emphasizes the role of research to adapt HIV vaccine studies to different contexts [124].

Although recognized the need to evaluate whether the most-at risk individuals for HIV infection would be willing to participate in HIV vaccine trials, as well as factors that could serve as barriers or facilitators for trial participation in a detailed and contextualized manner [101], which is crucial for the development of future vaccines, few studies have been conducted in low income countries in Africa [34, 35, 96], including Mozambique.

Different studies that assessed willingness to participate looked at the individual as a basis for understanding the decision-making process for hypothetical willingness to participate in HIV trials, which may have been driven by the fact that most studies were conducted in developed countries [101, 125-127], where the decision process to participate (or not) in an HIV vaccine clinical trial, takes an individual approach. In contrast, in developing countries, especially in the Sub-Saharan Africa region, including Mozambique, it is theorized that the decision-making process is largely influenced by social dynamics, cultural challenges and the environmental context, framed in a complex structure of relationships within the community [99, 106, 128-131].

Understanding the knowledge and beliefs associated with vaccines is essential for the successfully implementation of HIV vaccine clinical trials. Obtaining this knowledge will guide the design and implemention of HIV vaccine clinical trials. A complete assessment of the acceptability of stakeholders in the different key sectors is needed, to be involved directly or indirectly in the implementation of the clinical trials. Sexual risk behavior and other behaviors of the participants during the trials must be evaluated and measured safely, in order to control the possible impact of such factors on the results of the trials.

This study aims to address these issues with a view to strengthening the development of the HIV vaccine in Mozambique. Understanding what the perceptions about the HIV vaccine and the effects of implementing HIV vaccine clinical trials could help to reduce limitations and eliminate the negative results of future HIV vaccine trials.

3.1 General Objectives

To understand the socio-behavioral aspects regarding participation to HIV vaccine clinical trials among young people in Maputo, Mozambique.

3.2 Study Specific Objectives

3.2.1 Study I

1. To assess the expressed willingness to participate in future HIV trials among young adults at high risk for HIV infection, who participated in a HIV incidence study in Maputo (RV 363 Study).
2. To identify the associated factors, among young adults at high risk for HIV infection, who participated in a HIV incidence study in Maputo (RV 363 Study).

3.2.2 Study II

1. To understand the motives and experiences of HIV vaccine trial participants for participation in HIV vaccine trials, among young adults who participated in a previous phase II HIV vaccine trial (TaMoVac II) conducted in Maputo.
2. To identify potential social harms and changes in sexual behavior among volunteers due to study participation in the previous phase II HIV vaccine trial (TaMoVac II) conducted in Maputo.

4 Project Design, Methods and Procedures

This research project includes 2 studies, with a mixed methods approach, using quantitative and qualitative methods. In order to gain a complete understanding of a research problem through of convergence of qualitative and quantitative data, a convergent design was used [132]. This was a descriptive and exploratory research. Questionnaires, in-depth interviews and focus group discussion were administered to previous and potential future participants of HIV vaccines trials. In-depth interviews and focus group discussion were conducted to explore the motives for participation, sexual behaviour and potential social harm among volunteers who received an HIV vaccine candidate in a phase II HIV vaccine trial conducted in Maputo. The Health Behaviour Model was used to explain motives for participation in HIV vaccine trials. Awareness, knowledge and sexual behaviour was assessed in order to identify factors that can influence willingness to participate in HIV vaccine trials. This project research is divided in study I and study II.

4.1 The Health Belief Model

Originally developed in the 1950s, the Health Belief Model is one of the most widely used behavioural change models [133, 134]. Developed by Hochbaun with the aim of improving the effectiveness of health education programs, this model tries in a systematically way, to explain and predict preventive health behaviour. Health education is important to modify individual characteristics that help to predict preventive health behaviours and the use of health services. The model is based on the premise that an individual's likelihood of accepting a preventive health behaviour is based on their beliefs [14] about the relationship between the behaviour and the subsequent illness and their ability to weigh the risks and benefits of adopting or not adopting the preventive behaviour. This model proposes to guide the development of persuasive methods to change beliefs related to behaviours that in turn will consequently lead to an actual change in behaviour, particularly in the absence of disease. In the field of HIV prevention, this model has been used to evaluate the beliefs and perceptions of the target populations for the HIV preventive measures in relation to the same preventive measures, as well as to guide the development of strategies that facilitate their adoption, such as messages for recruitment and retention in HIV preventive strategies [133-135]. The health belief model postulates that understanding a person's motivation to undertake a health behavior can be divided into 5 main categories:

[14] Beliefs - Individual characteristics that shape behavior and can be acquired through primary socialization.

Perceived Susceptibility - each individual has their own perception of their risk/probability in relation to experiencing a disease, and this perception of susceptibility to a disease varies between individuals. Considering the assessment of their own risk in relation to a disease, such as HIV/AIDS, individuals who think they are less likely to become infected by HIV deny the possibility of being affected by the disease, individuals who think they have a moderate probability may admit to a certain degree of the possibility of becoming infected, and individuals with a high perception of susceptibility feel that there is a real danger of contracting the infection disease.

Perceived Seriousness - it refers to the beliefs that a person has in relation to the effects, mostly negative, that a certain disease would have on his life. These effects range from physical and psychological changes such as pain, discomfort, changes in appearance to social issues such as lost time at work, financial burdens, difficulties with the family, relationships and susceptibility to future conditions and even taking pills for the rest of his life, in the case of HIV/AIDS. It is important to include these emotional and financial burdens when considering the severity of an illness or condition.

Perceived Benefits of Taking Action - after accepting their susceptibility to a disease, the next step involves the individual taking steps to prevent the disease. The direction of action a person chooses will be influenced by beliefs about the action, if it is effective or not.

Barriers to Taking Action - even after recognizing one's risk in relation to a disease, that the disease is serious and that preventive measures are effective, it does not guarantee that the individual will adopt the measures or take action to adopt the preventive measures. This may be due to barriers, related to the characteristics of the measures, which can be inconvenient, expensive, unpleasant, painful or not accepted in his/her community. These characteristics can make it difficult or even prevent the person from performing the desired action.

Cues to Action - an individual's perception of the levels of susceptibility and seriousness provide the force to act. Benefits (minus barriers) provide the path of action. However, it may require a 'cue to action' for the desired behavior to occur. These cues may be internal or external [133].

4.2 Project Setting

4.2.1 Polana Caniço Health Research and Training Center (CISPOC)

Polana Caniço Health Research and Training Center (CISPOC) is a clinical research center under the National Institute of Health of Mozambique [122, 136], Ministry of Health of Mozambique. CISPOC was created in 2011 with the mission of generating and promoting the incorporation of scientific and technological solutions to the main health problems and conditions in Mozambique. The center has experience and the ability to conduct clinical research, including clinical trials, surveillance activities and program evaluation. CISPOC is actively involved in the training program for undergraduate and graduate students (master's and doctorate). This research project was implemented as part of its HIV vaccine research program. One of the objectives of CISPOC is to involve the community at all levels of research in the field of vaccines, using the Community Advisory Council (CCC) as a link between participants in clinical trials and the Maputo community, especially in Polana Caniço neighborhood where it is located. The main pillars of this activity are community education, recruitment and retention. This research project is innovative, as to our knowledge, it is one of the first in the country that aims to address questions about the knowledge, awareness and perception of the community about HIV vaccine research. The results of this research will reinforce Mozambique's preparation for conducting clinical trials of HIV vaccine efficacy and will strengthen the relationship between the center and the community of Polana Caniço, where it is based. This research project is the result of CISPOC's increased awareness of the need to continually update and improve its community engagement plan.

4.2.2 Maputo City

Maputo is the capital and largest city in Mozambique. Located in the south of the country, it has a strategic role at national and international level, because, among other things, it is the city that has the best infrastructure and services in Mozambique. It is equipped with a network of roads and railways that connect the main urban centers in the country. It has a population of 1.101.170 inhabitants [43]. HIV prevalence in Mozambique’s capital, Maputo City is 22% for women and 11% for men, aged 15-49 years [79]. The Polana Caniço neighbourhood is a low-income peri-urban area, with an approximately population of 90.000 people, and it is divided into Polana Caniço "A" and Polana Caniço "B" [43].

- Polana Caniço "A" - Has a population of 45,883 inhabitants.
- Polana Caniço "B" - Has a population of 46,184 inhabitants.

Figure 4.1 Map of Mozambique

Source: Wikimedia Common by André Koehne

4.2.3 Ethical Approval

Study I was approved by the Instituto Nacional de Saúde-Institutional Health Bioethics Committee and the Study II was approved by the National Health Bioethics Committee of Mozambique and by the Institutional Review Board Ethics Committee of the Walter Reed Army Institute of Research. Administrative approval was granted by the Ministry of Health of Mozambique. The PhD project was approved by the Ludwig Maximilian University of Munich medical ethics committee.

4.3 Study I

4.3.1 Study design and population

The RV363 study was a prospective observational HIV-incidence cohort study. It was conducted between November 2013 and February 2017 at CISPOC. Inclusion criteria were age 18-35 years, self-report of at least two sexual partners in the 3 months prior to screening and being HIV-uninfected. HIV status was assessed using the Alere Determine™ HIV-1/2 rapid test (Alere Inc, Waltham, USA) with reactive tests confirmed using the Uni-Gold™ Recombigen® HIV-1/2 - for HIV 1 and 2 (Trinity Biotech, Bray, Ireland). Women of child-bearing potential were required to have a negative urine pregnancy test. Co-enrollment in any other HIV prevention study was not allowed. Participants who answered the survey questions about willingness to participate in future HIV vaccine trials were included in these analyses (Figure 4.2).

4.3.2 The RV 363 Incidence Study

The RV 363 was a prospective observational cohort and site development to assess the incidence of HIV infection, retention rate, and willingness of adults to participate in future HIV vaccine trials in Mozambique. The study aimed to recruit and follow 500 HIV uninfected male and female participants aged 18-35 years old at risk of HIV infection, defined by being sexually active with two or more partners in the last 3 months, in Maputo city. Inclusion criteria included being HIV negative assessed using the Alere Determine™ HIV-1/2, with negative tests confirmed using the Uni-Gold™ Recombigen® HIV-1/2 - for HIV 1 and 2, willingness to be followed for a period of 24 months, intending to reside in Maputo city during the implementation of the study. Women of child-bearing potential had to have a negative urine pregnancy test. Volunteers were required to pass a test of understanding and to provide written informed consent. Co-enrolment in any other HIV prevention studies was not allowed. Recruitment staff included social scientists, focal points from key populations associations (lesbian, gay, bisexual and transgender, female sex works) and from local community-based organizations. A community-based recruitment strategy was implemented, that target schools with nigh shifts, bars and markets in Maputo city. Sensitization and mobilization activities included one-on-one interactions and the distribution of flyers containing information regarding the study purpose, target population (adults who did not knew their HIV status), the duration of the study and were the study was being conducted, to potential participants. At enrollment HIV assessment, HIV risk reduction behavior counselling and circumcision counseling for male volunteers was provided, followed by a clinical examination including sexual transmitted infections screening. From November 2013 to November 2014, 505 HIV negative participants and 50 HIV positive participants (for masking purposes) were recruited and included in the study. As part of the incidence study HIV assessment, HIV risk reduction behavior counselling were done every 3 months and a HIV risk behavior assessment every 6 months for up to 24 months (Figure 4.2). Questionnaires were administered to each volunteer by a trained staff member and collected data on demographic characteristics (age, sex, level of education, approximate income, marital status and occupation), medical history (history of sexually transmitted infections, blood transfusion, previous testing for HIV, alcohol use, and drug use). Sexual behavior (age of first intercourse, number of sexual partners, perceived risk for HIV infection, history of sex exchange for benefits, and sex under the influences of alcohol). Participants also answered to a willingness to participate questionnaire at screening and at the exit visit. HIV/AIDS awareness, vaccine knowledge, facilitators and barriers factors associated with WTP, where collected (Annex 1- Study I_RV 363 HIV/AIDS Willingness to participate

questionnaire). No additional information was given on HIV Vaccine or HIV vaccine trials to study participants. Blood samples were collected for blood count, HIV diagnosis, syphilis and herpes simplex virus-2. Urethral and vaginal samples was collected for human papilloma virus diagnosis [137].

4.3.3 PhD Student Role

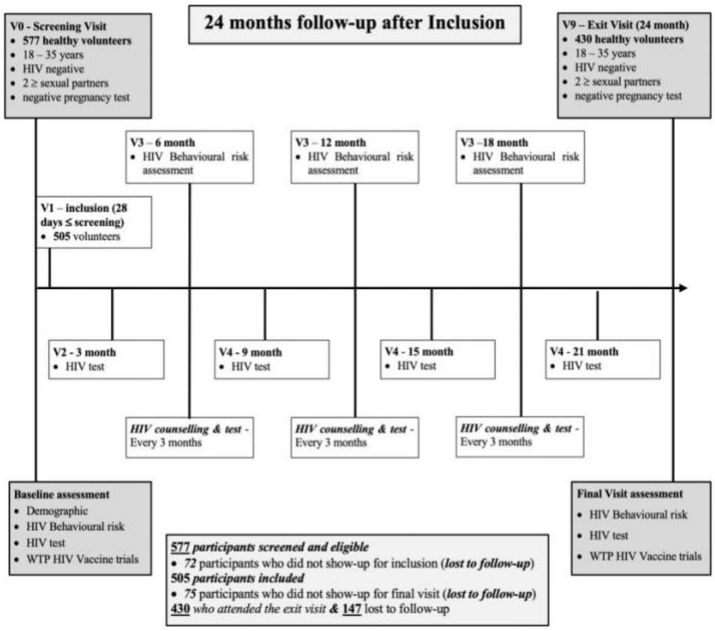
PhD student was one of the co-investigators in the RV 363 incidence study, supporting mainly retention activities strategies discussions and participating in cultural events organized for the participants, fairs and discussion of retention strategies. The RV 363 study materials were developed as part of the RV 363 incidence protocol. The PhD student oversaw the willingness to participate data cleaning, analysis and conceptualized and led the report manuscript writing.

4.3.4 Questionnaires

HIV vaccine knowledge. Participants were asked "*if a vaccine is meant to prevent illness*" (true/false) and if they had received information on HIV research (yes/no) prior to their participation in the study, including the source of information.

Willingness to participate questionnaire. First, the staff member would give a brief explanation of the purpose of HIV vaccine clinical trials to the participant, before proceeding to the main question, "*would you be willing to participate in such a study to test an experimental HIV vaccine?*" (yes/no/someone else should decide/refused to answer/don´t know). Barriers were assessed with the question "*how likely or unlikely would you be to enroll in a research study of a new experimental HIV vaccine*", and responses were collected on a 4-point Likert scale: very unlikely, somewhat unlikely, somewhat likely, and very likely. Facilitators to participation were assessed with the question "*how important are the following factors in making a decision about participating in a research study of an experimental HIV vaccine*", with responses also collected on a 4-point Likert scale: not important at all, somewhat important, important, and very important. The last question was if the participant thought that an HIV vaccine would be useful in controlling HIV infection (yes/no). Participants could select all applicable answers for questions with more than one option (annex 5).

Figure 4.2 RV 363 Study Procedures



4.3.5 Statistical analyses

Demographic variables (age, gender, level of education, marital status, income, main occupation, history of blood transfusion, desire to get pregnant) [35, 138] and sexual behavior variables (age of first sexual intercourse and perceived risk for HIV infection) [139, 140] included in the analyses were selected based on literature review. Expressed Willingness to Participate was the dependent variable and was determined by a "yes or no" question, with "do not know" and "refused to answer" as the other options, but these were removed for bivariate and multivariate analysis. Missingness account for less than 5%. Likert scale questions were dichotomized from a set of 4 categories: "unlikely" (questionnaire responses "very unlikely" and "somewhat unlikely") and "likely" (questionnaire responses "somewhat likely" and "very likely"); "not important" (questionnaire responses "not important at all" and "somewhat important") and "important" (questionnaire responses "important" and "very important"). Frequencies and proportions for all variables were calculated. Two analytical approaches were employed, based on the status of the participants' visit assessments. For the screening assessment, bivariate analysis was done between willingness to participate (yes/no), demographic, sexual behavior and willingness to participate factors. Differences were assessed with Chi-square and Fisher's exact test when appropriate. Willingness to participate factors that were statistically significant ($p<0.05$) in unadjusted logistic regression models were included in the adjusted logistic regression model at the baseline assessment. Analyses were performed among participants who stayed throughout the study, in

order to identify factors associated with willingness to participate. McNemar's exact test was used to assess the differences in responses within the participants, at screening and at the exit visit, and variables with $p<0.05$ were included in a *Generalized Estimating Equation* (GEE) logistic regression for binary outcomes model. Analyses were performed using STATA 15.1 (StataCorp, College Station, TX).

4.4 Study II

4.4.1 Study Design

A prospective exploratory cohort, using a convergent mixed study design with both quantitative and qualitative approaches were used, in order to obtain a profile on the participant´s motivators, sexual behaviors and experiences of participating [112, 132] in a previous phase II randomized, placebo-controlled, double–blinded HIV vaccine clinical trial, the TaMoVac II. This study was conducted between February 2017 and March 2018 at the *Centro de Investigação e Treino em Saúde da Polana Caniço* (CISPOC), where the first two Mozambican HIV vaccine trials, TaMoVac I and TaMoVac II, were conducted.

4.4.2 TaMoVac II

Was a phase II randomized, placebo-controlled, double-blinded, factorial design conducted at 1) the Muhimbili University of Health and Allied Sciences (MUHAS) in Dar es Salaam, 2) the National Institute for Medical Research-Mbeya Medical Research Center (NIMR-MMRC) in Mbeya, Tanzania, and 3) the CISPOC-INS in Maputo, Mozambique), to assess a prophylactic HIV vaccine with the HIVIS DNA prime administered ID by the Zetajet® device with or without the Derma Vax™ electroporation device at a dose of 0.6mg in a concentration of 3mg/ml or in a concentration of 6mg/ml, followed by IM MVA-CMDR 108pfu per ml either alone or given at the same time as IM 100 μg CN54 rgp140 adjuvanted with 5μg GLA-AF. At CISPOC, 38 Healthy subjects, aged 18 to 40 years, considered healthy - determined by medical history, physical examination, clinical judgment and by key laboratory parameters as judged by the study physician - HIV negative (antigen/antibody ELISA for HIV infection); not being pregnant nor planning to become pregnant during the study period. Participants also had to be considered at low risk for acquiring an HIV infection in the past 6 months, defined by the absence of the following identifiable risk factor/ behavior:

- sexual partner with HIV;

- sexual partner with unknown HIV serostatus who is also unwilling to use protective condoms consistently in all sexual relations;
- sexual partner is known to be at high risk for HIV;
- more than two sexual partners in the last 6 months;
- history of being an alcoholic [as medically defined or more than 35 units /week] or intravenous drug abuse or ongoing other chronic drug abuse (e.g. marijuana);
- history of STI within past 6 months;

At CSIPOC, volunteers were recruited at the Youth Clinic at Hospital Central de Maputo by study staff. Information sessions and briefings were held containing general information through power point presentations on the study. Participants who expressed an interest to participate in the HIV vaccine trial were then invited to CISPOC to discuss informed consent individually. After passing a test of understanding and signing the informed consent form, the screening process would take place. Eligible participants would then be enrolled (week 0) and receive their first immunization. Participants were required to make a minimum of 17 scheduled visits over the course of 52 weeks. Week 0 started on the day of enrolment, which was also the day of the first immunization, followed by 4 more immunizations. Adverse events were assessed during the enrolment visit following immunization and at every visit thereafter. Clinical safety follow-up visits were conducted 2 and 4 weeks after each immunization. Routine laboratory safety parameters were collected at screening, baseline, at every visit thereafter and at any other unscheduled visit if clinically indicated. Long term immunogenicity and safety visits was performed at a minimum of 12 weeks after the last immunization (Table 4.1). The unblinding process occurred after the trial completion. Participants received an individual unblinding session, indicating the immunization group. For participants with an ongoing post-immunization positive ELISA, were followed until the time the response has disappeared. All participants received a trial participation card indicating that they have participated in an HIV vaccine trial with the potential of false positive HIV tests due to immunization. Participants were instructed to present this card whenever he/she desired to have an HIV test. The unblind process took place in 2017, about 2 years after the end of the study [121].

Table 4.1 TAMOVAC II flow chart

	Weeks	-4-8	-1-4	0	2	4	6	8	12	14	16	24	26	28	40	42	44	52	64
	Target days			0	14	28	42	56	84	98	112	168	182	196	280	294	308	364	448
	Visits	V1	V2	V3	V4	V5	V6	V7	V8	V9	V10	V11	V12	V13	V14	V15	V16	V17	V18
		Screening 1	Screening 2	Enrolment + DNA 1	Safety	DNA 2	Safety	Safety	DNA 3	Safety	Safety	MVA 1+/- rgp140/GLA	Safety	Safety	MVA 2+/- rgp140/GLA	Safety	Safety	Long term	Long term
Study Procedures																			
Informed Consent		x																	
Test of Understanding		x																	
HIV Risk Assessment		x																	
Medical History		x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Complete Physical Exam		x																	
Immunization				x		x			x			x			x				
Adverse Events assessments					x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Lab Investigations		x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x

4.4.3 PhD student role

PhD student participated at TaMoVac I as study physician and was the site clinical coordinator for TaMoVac II at CISPOC. PhD student conducted information sessions, administered the informed consent, test of understanding, the clinical follow-up of the participants, and the administration of the vaccines. He was also responsible for reporting any adverse events, including any serious adverse events to the study team. PhD student carried out the individual unblinding sessions with the participants, which included counseling and study procedures review. As part of the PhD research project, a separate protocol was elaborate for study II. The fact that some clinical trials participants were diagnosed with sexually transmitted infections, including HIV infection, and some report inconsistent use of condom and/or had two or more sexual partners during their trial participation, led the PhD student to question the motivations that led young people adults to participate in HIV vaccine trials. These participants were included as being at low risk for HIV infection and received regular counseling for HIV risk behavior reduction. It was expected that all clinical trial participants would maintain the same low risk behavior for HIV infection that they reported at the enrollment visit, during their trial participation, however that was not what was reported by part of the participants. The PhD student developed and submitted the study II protocol for ethical approval. Authorization to contact the participants was requested to the trial sponsors. PhD student was also responsible for identifying funding and submitting proposals to acquire funds to cover the costs of implementing the study. The study coordination and supervision were in charge of the PhD student. The PhD student led the process of data analysis and writing the manuscripts of this study.

4.4.4 Study Population

All participants from the TaMoVac II trial were intentionally selected and invited to participate in this study after trial completion.

4.4.5 Study Procedures

For this study, participants were contact telephonically, and invited to the study site, were, after an explanation of the study's procedures and objectives, participants who expressed their desire to participate, signed an informed consent form. The data was collected in two visits, before and after the unblinding process - disclosure to the participant if he received the experimental preventive vaccine or placebo. The interval between the first and second round, was a minimum of 3 months

before and after the unblinding. The study II research materials, questionnaires (Annex 2), semi-structured guides for in-depth interviews (Annex 3) and focus group discussions guides (Annex 3) was developed by the PhD student (Igor Capitine - IC) based on a literature review and adapted to local context [98, 99, 106, 131, 139], following discussions with the clinical trial team, including the TaMoVac II trial counselors. Participants would first answer to the questionnaire, followed by the In-depth interviews and FGD. In-depth interviews and FGD was only done at the first visit. The first four interviews were heard by the IC with the aim of ensuring quality and consistency, before proceeding with the next ones. The questionnaires were administered by 2 counselors who knew the participants, and the in-depth interviews and focus group discussion were conducted by 4 social researchers, who were not involved in the TaMoVac II trial. Participants were asked if they had a preference to answer to the questionnaire, in-depth interviews and/or focus group discussion with a female or male interviewer. During the unblinding session participants received counseling on HIV risk reduction behavior. The HIV vaccine trials procedures was also discussed with the participants, including the possibility of a false HIV positive rapid test result.

4.4.6 Study Materials

Questionnaires. Questionnaires collected data on demographics, HIV vaccine knowledge (objectives of the different phase of clinical trials, if its guarantee that a participant who receive a study vaccine is protect, and whether participants would agree to be vaccinated with an HIV vaccine if one was discovered), sexual behaviors (if in the 3 months prior to the questionnaire the participant had more than one sexual partner, reasons for not using a condom, and how auto risk assessment of HIV infection acquisition) and social harm (if the participant informed someone about his participation in the clinical trial, what that person's reaction was, and wheter there is anyone the participant would have liked to have informed about his participation in the clinical trial, but did not) (Annex 2 - Study II_Questionnaire), and the same questionnaire was used in both rounds.

In-depth interviews. For the in-depth interviews one semi-structured guide (Annex 3 - Study II_In-depth interview) was developed, with three major questions: 1. *What is HIV, how it´s transmitted and how to you assess your risk of HIV infection acquisition?* 2. *Why did you participated in the TaMoVac II trial?* 3. *How was your experience of participating in a HIV vaccine trial, and do you think members of your community would support research to find preventive measures against HIV, including conducting clinical trials of HIV vaccines and why?*

Focus group discussion. The first question was: 1. *What is research, and what are the goals of a HIV vaccine clinical trial*? 2. *Why despite having received counseling, some participants acquire STIs'*? 3. *What do members of your community think about the participation of young people from the community in clinical trials of HIV vaccines, and what would their comments be?* (Annex 4 - Study II_Focus Group Discussion).

4.4.7 Data analysis

Quantitative analysis: Thematic analysis was used to identifying, analyzing, organizing, describing and reporting themes within data, in order to identify participants views, opinions, knowledge, experiences or values regarding their experiences and motives of participating in a HIV vaccine clinical trial. The analysis was guided by Braun & Clarck, 2006 six steps:

- ***Familiarization with the data*** - This component involves that the researchers (particular those who will be involved in the data analysis) know the data very well. This can be achieved by participating in the data collection, transcription of interviews and repeated reading of the data actively in search of meanings and patterns. Data was transcribed and entered to MAXQDA 2020 (VERBI Software, 2019) for data analysis. It involves writing down preliminary ideas that can then be tested – The PhD student listened to all interviews and corrected all transcripts. PhD student would first read the whole interview before proceeding to coding.
- ***Generating initial codes*** – After familiarizing with the data, the PhD student produced the codebook in an inductive way, based on the first 2 interviews [141]. The codebook contained code names, codes description (inclusion and exclusion criteria) and examples. The codebook was discussed with the study team. All interviews, and interviews sections were coded by two researchers independently, with meetings held to discuss the code agreement and emerging codes.
- ***Searching for themes*** – After all interviews were coded discussed and agreed between the two coders, the PhD student started the search for the Themes. PhD student did a vertical code analysis, meaning reading the all sections coded by the same code in the same interviews, followed by a horizontal code analysis of all the sections across different interviews coded by the same code. During the process all progress was registered in memos containing description of the participants views and opinions. Codes were them collated to form themes.

- ***Reviewing themes*** – Phd student developed the themes framework Themes and sub-themes were then revisited and reviewed and discussed with the team. Themes and sub-themes that did not had enough data to support were either collapsed to another theme and sub-theme or deleted.
- ***Defining and naming themes*** – during this phase, a description for each theme was elaborated. Description contained interesting aspects of what the data represented. Key messages were also identified. Also at this phase, modifications and redefining of themes occurred.
- ***producing the report –*** this was the final part wich culminated with the writing of the article. Here previous descriptions were selected and transcription data was add to support the themes [142]. Analysis was done in Portuguese, and then the codes, sub-themes, themes and quotes were translated to English.

Qualitative analysis: Descriptive analyzes were done for the sociodemographic, knowledge, sexual behavior and social harm data. Fischer's test was used for independence analyzes, and the McNemar´s exact test was used to assess differences between the first and second visit.

5 Results

5.1 Study I - RV 363 HIV-incidence cohort study

5.1.1 Demographic and sexual behavioral characteristics

From 1150 screened volunteers, 577 were eligible for inclusion, all of whom responded to the question about willingness to participate in a future HIV vaccine trial. Their characteristics are shown in Table 5.1. Briefly, 275 (48%) were female, the mean age was 22.2 (SD ± 3.9) years, 67% of the participants did not complete the secondary level of education. Most of the participants were single (82%) and 87% earned less than 5,000 meticais (~USD147) [143] per month, which is around the minimal national wage salary. Only 10% of the participants reported being older than 18 years of age when they had their first sexual intercourse, and almost all (94%) acknowledged that they had at least some risk of getting infected with HIV. Of the 577 eligible participants, 505 participants enrolled and of these 75 (15%) did not respond to the willingness to participate questionnaire at the exit visit. Independence test between levels of education revealed that participants with only primary school completed ($p<0.001$) were more likely to drop-out before the exit visit. The exit visit was completed by 430 participants who remained at risk for HIV.

Table 5.1 Demographic and sexual behavior characteristics of 577 eligible HIV negative participants screened in a HIV-incidence cohort study (RV363 study)

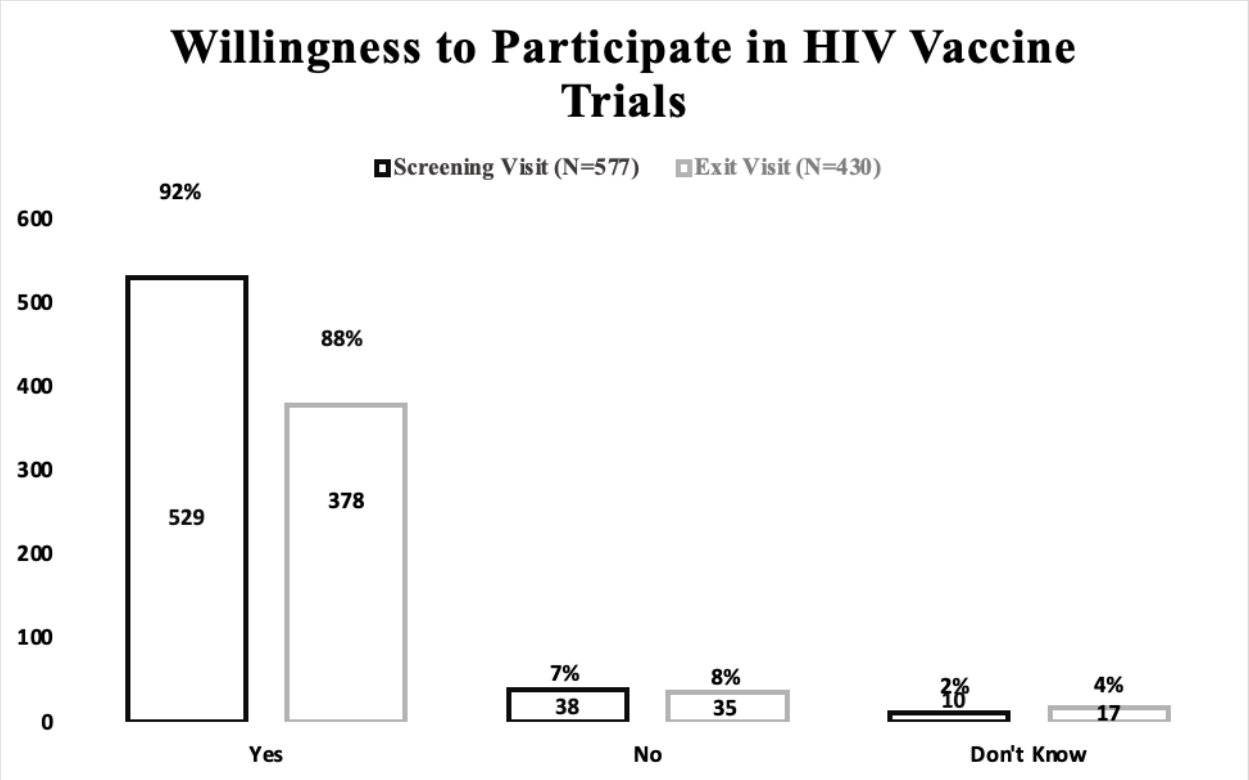
Socio Demographic Variables	Total Eligible (N=577)
Age (categorized), n (%)	
18-20	241 (42)
21-24	210 (36)
25-35	126 (22)
Gender	
Male	302 (52)
Female	275 (48)
Highest level of Education attained, n (%)	
≤ Primary school completed	57 (10)
Secondary school not completed	331 (57)
≥ Secondary school completed	189 (33)
Marital Status, n (%)	
Single	475 (82)
Cohabiting or married	83 (14)
Separated or divorced	18 (3)
Monthly income in metical's, n (%)	
≤ 5000	501 (87)
>5000	76 (13)
Main occupation, n (%)	
Student	321 (56)
Occasional Work	30 (5)
Permanent work	158 (27)
N/A [a)]	68 (12)
Ever received blood transfusion, n (%)	
No	550 (95)
Yes	22 (4)
N/A [a)]	5(1)
Desire to get pregnant in the next year (*n= 273 females only*), n (%)	
No	237 (87)
Yes	36 (13)
Age (years) of first sexual intercourse, n (%)	

< 15 years old	92 (16)
15 - 18 years old	393 (68)
≥ 18 years	58 (10)
N/A [a)]	34 (6)
Perceived risk for HIV infection, n (%)	
No risk	28 (5)
Some risk	500 (87)
High risk	39 (7)
N/A [a)]	10 (2)

5.1.2 WTP in a HIV vaccine study

Of the 577 HIV negative participants surveyed at screening, 529 (92%) said they would be willing to participate in an HIV vaccine study, 38 (7%) were not willing and 10 (2%) indicated that they did not know. Women who did not wanted to become pregnant in the following year (p=0.043) and participants younger than 15 years at first sexual intercourse (p=0.052) were more likely to not be willing to participate in an HIV vaccine study (data not shown). At the exit visit, 430 (75%) participants were still active in the study and willingness to participate in a HIV vaccine study remained high, with 378 (88%) willing to participate in an HIV vaccine trial, 35 (8%) not willing, and 17 (4%) who said that they didn't know (Figure 5.1). Among the 430 participants who stayed throughout the duration of the study, 392 indicated willingness to participate in a vaccine trial at enrollment visit. Of these 392, 360 (92%) maintained their willingness, 19 (5%) became not willing, and 13 (3%) became undecided. Of the 28 participants who initially were not willing to participate, 14 (50%) maintained their unwillingness, 12 (43%) became willing, and 2 (7%) became undecided. For 10 participants who initially stated that they did not know if they would participate in a HIV vaccine trial, 6 became willing, 2 became unwilling and 2 stayed undecided.

Figure 5.1 Willingness to Participate of 577 HIV negative participants at baseline, and of 430 HIV negative participants who completed the 24 months follow-up period



5.1.3 HIV vaccine knowledge

At screening, 546 (95%) participants indicated that the purpose of a vaccine is to prevent illness and 223 (39%) indicated that they had received any information on HIV vaccine research prior to study participation. The main source of information was radio/television in (n=143, 25%), followed by friends (n=71, 12%) and hospital (n=43, 7%) (Table 5.2). Friends/relatives became a less important source of information (n=56, 13%) vs. n=42, 10%), (p=0.016) at the end of the study; in contrast the internet become a more significant source of information (n=12, 2% vs. n=30, 7%), (p=0.001).

Table 5.2 Association analysis between HIV vaccine knowledge, motives and barriers with willingness to participate in HIV vaccine studies among the RV363 participants, by visit status

Willingness to Participate Factors	Total Eligible N=577	Visit Status		p-value[a]
		Screening Visit (n=430)	Exit Visit (n=430)	
Purpose of a Vaccine is to prevent illness - n/N (%)	546 (95) *	407(95) *	417 (97)	0.090
Had any previous information on HIV vaccine research, prior to participation - n/N (%)	223 (39)	175 (41)		
Source of Previous information regarding HIV vaccine research - n/N (%)				
Hospital/clinic/health worker	43 (7)	35 (8)	30 (7)	0.398
Radio/Tv	143 (25)	112 (26)	113 (26)	0.917
Friend/relative	71 (12)	56 (13)	42 (10)	0.016
Internet	12 (2)	10 (2)	30 (7)	<0.001
Poster	4 (1)	2 (0)	22 (5)	<0.001
Learned from a vaccine trial volunteer	3 (1)	3 (1)	4 (1)	0.706
Research center	7 (1)	7 (2)	24 (6)	0.002
Personal benefits of participating in Vaccine study- n/N (%)				
Learn how to avoid risky behaviour	529 (92)	398 (93)	352 (82)	<0.001
Feel protected from HIV infection	531 (92)	394 (92)	372 (87)	0.002
Get free HIV counselling and testing	496 (86)	369 (86)	273 (63)	<0.001
Receive updated information about HIV/AIDS	368 (64)	276 (64)	253 (59)	0.045
Get small reimbursement	83 (14)	67 (16)	18 (4)	<0.001

Be tested for sexually transmitted infection	527 (91)	389 (90)	311 (72)	<0.001
Receive regular health care related to research	373 (65)	289 (67)	206 (48)	<0.001
Get free pregnancy test every 3 months (N=275 females)	195 (71)	137 (50)	63 (23)	<0.001
Motives that could make you not participate in a vaccine study- n/N (%)				
Fear of needle	26 (5)	22 (5)	23 (5)	0.847
Fear of getting HIV	1 (0)	1 (0)	5 (1)	0.103
Fear of side effects	15 (3)	10 (2)	7 (2)	0.405
Fear of death	1 (0)	1 (0)	2 (0)	0.564
Fear of fetal abnormalities	10 (2)	9 (2)	7 (2)	0.480
Time required for visits	1 (0)	1 (0)	8 (2)	0.008
Fear of testing HIV positive	1 (0)	1 (0)	4 (1)	0.180
Fear of discrimination	2 (0)	2 (0)	1 (0)	0.564
How likely would you enrol in research study of a new experimental HIV vaccine if (*likely*[b]) - n/N (%)				
Required to come every 3 months to study center on a specific day	571 (99)	425 (99)	427 (99)	1.0000
Required to talk about study experiences with a nurse	571 (99)	425 (99)	427 (99)	1.0000
Required to test for HIV every 3 months	569 (99)	423 (98)	427 (99)	0.317
Required to be injected with a HIV study vaccine a few times	541 (94)	401 (93)	422 (98)	0.706
Required to give blood samples every time that you attend a study visit	554 (96)	413 (96)	422 (98)	0.564
The center was open for weekend visits	552 (96)	409 (95)	422 (98)	0.103
Required to use contraceptive during study participation (N=275 females)	214 (78)	153 (56)	172 (63)	0.178
Which factors are important for your decision to participate in a study of an experimental HIV vaccine (*important*[c]) - n/N (%)				

Helping vaccine research	548 (95) *	405 (94) *	429 (100)	<0.001
Helping fighting HIV/AIDS	549 (95) *	408 (95) *	429 (100)	0.003
Positive family support	463 (80) *	343 (80) *	426 (99)	<0.001
Meet new people	488 (85) *	359 (83) *	426 (99)	<0.001
Helping the community	553 (96) *	408 (95) *	429 (100)	0.002
Helping the country	556 (96) *	412 (96) *	430 (100)	0.002
Helping research of HIV Vaccine	554 (96) *	411 (96) *	429 (100)	0.007
Perceived as HIV positive	16 (3) *	11 (3) *	237 (55)	<0.001
Perceive as High-risk person for HIV infection	9 (2) *	7 (2) *	233 (54)	<0.001
Unable to have sex intercourse	19 (3) *	11 (3) *	231 (54)	<0.001
People refusing contact	16 (3) *	10 (2) *	227 (53)	<0.001
Preventive vaccine will work - n/N (%)	573 (99) *	426 (99) *	428 (100)	1.0000

a. McNemar's exact test
n/N= numbers participants who answered yes, likely or important/total numbers of participants who answered
b. Likely = composite of somewhat unlikely and very likely
c. Important = composite of important and very important
* Data missing

5.1.4 Facilitators and barriers for HIV vaccine trial participation

Table 5.2 also shows the perceived personal benefits and motives that could serve as facilitators for the decision to participate in an HIV vaccine trial for the 577 participants at screening. Feeling protected from HIV infection (n=531, 92%), learning how to avoid HIV infection (n=529, 92%), and free testing for sexually transmitted infections (n=527, 91%) were the three most commonly reported expected personal benefits of vaccine study participation. Important social motives for participants' decision to participate in a HIV vaccine study were helping the country (n=556, 96%), helping the research of HIV Vaccine (n=554, 96%), and helping the community (n=553, 96%). Perceived barriers to participation in an HIV vaccine study included fear of needles (n=26, 5%), fear of side effects (n=15, 3%) and fear of fetal abnormalities (n=10, 2%). When comparing data from screening visit to the 24-month visit (exit visit) among participants who provided information at both time-points, perceived personal benefits of study participation tended to decrease over time while motives for not participating increased (Table 5.2). No statistically significant differences over time were observed for barriers to participation.

5.1.5 Factors associated with WTP

Bivariate analysis among the participants at screening visit revealed that participants who had their sexual debut between the ages of 15-18 had an odds ratio (OR) of 2.27 (95% CI: 1.02 - 5.04) times more likely to be willing to participate in a HIV vaccine study when compared to those whose sexual debut was before age 15 (Table 5.3). Perceived personal benefits of participating in an HIV vaccine study that were significantly associated in analysis with WTP include learning how to avoid risky behavior (OR 9.37, 95% CI:4.42-19.89), and feeling protected from HIV infection (OR 7.17, 95% CI:3.31-15.50). We also found that HIV vaccine trial attributes, such as having to receive an experimental HIV vaccine (OR 14.84, 95% CI: 6.02-36.6), and being required to donate blood samples (OR 7.69, 95% CI: 2.53-23.35) were associated with WTP. Multivariate analysis was adjusted for variables with $p<0.05$ and age as controller (Table 5.3), and demonstrated that participants were more likely to express willingness to participate in HIV vaccine trials if they were required "to be injected with a vaccine candidate a few times" (aOR 104.74, 95% CI: 9.25-1186.59).

Table 5.3 Binary and multivariate logistic regression analysis of selected factors for willingness to participate in HIV vaccine studies, among participants of the RV363 study, at screening visit

Variables	Willingness to participate			
	Screening visit assessment (n= 577)			
	Bivariate Analysis		Multivariate Analysis[a)]	
	OR (CI 95%)	p-value	aOR (CI 95%)	p-value
Age (categorized ref: *18- 20 years*)				
21-24 years	0.85 (0.39-1.83)	0.675	3.63 (0.55-23.84)	0.179
25-35 years	0.70 (0.30-1.63)	0.412	1.34 (0.24-7.53)	0.736
Gender (ref: *male*)				
Female	1.45 (0.74-2.84)	0.280		
Education (ref: *≥ Primary school completed*)				
Secondary school not completed	0.74 (0.21-2.55)	0.632		
≤ Secondary school completed	0.78 (0.21-2.88)	0.712		
Age of first sexual intercourse *(ref: < 15 years old*)				
15 - 18 years old	2.27 (1.02-5.04)	0.043	2.14 (0.34-13.31)	0.416
≥ 18 years	1.01 (0.35-2.95)	0.988	0.78 (0.08-7.79)	0.831
Perceived Risk for HIV infection (ref*: No risk*)				
Some risk	1.72 (0.49-6.01)	0.395		
Previous to this study did you received information regarding HIV Vaccine research (ref: *No*)				
Yes	0.86 (0.44 1.68)	0.662		

Which of these sources have you received information about HIV vaccine research?				
Hospital/clinic/health worker	0.66 (0.22-1.95)	0.450		
Radio/Tv	0.80 (0.39- 1.66)	0.548		
Friend/relative	1.21 (0.42-3.52)	0.724		
Research center	0.42 (0.05-3.62)	0.433		
Benefits of participating in Vaccine study (ref*: No*)				
Learn how to avoid risky behavior	9.37 (4.42-19.89)	<0.001	8.79 (0.72-106.81)	0.088
Feel protected from HIV infection	7.17 (3.31-15.50)	<0.001	0.15 (0.01-2.25)	0.170
Get free HIV counselling and testing	2.81 (1.33-5.93)	0.007	0.66 (0.05-8.51)	0.747
Receive updated information about HIV/AIDS	1.69 (0.87 3.27)	0.121		
Get small reimbursement	1.43 (0.49 4.13)	0.513		
Be tested for sexually transmitted infection	5.26 (2.43-11.42)	<0.001	2.01 (0.19-21.57)	0.563
Receive regular health care related to research	1.76 (0.91 3.41)	0.094	0.96 (0.20-4.67)	0.959
Get free pregnancy test every 3 months	2.02 (0.91-4.49)	0.086	1.79 (0.42-7.63)	0.431
How likely would you enroll in research study of a new experimental HIV Vaccine if (ref: *Unlikely)*				
Required to receive HIV study Vaccine a few times	14.84 (6.02-36.6)	<0.001	104.75 (9.25-1186.59)	<0.001
Required to donate blood samples	7.69 (2.53-23.35)	<0.001	10.36 (0.68-158.34)	0.093
Required to use contraceptive	3.42 (1.18-9.85)	0.023	2.55 (0.58-11.13)	0.214
How important are the following factors in making a decision about participating in a research study of an experimental vaccine? (ref: *Not Important)*				

Helping vaccine research	0.82 (0.11-6.31)	0.848		
Receiving support from family and friends	1.17 (0.49-2.76)	0.726		
Meet new people	1.34 (0.54-3.36)	0.530		
Helping the community	1.00 (0.13-7.78)	1.000		
Perceived as HIV positive	0.94 (0.12-7.31)	0.949		
Perceive as High-risk person for HIV infection	0.43 (0.05-3.6)	0.436		

a) Adjusted for all significant variables with p<0.05 and age as a controller;
OR Odds Ratio;
CI Confidence Interval;
aOR Adjusted Odds Ratio

Among the 430 participants who stayed through the course of the study, results from the GEE binary logistic regression (screening visit and exit visit) showed that perceived risk for HIV infection (aOR 1.90, 95% CI: 0.99-3.63), wanting to learn how to avoid risk behaviors (aOR 3.33, 95% CI: 1.61-6.86) and feeling protected against HIV infection (aOR 2.24, 95% CI: 1.07-4.7) were associated with willingness to participate in HIV vaccine studies (Table 5.4).

Table 5.4 Multivariate analysis using generalized estimation equation of factors associated with willingness to participate in HIV vaccine studies, among participants who complete the RV363 study (screening visit and exit visit)

Variables	**GEE Analysis**	
	aOR (CI 95%)	**p-value[c)]**
Age (categorized ref: *18- 20 years*)		
21-24 years	0.88 (0.41-1.89)	0.743

25-25 years	0.77 (0.34-1.71)	0.515
Gender (ref: *male*)		
Female	0.81 (0.42-1.58)	0.545
Age of first sexual intercourse *(ref: < 15 years old*)		
15 - 18 years old	1.76 (0.77-4.05)	0.181
≥ 18 years	1.32 (0.41-4.21)	0.643
Perceived Risk for HIV infection (ref: No risk)		
Some risk	1.90 (0.99-3.63)	0.053
Which of these sources have you received information about HIV vaccine research?		
Friend/relative	1.61 (0.4-6.44)	0.503
Benefits of participating in Vaccine study (ref*: No*)		
Learn how to avoid risky behavior	3.33 (1.61-6.86)	<0.001
Feel protected from HIV infection	2.24 (1.07-4.7)	0.032
Get free HIV counselling and testing	0.62 (0.27-1.44)	0.267
How important are the following factors in making a decision about participating in a research study of an experimental vaccine? (ref: *Not Important)*		
Helping the community	2.62 (0.55-12.42)	0.225
Perceive as High-risk person for HIV infection	0.34 (0.06-2.01)	0.236
Unable to have sex intercourse	3.12 (0.76-12.85)	0.115
Not being able to contact people	2.17 (0.63-7.42)	0.217

a) Adjusted for age; gender; age of first sexual intercourse; perceived risk for HIV infection; which of these sources have you received information about HIV vaccine research?; benefits of participating in vaccine study; How important are the following factors in making a decision about participating in a research study of an experimental vaccine?

GEE Generalized estimation equation for binary logistic regression for screening and exit visit

aOR Adjusted Odds Ratio;

CI Confidence Interval;

5.2 Study II

5.2.1 Participants Characteristics

Between February 2017 and March 2018, 31 of the 38 TaMoVac II subjects were enrolled in this study (study II) and answered the questionnaire, 10 participants did not return for the 2 visit, and 21 answered the same questionnaire at visit 2. At visit 1, 12 IDI were conducted (6 female vs 6 male) participants, and 3 FGD, 1 with women only (4 participants), 1 with men only (6 participants) and a mixed group (2 female vs 3 male participants). Of the 31 participants who accepted to participate in this study, 11 (35%) were men, with the median age being 24 years. Most of the participants were single (74%), of whom 65% (n=15/31) were women. Of the 11 (35%) participants that were attending or completed university, 64% (n=7/11) were women (Table 5.5). The reason for participants drops out was lack of time, and 60% (n=6/10) were women under 24 years old.

Table 5.5 Socio-Demographic variables of 31 previous participants of a Phase-II HIV vaccine clinical trial conducted in Maputo City

Socio Demographic Variables	**Visit 1 N=31**	**Visit Status [b)]**	
		Drop-out (n=10)	**Completed Visit 2 (n=21)**
Mean age in years (±SD)	24.2 (2.41%)	23.6 (2.22)	24.5 (2.5%)
Age, categorized			
21-24	21 (68%)	7 (70%)	14 (67%)
25-31	10 (32%)	3 (30%)	7 (33%)
Sex			
Male	11 (35%)	1 (10%)	10 (48%)
Female	20 (65%)	9 (90%)	11 (52%)
Marital status			
Single	23 (74%)	8 (80%)	15 (71%)
Cohabiting/Married	8 (26%)	2 (20%)	6 (29%)
Monthly Income (metical's)			
None	15 (48%)	6 (60%)	9 (43%)
2.500 – 20.000	11 (36%)	4 (40%)	7 (33%)
> 20.000	4 (13%)	0	4 (19%)
Refused to answer	1 (3%)	0	1 (5%)

Level of Education [a)]			
Primary	1 (3%)	1 (10%)	0
Secondary	19 (61%)	8 (80%)	11 (52%)
University	11 (36%)	1 (10%)	10 (48%)

a) For the university level included those that have finished the secondary level but were taking a university degree or already had one. For the primary and secondary level, we included those that had finished that level and were not enrolled in any the next level.

b) Visit status - between participants that did not return for the second visit (dropouts) and those that returned (completed visit 2).

5.2.2 HIV Research Knowledge

HIV Knowledge. The results of the in-depth interview showed that participants knew that HIV is caused by a virus, and that progression to the Acquired Immunodeficiency Syndrome (AIDS) is when the person is infected and does not comply with the treatment and has harmful habits (drinking and smoking).

" *It is a virus that, a virus that when it is not treated, with time, that is, when it is not discovered in time, it ehhh how it is, it grows until it reaches a very complicated phase … is that it is, HIV/AIDS, is in´t*?" – Male participant (IDI)

The most common ways of transmission described by the participants where sexual intercourse without using condom, and the use of sharp objects.

"*anyone can get HIV, as long as they are in a vulnerable situation. . ., unprotected relationships, contact with blood, contaminated objects, needles, etc. blood transfusion too*" – Female participant (IDI).

Participants stated that the most affected by HIV are children, young women and pregnant women.

"*I think that women have to be more aware, especially pregnant women, because sometimes they have HIV-AIDS and sometimes they have so much psychological damage, they even think that if the child is born with a virus HIV, whether born or not, does not change anything and then as for teenagers, I believe they are the most affected* " – Female participant (IDI).

HIV Research Knowledge. In general, the participants were aware of what research was, and had a good knowledge of the objectives and procedures of clinical trials.

"*they explained it well, they had the patience to explain, from what I realized, I participated in TaMoVac II. TaMoVac I, was to study if the vaccine candidate was safe, now at TaMoVac II, it´s*

also to know if it was safe and to know when they give the vaccine to someone, if it´s possible to know if that vaccine candidate produces antibodies or antibodies in the body of that person" – Male participant (mixed FGD).

"*From what I remember they explained that ahh, this study was to study the safety of the vaccine to see the immune response of the organism, how will the organism react to the vaccine, also know what the dosage would be for each person , depending on the immune system of each one*" – Female participant (mixed FGD).

HIV Vaccine Trial Knowledge. When asked if an experimental HIV vaccine could protect against HIV infection, 6 out 31 participants answered yes, 5 out 31 believed that when receiving the candidate HIV vaccine, they could easily become HIV infected. If a participant had a HIV positive result in a rapid test, 3 out 31 participants believed it meant that they are protect from HIV infection, and 5 out 31 that it meant that their children would be protect as shown in Table 5.6.

Table 5.6. Independence analysis between HIV vaccine knowledge by visit status, among 31 participants of a previous HIV vaccine trial

HIV Vaccine Knowledge Variables - *ref: No* [a, b]	Visit 1 N=31	Visit Status [c] (N=21)		p-value[d]
		Visit 1	Visit 2	
1. **Is it proven that the candidate HIV Vaccine used in TaMoVac II, can protect against HIV infection?**	6 (19%)	2 (10%)	1 (5%)	0.564
2. **HIV vaccine Phase I and II clinical trials, can include people who are HIV-negative?**	26 (84%)	17 (81%)	20 (95%)	0.179
3. **HIV vaccine Phase I and II clinical trials, can include people who are HIV negative, but at risk of getting infected with HIV.**	10 (32%)	7 (33%)	5 (24%)	0.527
4. **HIV vaccine Phase III clinical trials, can include people who are HIV negative, but at risk of getting infected with HIV.**	13 (42%)	10 (48%)	5 (24%)	0.132
5. **HIV vaccine Phase III clinical trials, can include people who are HIV -positive?**	6 (19%)	3 (14%)	2 (10%)	0.655
6. **The goal of HIV vaccine clinical trials, is to find a HIV vaccine that can protect against HIV infection?**	30 (97%)	20 (95%)	21 (100%)	0.317
7. **A preventive HIV vaccine, can be used to cure people infected with HIV?**	4 (13%)	2 (10%)	2 (10%)	1.000
8. **In clinical trials, Placebo can be used as research product?**	25 (81%)	16 (76%)	19 (90%)	0.257
9. **In clinical trials, Vaccines can be used as research products used?**	29 (94%)	21 (100%)	21 (100%)	1.000
10. **One of the goals of clinical trials, is to evaluate if the vaccines are safe?**	30 (97%)	21 (100%)	20 (95%)	0.317

11. **The fact that you received a candidate for HIV vaccine, makes it easier for you to become HIV infected?**	5 (16%)	3 (14%)	2 (10%)	0.655
12. **Is it very likely that because you received a HIV vaccine candidate, you may have health problems caused by the candidate vaccine?**	4 (13%)	2 (10%)	1 (5%)	0.317
13. **A person who received the candidate for HIV vaccine may have a HIV-positive result in the rapid tests, even if not infected?**	27 (87%)	18 (86%)	20 (95%)	0.317
14. **If a TaMoVaC II participant has an HIV-positive result in the rapid test, is the same as saying that he is protected by the vaccine against HIV infection?**	3 (10%)	0	2 (10%)	0.157
15. **If a TaMoVaC II participant has an HIV-positive result in the rapid test, is the same as saying that he is infected with HIV?**	3 (10%)	2 (10%)	1 (5%)	0.564
16. **A HIV-positive test result induced by the HIV vaccine candidate can last for more than 5 years, in a volunteer who received a HIV vaccine candidate during the clinical trial?**	6 (19%)	5 (24%)	2 (11%)	0.257
17. **If a TaMoVaC II participant has an HIV-positive result in the rapid test, is the same as saying that is sexual partner is protected?**	3 (10%)	2 (10%)	2 (10%)	1.000
18. **If a TaMoVaC II participant has an HIV-positive result in the rapid test, it means that his children may be protected by against HIV infection**	5 (16%)	4 (19%)	1 (5%)	0.1780
19. **If a TaMoVaC II participant has an HIV-positive result in the rapid test, it means that his children may have malformations at birth?**	3 (10%)	2 (10%)	21 (100%)	0.157

20. If a vaccine that protects against the HIV infection was discovered, would you like to be vaccinated?	28 (90%)	19 (91%)	21 (100%)	0.157

a. One answer per question and presented the participants who answered for yes.

b. **Correct answers (a=yes; b=no):** 1b; 2a; 3b; 4a; 5b; 6a; 7b; 8a; 9a; 10a; 11b; 12a; 13a; 14b; 15b; 16a; 17b; 18b; 19b (we don´t know)

c. Analysis performed among participants that responded to the questionnaire at visit 1 and visit 2

d. McNemar's exact test for those that did visit 1 and 2.

When asked if they would like to be vaccinated, if a vaccine that protects against the HIV infection was discovered, 3 out 31 participants said no, mainly because they considered themselves to be at low risk for HIV infection and because they don´t like vaccines. As for the other participants that would be interested in being vaccinated, 19 were interested because they would want some protection from HIV infection, and 9 because they would like full protection against other form of HIV transmission, other than sexual transmission (data not shown). Between visit 1 and 2 we did not show a significance difference regarding HIV vaccine knowledge.

5.2.3 HIV Stigma

HIV infection perception. HIV infection is seen as a problem, not as a serious disease by the participants and society. Mainly because: unprotected sexual intercourse with multiple partners have been publicized as one of the main forms of transmission; talking about sexual relations is a taboo in the society; and because the infected person must change its habits and routines and must take pills for the rest of his life, to prevent AIDS which is seen as a serious disease by the participants.

"Because you are going to die taking pills, you are going to die taking pills and the society, I think it is the way the disease was disseminated nor, there is still a lot of preconception, when... someone knows that you have HIV, it was because you had unprotected sex, but there are many other ways of contracting HIV, but people all stop right there and discriminate against people who have HIV, they have many problems to socialize with, is it a problem because the people when they have that disease never feel good, never have support from people, so it's a problem" - Female participant (IDI).

Stigma as a barrier for trial participation. Social stigma is a barrier to the adoption of preventive measures and participation in studies of experimental HIV vaccines. It inhibits young people from obtaining condoms, even if they are free, because they do not want to be associated with people who have multiple sexual partners.

"Even in hospitals there are people who are afraid to take the condoms away… Humm, because there are a lot of people who will see them, and they are afraid, if I take the condom what will those people think" – Male participant (IDI)

It could also impair participation in studies of experimental HIV vaccines, because people might look at the participants as being HIV positive, consider that participants have risky sexual behaviors due to their participation in clinical trials or have distrust towards the objectives and procedures of experimental HIV vaccine studies.

"*They will not understand (referring to clinical trials), they will say hmm this guy has AIDS, they are injecting this guy with something, because the vaccine application comes with... how you call it ... comes with ... there are some let's say, HIV substance in it, is what they explained to us" –* Male participant (IDI)

"*There is still a lot of taboo in relation to the disease, so for people to accept it (referring to clinical trials) would be a little difficult"* – Female participant (IDI)

5.2.4 Sexual Behavior

Risk Behavior. Was defined by the participants as having sex without using a condom, having multiple sexual partners, exchanging sex for money and the use of injectable drugs.

" *in my opinion the people who are most at risk are people who have risky behaviors, and what are risky behaviors, it's having multiple partners ... people who share piercing objects, in this case I mean people who consume injectable drugs in this case and also, to some extent, sex workers these are the potential potentials"* – Male participant (IDI)

"*…unprotected relationships, contact with blood, contaminated objects, needles, etc. blood transfusion too… If I am going to have unprotected sex with my boyfriend from the moment, I go unprotected I am vulnerable"* – Female participant (IDI)

The groups that were mentioned as having a high risk for HIV infection are women, especially adolescents and young people, as they are economically vulnerable and/or dependent on their partners, and therefore are unable to negotiate condom use, young men who, due to peer pressure (from other young men), have several sexual partners to maintain a virile status in society.

"*... We people like things a lot you know, people like things a lot, I think there are a lot of people who do … Especially girls … They like things, a girl that at home, for example, does not receive any value, … then a guy promises I'll give you 100 metical's, 500 metical's, she will be able to show her friends that she has lunch, she'll buy a hamburger she'll also buy*" – Male participant (IDI)

"*Some people think of themselves as superheroes, super men, … They can't catch these diseases, , they do and undo . . . people who say like this, I can be with that woman, I can be with this one, I do whatever I want, I have nothing to do with protection, whatever, … Whatever I want , as I want*" – Male participant (IDI)

HIV Risk Assessment. Almost all participants recognized that they had some risk, which they considered was higher before entering the study, because they did not use condoms regularly and had multiple sexual partners.

"*I currently evaluate myself as a low risk person... before I was part of the study, or rather, before being part of the study, I could consider myself a middle-level person because ready, I didn't have, I didn't have several partners but I was one person who had relationships, relationships with a short time span that involved several partners, even though they were not multiple, but because they were several, that already put me in this situation… Nowadays I have a single partner, a person who lives with me and with the knowledge I have acquired allows me to make a self-*

assessment, analyze to better evaluate the conditions so that I do not expose myself" – Male participant (IDI).

Some participants, 4/31 (13%) had more than one sexual partner, and 20/31 (65%) did not use condoms regularly, mainly because they trusted their partner. Study participation influenced participants sexual behavior, with 24/31 (77%) acknowledging that they changed their behavior (Table 5.7).

Table 5.7 Sexual Behavior analysis of 31 participants of a previous HIV vaccine clinical trial, by visit status

Sexual Behavior *ref: No* [a)]	**Visit 1 N=31**	**Visit Status[c)] (n=21)**		**p-value[d)]**
		Visit 1	**Visit 2**	
In the past 3 months have you had vaginal or anal sexual intercourse?	31 (100%)	21 (100%)	20 (95%)	1.000
In the past 3 months have you had sex with more than one sexual partner?	4 (13%)	4 (19%)	2 (10%)	0.4142
In the past 3 months, did you use condom during sexual intercourse?				0.566
Never	4 (13%)	2 (10%)	2 (10%)	
Rarely (less than half of sexual intercourse)	1 (3%)	1 (5%)	3 (15%)	
Sometimes (half of sexual intercourse)	15 (48%)	9 (43%)	7 (35%)	
Always (all sexual relations)	11 (35%)	9 (43%)	8 (40%)	
The reason why you did not use a condom:				
Sexual partner does not want to use a condom	2 (6%)	0	2 (10%)	1.000
Because you trust your partner	13 (42%)	8 (38%)	8 (38%)	1.000
Don´t know	2 (6%)	1 (5%)	0	1.000
In the last 3 months, of the people with whom you had sex, there was someone who was HIV positive or who you suspected?				
Yes	1 (3%)	11 (5%)	0	1.000
Don´t know	2 (6%)	2 (10%)	3 (15%)	
In the past 3 months, have you been diagnosed with any sexually transmitted infections?	1 (3%)	1 (5%)	0	0.3173
Regularly drink alcohol [c)]	6 (19%)	5 (24%)	0	0.0253

During the past 3 months, have you had sex while under?				
The effect of alcohol	10 (32%)	7 (33%)	3 (14%)	1.000
The effect of drugs	0	0	0	1.000
During the past 3 months, how would you rate your risk of acquiring HIV infection?				
None	2 (7%)	1 (5%)	1 (5%)	1.000
Low	20 (67%)	13 (65%)	12 (57%)	
Moderate	6 (20%)	4 (20%)	8 (38%)	
High	2 (7%)	2 (10%)	0	
The reason you rate your risk of acquiring HIV infection is:				
Trust the partner	2 (6%)	0	1 (5%)	1.000
Only had sexual intercourse with one partner	8 (26%)	8 (38%)	5 (24%)	
Did not had risk behavior/Has protected sexual intercourse	11 (35%)	5 (24%)	11 (52%)	
Has risk behavior/Had unprotected sexual intercourse	6 (19%)	4 (19%)	3 (14%)	
Can´t guarantee 100% protection	3 (10%)	3 (14%)	1 (5%)	
Suspects the partner is HIV positive	1 (3%)	1 (5%)	0	
Do you think that the fact that you participated in a clinical trial of the candidate for the HIV vaccine, influenced in your sexual behaviour?	24 (77%)	16 (76%)	15 (71%)	0.7630
Why do you think that the fact that you participated in a clinical trial of the candidate for the HIV vaccine, influenced in your sexual behaviour?				
Nothing changed – it always protecting himself	7 (23%)	5 (24%)		
Learned to prevent itself better	14 (45%)	8 (38%)		
Changed behaviour, before it had many sexual partners	9 (29)	7 (33%)		

Don't trust his/her sexual partner	1 (3%)	1 (5%)		
Risk Behaviour assessment[c)]				
None	8 (26%)	4 (19%)	7 (33%)	0.3657
Some	23 (74%)	17 (81%)	13 (62%)	

a. One answer per question and presented the participants who answered for yes.
b. defined as more than 35 units per week for men, or 14 units per week for women. 1 unit = 1 beer or 1 glass of wine or a measure of strong alcohol.
c. Analysis performed among participants that responded to the questionnaire at visit 1 and visit 2
d. McNemar's exact test for those that did visit 1 and 2.

5.2.5 Clinical Trial Participation

Interest towards HIV Trial. The decision to participate was individually but being invited by a friend/peer and the curiosity triggered by the knowledge that studies are being carried out to discover an HIV vaccine in Mozambique, led them to seek more information.

"*… I believe that first, if I'm not mistaken, I received an invitation from my colleagues because … I received a little idea, let's participate in the lecture (referring to the information sessions as part of the recruitment process), it is something interesting, I went there too, I heard the lecture, I was interested in wanting to have more detailed information about it and that's when I decided that I want to enter this study too* " – Male participant (mixed FGD).

" *... I, I arrived at CISPOC, an invitation from a TAMOVAC II participant who is part of the study, even at the beginning, my college she said she was taking part in the study and it would be good for me to participate and said she had an appointment scheduled for a few minutes later and said come on, I said come on, I got here, they treated me very well and explained it to me and I stayed*" – Female participant (mixed FGD).

Motives for Trial participation. Being able to actually do something to help to reduce the number of infections in their communities and in the country and contributing to the research for the discovery of an HIV vaccine, where the most common reasons reported by the participants for trial participation. Knowing someone infected with HIV and receiving monetary compensation to pay for transport to come to study site contributed for trial participation and to comply with study visits.

"For me, since I was a kid, I always had that thing about watching superhero movies, Super Man, BatMan, so when this opportunity came I said, I can't be born in this world here and die without doing something positive, I said no , this is also an opportunity to be a super hero, a super hero is not only one who has powers, he is one who helps researchers or helps professionals. Collaborating for a certain just cause, you can also be considered a superhero, no matter how much people say ehh no… are you going to be a guinea pig?" – Male participant (mixed FGD).

"*At first ehhh I didn't know that there would be any compensation, I came for my own motivation after I saw that there would be a hallelujah compensation is an advantage. Tomorrow I don't have to complain that I don't have money (for transportation)*" – Female participant (mixed FGD)

"*Yes, I can say that It was it the reason, yes, to have or know someone close to them who was suffering from this disease that served as motivation for them to stay … I met some relatives who are unfortunately suffering from the same disease*" – Male participants (mixed FGD)

Positive experiences of Participating in a Clinical Trial. Participation in the TaMoVac II was a positive experience for the participants because they were well received by a young and friendly team of research's, received free counselling and learned a lot about HIV prevention. Signing the informed consent was seen as an agreement between the center and the participants, were the duties and rights of the participants and the centers were clear, including the fact that they could leave at any time if they wanted to.

"*No, they were always very good, … that is attention because that is a commitment that we have and we have to honor it, they always treated me very well Dr. Igor, Dr. Patrícia…*" – Female participant (IDI).

" *because when there are normally two young people many times the conversation is better, the conversation is better*" – Male participant (IDI)

"… before participating in the study… That's it, is hearing about it and thinking it is a utopia (HIV infection), and then arriving here to receive explanation - Humhm… concrete examples and simple examples, say look this can be contaminated unprotected, contaminated and everything and call my responsibility…" - Female participant (IDI).

"*One of the rights we had was to know that we could leave the study at any time. We are not in prison, simply because we sign the consent, it does not mean that we should be in prison, we are free to make our own choices*" – Male participant (male FGD)

Negative experiences of Participating in a Clinical Trial. Blood collection discomfort and the duration of study visits were the most common negative experiences participants had. Participants also felt abandoned at the end of the study, by the study team.

"*I don't know if it's still the lady who stayed there, for the collection (blood collection)… and that hurt …you know that there was a time when she even had to prick both arms, to be able to draw blood and it wasn't nice… You had to take a needle and return it to the same arm. I will never forget that day… It was terrible… then the person who is going to do the collection should be skilled"* - Male participant (IDI).

"I have a friend she was outside the country she came back last year when she came back when she came across me the first thing that she asked me, was how was it?... I said I am disappointed, because, the study happened, and we simply serve their interests, the rest no longer matters if they reached those objectives … they should continue to give us that warmth even if it is once a monthly call …, call us and invite us to come here sit discuss and talk about our experiences" – Female participant (IDI)

Social Harm. Nearly all participants 30/31, (97%) revealed to someone that they were participating in a HIV vaccine trial, with parents 21/31 (70%) and siblings 17/31 (57%) being the main people they told. Almost half of the participants 12/31 (41%), did not revealed that they participated because they feared that people would think that they were infected with HIV/AIDS 6/31 (19%) or could become infected at some point 4/31 (13%) (Table 5.8). In general participants received support for important people for them, when they revealed that they participated in a HIV vaccine trial, but they also had some negative experiences, such as receiving negative comments, or be seen as guinea pigs, mainly by family members, peers, colleagues and even health care professionals.

"They called me a coward. I went to this hospital with my boyfriend to do HIV tests and they (referring to health care professional) asked me why you don't do it, I explained if I do it I will be positive because I am participating in TAMOVACH, so they said you are guinea pigs … that will not do anything, they are just making animals of you… they were nurses: Yes, it happens (another Female participant). It happened to me too (another Female participant)" – Female participant (female FGD).

"(*Wowww. Ahhhh.) Are you crazy (mothers' reaction)? What are you thinking about life? What do you want?" - Female participant (IDI).*

"some schoolmates with the time, because sometimes I had to leave a bit early to get there, and I couldn´t do some work with them, so when I told them, they just said you agreed to be a guinea pig … sometimes they even called me a guinea pig" - Female participant (mixed FGD).

Table 5.8 Social Harm descriptive analysis of 31 participants of a previous HIV vaccine clinical trial

Social Harm Variables	**Visit 1 N=31**
The following questions refer to the period during your participation in the trial (from the beginning to the end of the study)	
Have you ever told anyone that you participated in a HIV vaccine candidate's clinical trial?	30 (97%)
Father/Mother	21 (70%)
Siblings	17 (57%)
Cousins	3 (10%)
Partner (Boyfriend/Husband)	16 (52%)
Classmate	11 (37%)
Work Colleague	2 (7%)
Boss	0
Doctor	2 (7%)
Nurse	2 (7%)
Church / Religion / Worship Staff	2 (7%)
The person you told you agreed with your participation in the HIV vaccine clinical trial?	28 (93%)
Was there anyone you did not tell about your participation in in the HIV vaccine clinical trial, but you would have like it to?	13 (42%)

The reasons you did not tell that you participated was because the person could think that:	
You were infected with HIV / AIDS, because you participated in the trial vaccine clinical trial	6 (19%)
That you had a promiscuous behavior, such as exchanging goods, money or services by sex, because of your participation in a HIV Vaccine clinical trial	2 (7%)
That you have multiple sexual partners	1 (3%)
That you could be infected because of your participation in a HIV Vaccine clinical trial	7 (23%)
That you could have health problems because of your participation in a HIV Vaccine clinical trial	2 (7%)
That you are being a "guinea pig" in an experiment, with foreign scientists	4 (13%)
Would not be able to explain that you could have a positive result in the HIV rapid test and not being infected with HIV	1 (3%)
It is a personal matter, and it does not concern other people	1 (3%)
What would be the consequences if you had revealed that you participated in *in a HIV Vaccine clinical trial*?	
Being rejected by family members	2 (7%)
Be rejected by your partner	2 (7%)
Failing to have a new relationship	1 (3%)
During your participation in *in a HIV Vaccine clinical trial* have you received/ heard any negative comments or reactions for example?	
Your principal sexual partner left you because of your participation in the HIV Vaccine clinical trial	1 (3%)
Jokes of you being a "guinea pig" in an experiment, with foreign scientists	4 (13%)
Being discriminated in your workplace, by your colleagues don't want to hang out with you because of your participation in the HIV Vaccine clinical trial or losing your job	1 (3%)
Community comments on the negative effects of the HIV vaccine candidate	1 (3%)
The following questions cover the period from the end of the HIV Vaccine clinical trial until the time of the interview	
After the completion of the HIV vaccine clinical trial, did you tell someone about your participation in the HIV vaccine clinical trial?	17 (55%)
Father/Mother	1 (3%)
Siblings	3 (10%)

Cousins	1 (3%)
Partner (Boyfriend/Husband)	4 (13%)
Classmate	2 (7%)
Work Colleague	3 (10%)
Boss	0
Doctor	0
Nurse	0
Church / Religion / Worship Staff	1 (3%)
In your opinion the reaction was	
Positive (approval or other positive comment)	4 (13%)
Neutral (did not express any feelings or opinions)	10 (32%)
Negative (did not express any feelings or opinions)	3 (10%)

a. One answer per question and presented the participants who answered for yes.

5.2.6 Decision process to participate in HIV vaccine trial

Decision-making process to participate in the HIV vaccine trial can be explaining using the 5 constructs of the Health Belief Model (Figure 5.2). Awareness of HIV and HIV prevalence in the country – *HIV knowledge theme* - associated with knowing the behaviors that increase the risk to HIV acquisition – *HIV risk theme*- and being able to assess one´s own risk to HIV infection - *HIV risk assessment theme*- contributes to HIV susceptibility construct. Participants perception that HIV infection is a problem because if affects the way of life and that AIDS is in fact the serious problem – *HIV infection perception theme*- which influences HIV infection severity construct. Barrier's construct is composed by *stigma as a barrier for trial participation theme, by social harm theme* and *negative experiences of participating in a HIV vaccine clinical trial theme*. Free and regular medical care and counseling as part of the *positive experiences of participating in a HIV vaccine clinical trial theme* plus transport compensation and personal benefits as part of *motives for trial participation theme* contrive the Benefits construct (Figure 5.2). Triggering stimuli that directly influenced participation were supported by *interest regarding HIV clinical trial* theme and motives *for trial participation themes.*

Figure 5.2 Description of the decision-making process to participate in a HIV vaccine trial using the components of a Health Belief Model among 31 participants of a phase II HIV vaccine trial

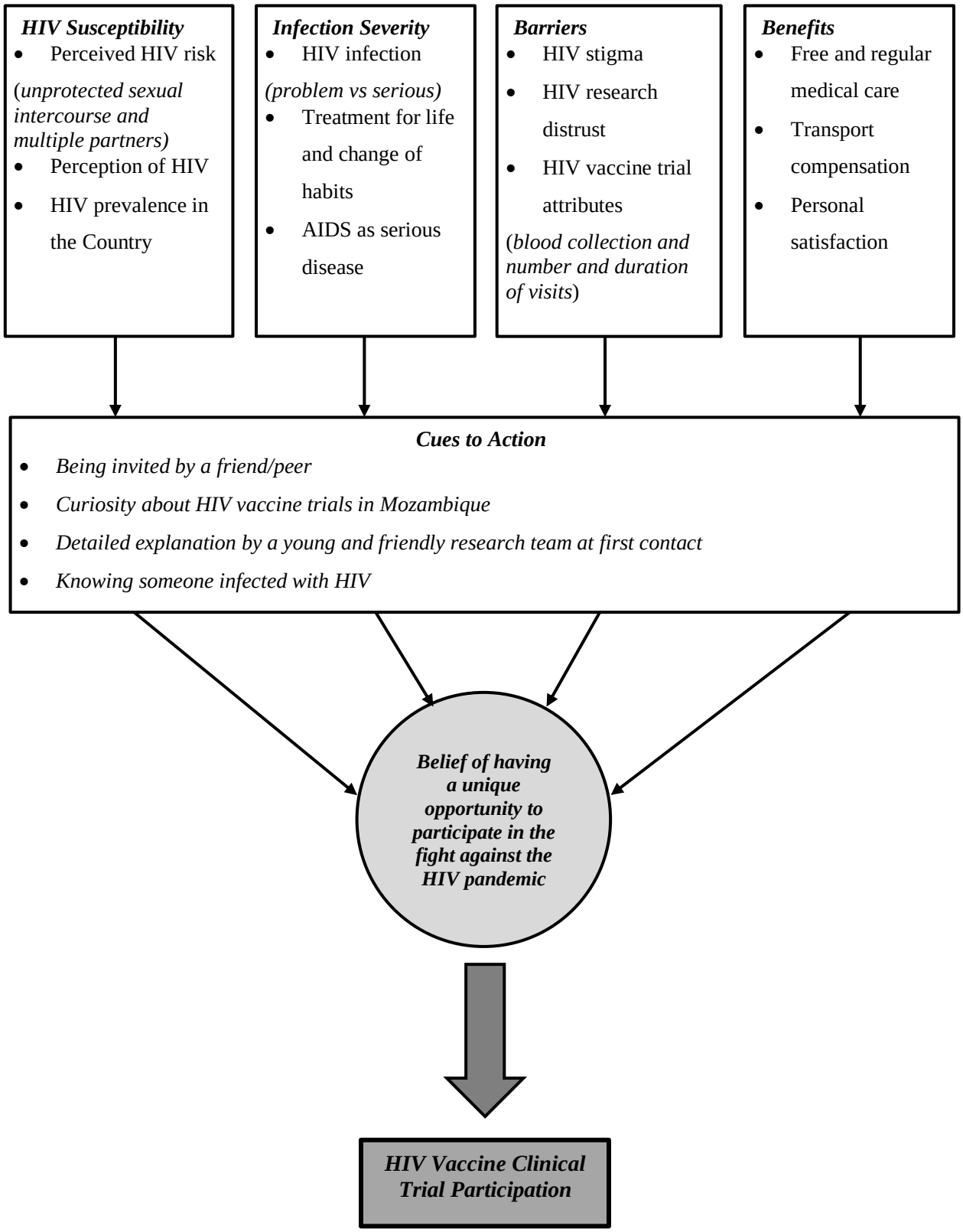


Table 5.9 provides a profile of the sexual behavior and experiences that participants had during the HIV vaccine trial. Of notice is the self-reported reduction in the perception of the risk of HIV infection acquisition and the fact that participants felt abandoned after the trial completion.

Table 5.9 Sexual Behavior and HIV vaccine trial experiences profile of 31 participants of a previous phase II HIV vaccine trial

Sexual Behavior Profile	Clinical Trial Experiences
• *Participants had some risk behaviors and were aware of their risk for HIV infection* • *Most of the participants did not use condoms and some had multiple partners* • *Sexual behavior changed due to trial participation*	• *Participants learned more about HIV infection and their health* • *Participants had negatives experiences related to blood collection and visit duration* • *Participants suffered negative comments from family and peers/colleagues*

6 Discussion

Hypothetical willingness to participate in HIV vaccine studies was high among young adults at risk for HIV in a low-income peri-urban area in Maputo, Mozambique. The results of the RV 363 incidence study (study I) reinforce the practicality of conducting HIV vaccine trials in Maputo, already established by the successful implementation of the first 2 HIV vaccine trials in Maputo. Despite a high prevalence of hypothetical willingness to participate among potential participants of future HIV vaccine trials does not guarantee actual willingness to participate, this information is still important. Knowing where there is the greatest likelihood of finding volunteers with the intention to participate in future preventive trial of a vaccine against HIV can guide recruitment strategies. More important is to describe the decision-making with actual willingness to participate, which can be achieve by evaluating the motivations for trial participation among participants of previous HIV vaccine trials conducted in Maputo city. This can result in reducing both the time needed for recruitment and the costs of implementing trials, accordingly.

In a survey conducted in China with man who have sex with man 76.6% (n=626) were willing to participate in a preventive HIV vaccine trial [113]. In contrast only 50.6% (n= 450) of young adults years old recruited at a youth clinic in Tanzania expressed their willingness to participate in a HIV vaccine trial [139]. Still in Tanzania, 61% (n=329) of police officers stated that they would volunteer to participate in a HIV vaccine trial [98]. Both studies were conducted in the capital city, Dar es Salam. Willingness to participate among fisher-folk communities in Uganda was 89.3% (n=2191), but it varied between island communities (90.4%) and the lakeshore communities (85.8%) [144]. These results are consistent with findings from Inugu et al. [35], where the authors concluded that willingness to participate in HIV vaccine trials varied by region population, and within countries.

Young adults and women tend to have a high incidence of HIV infection, and play an important role in the ongoing transmission of HIV [9, 91]. This reinforces the need for HIV vaccine trials and willingness to participate studies to target the largest number of women and young volunteers [92-94]. Participants from the RV 363 study (study I) consisted of young adults most-at-risk for HIV infection, of whom almost half were women, identified and recruited from the general community. In contrast, other HIV vaccine preparedness studies specifically targeted populations that are vulnerable and socially stigmatized such as man who have sex with man and female sex workers [101, 113, 140]. Despite being considered at low-risk for HIV infection at

enrollment, participants from a previous phase I and II HIV (TaMoVac I and II) vaccine clinical trials conducted in Maputo were also recruited from a cohort of young adult's set-up specifically for these trials [114, 115, 121], confirming the capacity to recruit young adults to participate in HIV vaccine trials in Maputo city. We found high rates of willingness to participate results for both males and females. Meque, et al. [128] in a study conducted in another province in Mozambique, found that WTP was 77.8% (n=1019) for females and 57.6% (n=97) for males, whereas in the fisher-folk communities study in Uganda, willingness to participate was lower in women when compared to man (87.3% vs 91.2%) [144].

HIV risk has been associated with willingness to participate in HIV vaccine trials in different directions. In a study conducted with both males and females (61.6% vs 38.4%) in Kenya, they found perceived risk to HIV infection to be associated with wanting to participate in HIV vaccine trial [145]. In a survey conduct in India perception of not being at risk was the major reason for married women not wanting to participate in preventive HIV vaccine clinical trial [146], in contrast in a study conduct with black man who have sex with man and transwomen in the USA, those who reported engaging in risk behaviors were less likely to participate in a HIV vaccine trials[140]. In both study I and study II, the majority of our participants (both male and female) acknowledge at least some risk for HIV acquisition which corroborates the theory that perceived risk for HIV infection is related to willingness to participate [140, 147, 148].

Altruism was the most frequent motivator for WTP among the RV 363 incidence study and for actual participation among the TaMoVac II participants, and much of the same results were reported in other studies [105, 128, 138, 145], meaning that study participants see their participation as their personal contribution to the fight against HIV. Perceived personal benefits of participating in HIV vaccine trial, such as feeling protected from HIV infection, learning how to avoid HIV infection, free testing for HIV and sexual transmitted infections have also been reported [105]. Receiving monetary compensation for transportation costs contributed to trial participation and was also reported in other studies [145]. The most common barrier reported among participants of the HIV incidence cohort study was fear of needles, similar to other reported results [147]. Fear of fetal abnormalities was also stated, but we did not find it in other reported results. This is important, as it can impede young women from participatingm especially young women, whom in the sub-Saharan Africa context are pressured to establish a family in the early stages of their lives, which includes becoming pregnant. Stigma associated with HIV was identified by the study II participants as a potential powerful barrier, since participants might be seen as being HIV

positive or considered to have promiscuous sexual behavior due to their participation in HIV vaccine trials. Distrust towards HIV trial procedures and objectives was another potential barrier reported.

Low-HIV infection and HIV vaccine trial research knowledge has been associated with stigma and distrust regarding HIV vaccine research and HIV vaccine [149, 150]. Knowing how HIV can be transmitted and being able to assess one´s own risk is the first step to adopt any prevention strategy, including participating in HIV vaccine trials. Mozambican adolescents and young people have a low knowledge regarding HIV infection and HIV prevention[15] [50]. This highlights the need to increase national communication strategies with the aim of increasing HIV infection awareness and knowledge. Almost all participants indicated that the purpose of a vaccine is to prevent illness, but only a small portion of the participants of the RV 363 study reported having received information about HIV vaccine research prior to their participation. The proportion of sources of information changed significantly from screening to exit visit, as information from friends and relatives dropped, but internet, poster and research center information increased. In a study conducted in a rural population cohort with high HIV prevalence in Rakai, Uganda, awareness of HIV vaccines increased between baseline and follow-up (68% to 81%), and the main source of information was the study education program, followed by radio/television and hospitals/newspapers [151]. One hypothesis could be that because of their participation in the RV 363 study, participants learned how to use more accurate sources of information and, consequently, to discern what they thought was the correct information related to HIV vaccine research. This may have led them to assume that, whatever information they learned about HIV vaccine research prior to their participation, which they thought was correct during screening, at the exit visit it was no longer valid. Important to highlight is that the RV 363 incidence study did not have any educational program that aimed to increase HIV vaccine awareness among its participants. Participants from the phase II HIV vaccine trial (study II) reported that one of the biggest benefits of their trial participation was that they have acquired more knowledge about HIV and HIV research including clinical trials. De Bryun et al [152] in an assessment conducted among 240 school-going youths from Soweto, South Africa reported that

[15] Knowing that the correct and consistent use of condoms during sexual intercourse and having only one uninfected sexual partner can reduce the risk of contracting HIV, knowing that a healthy-looking person can have HIV and rejecting two most common misconceptions related to HIV prevention or transmission (contracting HIV through mosquito bites or eating together with an HIV-infected person).

receiving update information about HIV infection was associated with willingness to participate in future HIV vaccine trials.

Willingness to participate remained high among the participants who completed the 24-month follow-up, but no assurance should be taken that actual WTP will be high. In a 2-year follow-up cohort study conducted in Kenya, Nyasani et al. [138] reported that 86 of 100 participants who expressed their willingness to participate in a HIV vaccine trial and were contacted afterwards, only 30% (n=26) actually consented to participate in a phase-I HIV vaccine trial. As in study I (RV 363 incidence study), they also did not provide cohort participants with HIV vaccine research information. Asiki et al. [153], found that willingness to participate among high-risk men and women in Uganda decreased after the participants received information regarding HIV vaccine trials attributes. The principal barriers were number and duration of visits, being injected with an experimental vaccine, being required to delay pregnancy, and blood collection [138, 153]. In study I, feeling protected against HIV infection, being required to receive the HIV experimental vaccine a few times and being required to donate blood samples were independently associated with greater willingness, highlighting the need to consider the high rate of willingness to participate with caution. Equally important, was the fact that the rate of perceived benefits associated with willingness to participate decreased at the end of the study. This could be for several reasons: 1) participants felt that there was not more to learn, since they received counselling for HIV risk behavior reduction during the cohort study and 2) participants might have learned more about HIV vaccine trials and, especially the fact that there is no guarantee of protection from an experimental vaccine.

Paramount to highlight, is the erroneous perception that receiving an experimental HIV vaccine, could provide protection against HIV, which can lead to risk compensation due to trial participation. This can be explained by the fact that no information was given on HIV vaccine research and its goal to prove the efficacy of experimental vaccines among participants of study I. Study II objectives and procedures were discussed as part of the informed consent process during immunization and follow-up visits, but still, few participants believed that if it was confirmed that they received the experimental vaccine they could be protect against HIV infection and/or become easily infected. Meaning that clinical trial staff must provide clear messages regarding HIV vaccine study procedures and ensure that they are review and discuss throughout the duration of the study.

Different factors associated with the intend to participate in HIV vaccine trials have been identified, and their importance varies between populations and time [35]. Identifying motives and barriers alone cannot guarantee that potential participants of future HIV vaccine trials can participate in HIV vaccine trials. This approach focuses more on the outcomes, instead, focus should be on the process of decision-making. It is important to contextualize the decision-making process to participate in a HIV vaccine trial in order to develop clear frameworks for recruitment strategies [33]. Knowing how participants reason their decision to participate in a HIV vaccine clinical trial can be understand by using the components of the Health Belief Model. HIV transmission and prevention knowledge enable the participant to evaluate his own risk of HIV acquisition. HIV susceptibility is also influence by HIV prevalence awareness that HIV is a common disease. HIV it's a discomfort condition especially because, the infected person has to change is way of life, having to take pills for the rest of his life since currently there is no cure. In a context where access to healthcare services is not equal to all, free and regular care provide by the vaccine trials is clearly a benefit. Removing the constrain of not having to worry about the cost of transportation is important, especially if we consider that most of the participants in the Maputo city are students and were unemployed. Despite being a potent barrier HIV stigma can be outweighed by personal satisfaction of contributing to HIV vaccine research. Where, how and who conveys HIV vaccine research information to the volunteer can stimulate their interest in participating or not. Being able to identify himself with other participants and the study team staff proved to be important. Noteworthy was the fact that the participants felt at ease with the study team, as they were able to identify with the researchers, since in the eyes of the participants, the study team was composed of many young people. Knowing someone infected with HIV who might suffer stigma associated with HIV infection and the belief that participating in a HIV vaccine trials presents itself as a unique opportunity to contribute to the reduction of HIV infection through participation in a HIV vaccine trial, led to actual participation in a phase II HIV vaccine clinical trial.

Ensuring that participants stay through the duration of a study is crucial for the successfully implementation of HIV vaccine clinical trial [33], and its necessary to evaluate and develop retention strategies to inform the implementation of future trial [148, 154-156]. Retention in the study can be affected by participants sexual behavior and the experiences lived during the implementation of the trial [107]. Most HIV vaccine trials offer a preventive package that includes HIV risk behavior reduction counselling which aim to maximize prevention [157]. Another concern is the risk compensation behavior, when participants engage in higher risk sexual behavior

due to their participation in a HIV vaccine study [102-104]. Experiences lived during trial participation can include negative effects on the personal and social life of participants as result of their participation. This can result in the participants withdrawing the study in order to avoid more discomfort [33, 105, 107]. Addressing these issues can prevent high rates of lost to follow-ups during clinical trial implementation. It is important to characterize the participants who have withdrawn from study participation and understand their reasons, as well as to assess the effects of participating in clinical trial of an experimental vaccine in order to identify the potential factors that could influence the decision to withdraw or originate some discomfort in the participants' lives.

Although willingness to participate (hypothetical) was high and remained high among the participants of the RV 363 incidence study, 25% (n=147) of the participants did not complete the willingness to participate questionnaire at the final visit. This group had the highest proportion of individuals with the lowest levels of education. We postulate that these 147 individuals who did not respond to the willingness to participate questionnaire at the final visit, can resemble actual drop-out individuals in actual HIV vaccine trials, therefore, making it important to characterize this group, in order to identify potential factors associated with HIV trials loss to follow-up. In an HIV incidence study conducted in Kenya, Nyambura et al [158] found that being female and having a higher level of education was associated with greater risk for missing a study visit.

Participants from the TaMoVac II trial knew how to define risk behavior and considered themselves to be at low risk for HIV infection, even thought, some participants reported having unprotected sexual intercourse's and some participants had multiple partners. Reasons for not using condom were being in a monogamous relationship and trusting the partner. Although some participants believe that they were protected from HIV infection, and some had unprotected sexual intercourse with multiple partners, the vast majority of our participants were also aware that they were not protected by HIV infection as result of their participation in the trial, which demonstrates that participants did not had risk compensation behavior. Most participants stated that the risk reduction behavior counseling they received in the study gave them confidence to adopt a low risk behavior for HIV infection. Similar findings were found in other studies conducted in Africa, in which they reported a reduction in risky behavior, attributed to counseling to reduce risky behavior, but also, it was not observed in all participants.[159, 160].

Participation in a clinical trial can evoke positive and negative experiences. Learning more about HIV and their health, and receiving risk reduction counseling, and the fact that it was clear

to them that they could withdraw at any time, made the participants felt empowered. Also having a young team of researchers following them was pleasant. Results of recent studies conducted by Tarimo et al [105, 108] in Tanzania among participants of a phase HIV vaccine clinical trial I/II reported that vaccine trial participants appreciated regular health check-ups, knowledge acquisition and engage in less risky behavior.

Blood collection and duration and number of visits was cited as negative experiences. Blood collection and duration and number of visits have been identified as barriers for trial participation, but we did not found studies that reported this factors influencing participants retention [35]. HIV vaccine trial participants must donate considerable amounts of blood repeated times over a long period. This must be clear to them before trial implementation as well as the reasons for it. Effort should be made by the study team to identify qualified personnel in order to reduce any physical discomfort. In general, clinical trial visits require some time. Studies must envisage strategies to ensure that the participant does not spend too much time at the site, such as having a dedicated staff to guide the participants through the various steps of the visits and having multimedia devices available to distract the participants. All strategies should be discussed with the participants.

Social harm, as a result of distrust to HIV vaccine research and also HIV stigma can heavily affect participants retention [107]. During and after trial completion, participants received negatives comments, from family members, partners and colleagues related to their participation in a HIV vaccine study. This can force participants to withdraw, or it can lead to the participants not being able to attend their follow-up visits in a timely manner, or even not being able to attend at all. The most common negative impact was that participants were seen as *guinea pigs* who served the proposes of foreign scientists. Confirming the distrust towards HIV research. Some participants would have liked to have told someone that they participated in the clinical trials, during the time they were enrolled in the study, however the fear of negative comments or reactions by important people in their lives, prevented them from doing so. Negative comments from healthcare professionals are something to take notice. This is very important since it can impair participant access to healthcare, especially after the trial completion. In general, these results were reported in studies conducted in different countries [161]. In a review conducted by Inungu et al [35] they found that social harm is frequent in most HIV vaccine trials, but the effect and extent varies. [105]. In one study conducted in Johannesburg, South Africa, with 150 women who were participating in the microbicide development program trial, it reported that more than a

third of the 150 women suffered violence committed by their intimate partners. In another study conduct in Tanzania reported negative social impacts at the earl stages of trial implementation, when the participant is still not confident enough to discuss and explain negative attitudes towards him. Findings from TaMoVac II demonstrat that participants also received positive comments regarding their participation in the trial, mainly approval by family members- mothers and siblings.

Research teams must adopt different strategies to address potential social harm in order to protect study participants. Strategies should be developed with participants as suggested by a study in Tanzania, where participants of a previous phase I/II trial suggested wider dissemination of HIV vaccine trial procedures and results to the community [131].

Participants felt abandoned after the trial completion, and we could not find these results in other studies. In a study conducted in Tanzania participants suggest that trial participants can become advocates for trial participation, as they fell it would reduce concerns related to HIV vaccine clinical trial implementation in Tanzania [108]. As show by study II results, peers support can have a positive association with actual willingness to participate in HIV vaccine trials. Knowing that other young adults have participated from the same community have participated in previous HIV vaccine trials can eliminate suspicion surrounding HIV vaccine clinical trial implementation. The good participatory practice guideline for biomedical HIV prevention encourages sites that conduct HIV vaccine research trials to include previous participants of in their community advisory board. Is will ensure that a voice representing the participants will be able to discuss and defend the rights of HIV vaccine trial participants [124].

The main limitation of study I was that participants had not received any information regarding HIV vaccine research that could underestimate their knowledge and bias the responses, as the main objective of RV 363 incidence cohort study was to describe the HIV epidemic in the *Polana Caniço* area. The high loss to follow-up from the cohort could overestimate the willingness results. The main limitation of study one was the interval between the end of the study and the first interview, and the fact the low sample size can´t permit any generalization. Also, these studies were conducted in Maputo city, which is the capital of the country, were most of the educational resources are available when compared with the rest of the country, and thus we should assume that these results might need to be adapt and contextualized, if to be applied in other parts of the country.

7 Conclusion

This research project determined the expressed willingness to participate in future HIV vaccine clinical trials and described the actual motives for participating in HIV vaccine trials among young people in Maputo city. Based on a qualitative and quantitative analysis and the use of the Health Belief model this research project demonstrated that behavior and social factors influence young adults' participation in HIV vaccine clinical trials. These results provide evidence of the practicality of conducting HIV vaccine trials in Maputo and tools to enhance its implementation.

The high rate (92%) of expressed willingness to participate in HIV vaccine clinical trials, among most-at risk men and women reported in this project confirm that HIV vaccine trials can recruit a large number of students as potential participants, even though fear of needles was presented as a potential barrier for trial participation. This research clearly illustrates that young people who acknowledge their risk to HIV infection, want to participate in the fight against HIV and contribute to research aimed at finding a preventive HIV vaccine. Attention should be given regarding to the expectation that receiving an experimental HIV vaccine during trial participation can provide protection.

Continuous high rate of expressed willingness to participate in HIV vaccine trials does not guarantee actual participation in HIV vaccine trial. This can only be evaluated among those who actual decide to participate or participated in a HIV vaccine trial. The health belief model was used to explain the decision-making progress to participate in a HIV vaccine study. HIV susceptibility, infection severity and benefits of participating in a HIV vaccine trial must outweigh barriers for trial participation in order to promote the switch from intention to action.

Counseling to reduce HIV risk behavior, which is appreciated by participants, is effective, but it does not warranty that all participants will engage in low-risk behavior, particularly women. Decision to engage in high-risk behaviors is associated with the type of relationship. Reports from this research did not show any risk compensation behavior. Retention in HIV vaccine trials can be negative affect by stigma from family and peers towards HIV vaccine trial participants. Participants want to be involved with HIV research even after HIV trial completion.

In conclusion, the present research reports a continuous high intention to participate in HIV vaccine trial among young adults in Maputo city and identified the factors associated with it. It

also describes how actual participants of a phase II HIV clinical trial reason their participation and the factors associated with their retention participation in the HIV vaccine trial.

8 Recommendations

The results from these studies should be disseminated and findings should be used to develop recruitment and retention strategies and guide future research. Knowing that young adults, students could potentially have a high willingness to participate in HIV vaccine trial, must guide recruitment strategies to target this population. Because Mozambique has a generalized HIV epidemic, research is needed to describe socio-behavioral aspects for participation in HIV vaccine trial with different populations. Research should focus on willingness to participate in hypothetical scenarios of HIV research. New and contextualized change behavioral models should be used to access the influence of communities, including parents, teachers, peers, and different types of leaders in the society.

CISPOC should develop and implement a HIV infection and HIV research educational community-based plan that should target potential participants of HIV vaccine clinical trials. This plan should develop the tools to enable participants to realize their own risk for HIV infection, which will increase their interest in HIV preventive strategies including HIV vaccine research.

After almost 10 years implementing HIV vaccine clinical trials, it would be expected that in the neighborhoods surrounding CISPOC, were most of the participants to HIV preventive studies come from, HIV vaccine knowledge would be higher HIV. Educational program should be part of a specific plan, which should involve different stakeholders with clear indicators, that would need to be evaluated over time.

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10 List of Publications

1. Deus N[Θ], **Capitine I**[Θ], Bauhofer A, Marques S, Cassocera M, Chissaque A, Bero D, Langa J, Padama M, Jeyaseelan V, Oberste M, Estivariz C, Verma H, Jani I, Mach O, Sutter R. Immunogenicity of reduced-dose monovalent type 2 oral poliovirus vaccine in Mocuba, Mozambique**.** Submitted to The Journal of Infectious Diseases. [Θ] These authors contributed equally to this work
2. Chitio J, Baltazar C, Langa J, Baloi L, Manuel J, Ramos B. J. Mboane R, Sadate Assane S, Omar A, Manso M, **Capitine I**, Naira Luiz N, Vittal Mogasale V, Marks F, Park S, Beck N. A pre-emptive Oral Cholera Vaccine (OCV) mass vaccination campaign in Cuamba District**,** Niassa Province, Mozambique: feasibility, costs, and vaccination coverage. To be submitted.

10.1 Statement on Pre-release and Contribution

1. **Young at risk-people in Maputo City, Mozambique, present a high willingness to participate in HIV trials: results from an HIV vaccine preparedness cohort study.** Submitted to **Vaccine** journal.

   PhD Role: data cleaning, data analysis and data interpretation, manuscript conceptualization and writing, manuscript submission.

2. **Profile of motives, sexual behavior, and experiences of participating of young uninfected participants of a previous phase II HIV vaccine clinical trial conducted in Maputo City, Mozambique.** Under internal review – ***included in the PhD methods and discussion***. Journal **PlosOne (**To be submitted**)**

   PhD Role: Conceptualization of the study; development of the study protocol and instruments, data analysis and data interpretation, manuscript conceptualization and writing, manuscript submission.

3. **A social-ecological model approach to understand the intention to participate in HIV vaccine trials among young students in Maputo, Mozambique**. Data analysis and manuscript writing.

   Aim: This study used mixed methods to collect data on 320 students (questionnaire). In-depth interviews were also conducted with students, their parents, teachers, religious leaders, traders, community leaders and policy makers were also interviewed, in order to understand the willingness to participate in clinical trials and the socio-cultural factors involved. In all, about 70 interviews and 6 focus discussion groups were conducted – data collected, transcribed.

   PhD Role: Conceptualization of the study; development of the study protocol and instruments, data analysis and data interpretation, manuscript conceptualization and writing, manuscript submission.

All these studies were possible with the help of INS collaborators. Supervisors were instrumental in guiding the PhD theoretical perspective, aims, methods and identifying potential research grants. Supervisors support includes:

- Protocol and instruments review.
- Supervision of data collection and data analysis;

10.2 Acknowledgments

This was, by far, the most strenuous challenge of my professional and academic career, which happened in parallel with some of the most excruciating moments of my personal life, and I would not have been able to implement this life project without the support, encouragement and guidance of many different people who have always believed in me.

First, I would like to thank God for giving me health, strength and enlighten through this period.

My supervisors, **Dra. Caroline De Schacht, Dr. Arne Kroidl** and **Prof. Dr. Martin Fischer,** for the words of encouragement, dedication, guidance, and wisdom during this project, and mainly for their availability. For always pushing me to see the big picture, and to present my ideas in a simple and clear way. One word to describe their efforts – **Outstanding**.

My family, especially my mother **Almingarda Paulo Ubisse** (in memoriam), for having taught me values that I carry with me at all times. My father **Valeriano Pedro** (in memoriam)**,** my forever role model, for always demanding from me much more than I imagined, and for your time and experience. My sisters **Carina** and **Kathleen** for always being present in my life and for their unconditional love.

I would like to thank the CIH team and all the teachers, and my colleagues for the hospitality, logistic and technical support, and unforgettable life experiences. A special thanks goes for previous PhD student **Celso Khosa**, for being a splendid alumni.

This project would not have happened without the research participants, in particular the **TaMoVac II study participants**- they are the main reason for this PhD project implementation.

Finally, my colleagues from CISPOC, **Patricia Ramgi, Luis Aires Nhambizo, Raquel Matavel and Nilesh Bhatt**. From the National Institute of Health, **Sergio Chicumbe, Jose Paulo Langa and Júlia Sambo Assiat**. For your support, affection, guidance, and *shoulder*. I have no words.

I would like to thank ***Trud Marlene (my wife)*** for the love and support. For believing in me, for the words of encouragement that helped me stay focused. For being understanding, for the many absent moments, when I had to dedicate myself to my PhD. For the positive energy that you always transmitted to me, and that helped make this journey less heavy and fun. Thank you, my love.

10.3 Study Materials

10.3.1 Annex 1- Study I_Willingness to participate questionnaire

RV-363 HIV/AIDS Awareness, Vaccine Knowledge and Willingness to Participate Questionnaire

Site ☐1 ***CISPOC*** ☐2 ***CIDI*** **Visit: _____**

Subject Number ___ ___ ___ ___ ___ ___

INTERVIEWER TO READ THIS

Before we start, I would like to remind you about the interview process. Your participation in this interview and every aspect of the research study are completely voluntary. You may skip any question that you prefer not to answer, but I would appreciate if you answered all the questions. You can also ask me anytime to clarify questions that you do not understand, or you can decide to stop the interview at any time.

Any information you provide for this study will be kept confidential and cannot be shared with any individual, including your employer/boss, spouse, friends, or relatives. The responses that you provide to these questions will only be identified by a unique number, not by your name or any other identifying information.

Today I am going to ask you to tell me what you know about HIV infection, and some questions on what you know about vaccines. This questionnaire has only two sections.

If you have any questions, please do not hesitate to ask me anytime as we go through the questions.

Thank you. Let us begin!

Time Interview Started: ___ ___:___ *hh:mm (24 hour clock time)*
___

Form Completed By: ☐☐☐ **Date Completed** *DD/MON/YYYY* __ __/__ __ __/__ __ __ __

**** All Questions OTHER (SPECIFY) = Responses which do not fit into any category. Should occur in minimal cases. REFUSED TO ANSWER = Respondent refused to answer the question for any reason. Should occur in minimal cases. DO NOT KNOW = Respondent states they do not know. He/She may actually know but does not want to give the answer. Should occur in minimal cases.**

RV-363 HIV/AIDS Awareness, Vaccine Knowledge and Willingness to Participate Questionnaire

Site: ☐1 ***CISPOC*** ☐2 ***CIDI*** **Subject Number** ___ ___ ___ ___ ___ ___ **Visit:** _____

ADMINISTRATIVE INFORMATION

1. Visit Date	☐☐ DAY ☐☐☐ MONTH ☐☐☐☐ YEAR

2. Volunteer's residence (Identify code and record code number in boxes)

District code : ☐☐☐ **Neighborhood Code:** ☐☐☐

INSTRUCTION FOR FORM COMPLETERS

**** **DO NOT** READ ANSWER CHOICES OUT ALOUD TO A PARTICIPANT UNLESS INSTRUCTED ****

WITH
***READ** SIGN*

******HOWEVER, **DO NOT** READ******

*'**REFUSED TO ANSWER**' and '**DO NOT KNOW**' answer choices*

***** FOR SOME QUESTIONS YOU WILL SEE THE **ARROW** SIGN FOLLOWED BY A LETTER **'Q'** AND **NUMBER** OR **SECTION.** IT IS INSTRUCTING YOU TO '**SKIP**' TO ANOTHER QUESTION OR SECTION.*
PLEASE FOLLOW THE SKIP PATTERN CAREFULLY** *

□Q *Means **Skip*** to another **Question***

□SEC *Means **Skip*** to the next **Section***

RV-363 HIV/AIDS Awareness, Vaccine Knowledge and Willingness to Participate Questionnaire

Site: ☐1 ***CISPOC*** ☐2 ***CIDI*** **Subject Number** ___ ___ ___ ___ ___ ___ **Visit:** _____

Section 1: AIDS AWARENESS

1.1	I am going to read you a list of some ways people believe you can become infected with HIV. Please tell me which of the ways you agree that you could become infected with the HIV virus. **Read** (CHECK ALL APPLICABLE ANSWERS)	□ HAVING PENILE-VAGINAL SEX WITH SOMEONE WHO HAS THE HIV VIRUS □ PLACING YOUR MOUTH ON YOUR PARTNER'S GENITALS □ PLACING YOUR PENIS IN THE ANUS OR LETTING YOUR PARTNER PLACE, HIS PENIS IN THE ANUS □ KISSING MOUTH TO MOUTH □ INJECTING DRUGS WITH SYRINGES OR NEEDLES, USED BY SOMEONE WHO HAS THE HIV VIRUS □ SHARING RAZORS, SCISSORS, NEEDLES WITH SOMEONE WHO HAS THE HIV VIRUS □ CONTACT WITH BODY EXCRETIONS FROM SOMEONE WITH THE HIV VIRUS □ GETTING BLOOD TRANSFUSION FROM SOMEONE WHO HAS THE HIV VIRUS □ A BABY BREAST FED BY MOTHER WHO HAS THE HIV VIRUS □ EXPERIMENTAL HIV VACCINES □ NONE OF THESE □ REFUSED TO ANSWER □ DO NOT KNOW
1.2	I am going to read a second list of some ways people believe you can become infected with HIV. Please tell me which of the ways you agree that you could become infected with the HIV virus. **Read** (CHECK ALL APPLICABLE ANSWERS)	□ CONDOM □ WORKING NEAR SOMEONE WHO IS INFECTED WITH HIV □ SHARING EATING UTENSILS □ USING SAME TOILET WITH SOMEONE WHO HAS THE HIV VIRUS □ MOSQUITOES □ NONE OF THESE □ REFUSED TO ANSWER □ DO NOT KNOW

RV-363 HIV/AIDS Awareness, Vaccine Knowledge and Willingness to Participate Questionnaire

Site: ☐1 ***CISPOC*** ☐2 ***CIDI*** **Subject Number** ___ ___ ___ ___ ___ ___**Visit:** _____

1.3	From this list that I am going to read, tell me which ways you think a person can avoid or prevent getting infected with HIV? (CHECK ALL APPLICABLE ANSWERS)	□ HAVE SEX ONLY WITH HEALTHY- LOOKING PERSONS □ USE CONDOMS □ USE FAMILY PLANNING SPERMICIDES BEFORE SEX □ CLEANING/DOUCHING AFTER SEX □ WITHDRAW BEFORE EJACULATING □ ABSTAIN FROM SEX □ DON'T SHARE NEEDLES □ REFUSED TO ANSWER □ DO NOT KNOW **Read**
1.4	Can you tell by looking at someone if they have the HIV virus? ☐☐	NO 00 YES 01 REFUSED TO ANSWER 88 DO NOT KNOW 99
1.5	If you tested HIV positive and chose to disclose your status to others, which of the following things do you think would happen in your life? (CHECK ALL APPLICABLE ANSWERS)	□ BREAK UP OF MARRIAGE □BREAK UP OF SEXUAL RELATIONSHIPS □ PHYSICAL ABUSE BY SPOUSE/SEXUAL PARTNER □ INCREASED SUPPOR FROM SPOUSE/SEXUAL PARTNER □ DISCRIMINATION BY EMPLOYERS □ INCREASED SUPPORT FROM EMPLOYERS □ NEGLECTED BY FAMILY □ DISOWNED BY FAMILY □ INCREASED SUPPORT FROM FAMILY AND RELATIVES □ ESTRANGED FROM MY PEERS □ INCREASED SUPPORT FROM PEERS □ OTHER (SPECIFY) _____ □ REFUSED TO ANSWER □ DO NOT KNOW **Read**

1.6	Prior to coming in for this study, which of the following ways did you receive information about HIV/AIDS? (CHECK ALL APPLICABLE ANSWERS)	□ NO INFORMATION ABOUT HIV/AIDS □ NEWSPAPER OR MAGAZINES □ RADIO □ TELEVISION □ FRIENDS/NEIGHBOURS □ FAMILY □ SCHOOL □ HEALTH PERSONNEL □ POSTER/PAMPHLET □ NGO OUTREACH □ INTERNET □ SITE RECRUITMENT STAFF □ COMMUNITY EVENT □ OTHER (SPECIFY) _____ □ REFUSED TO ANSWER □ DO NOT KNOW **Read**	
2.1	Can you please tell me if the following statement is true or false? "**A vaccine is meant to prevent illness**" ☐☐	FALSE 00 TRUE 01 REFUSED TO ANSWER 88 DO NOT KNOW 99	
2.2	Prior to coming to this study, have you ever received education/information on HIV vaccine research? ☐☐	NO 00 YES 01 REFUSED TO ANSWER 88 DO NOT KNOW 99	□**Sec.3**

RV-363 HIV/AIDS Awareness, Vaccine Knowledge and Willingness to Participate Questionnaire

Site: ☐1 ***CISPOC*** ☐2 ***CIDI*** **Subject Number** ___ ___ ___ ___ ___ ___**Visit:** _____

2.3	From this list I'm going to read, which of these sources have you received information about HIV vaccine research? [1 SEP] (CHECK ALL APPLICABLE ANSWERS)	□ HOSPITAL/CLINIC/HEALTH WORKER □ RADIO/TV □ NEWSPAPER/BROCHURE/MAGAZINES □ FRIEND/RELATIVE □ INTERNET □ NGO □ POSTER □ LEARNED FROM A VACCINE TRIALVOLUNTEER □ I WAS A VACCINE TRIAL VOLUNTEER □ RESEARCH CENTER □ SCHOOL □ OTHER (SPECIFY) _____ □ REFUSED TO ANSWER □ DO NOT KNOW **Read**	
3.1	Would you be willing to participate in such a study to test an experimental HIV vaccine? [ ][ ]	NO 00 YES 01 SOMEONE ELSE WOULD DECIDE 02 REFUSED TO ANSWER 88 DO NOT KNOW 99	□Q3.3
3.2	Please tell us why you will not be willing to participate in a vaccine study? (CHECK ALL APPLICABLE ANSWERS)	□ FEAR OF NEEDLE □ FEAR OF GETTING HIV □ SPOUSE/SEXUAL PARTNER REFUSAL □ FEAR OF SIDE EFFECTS □ FEAR OF DEATH □ FEAR OF FETAL ABNORMALITIES □ TIME REQUIRED FOR VISITS □ FEAR OF TESTING HIV POSITIVE □ I KNOW I AM HIV POSITIVE □ FEAR OF DESCRIMINATION □ OTHER (SPECIFY) _____ □ REFUSED TO ANSWER □ DO NOT KNOW **Read**	

3.3	From this list I'm going to read, can you please choose some of personal advantages of participating in a study of an HIV vaccine? **Read** (CHECK ALL APPLICABLE ANSWERS)	□ LEARN HOW TO AVOID RISKY BEHAVIOR □ FEEL PROTECTED FROM HIV INFECTION □ GET FREE HIV COUNSELING AND TESTING □ RECEIVE UPDATED INFORMATION ABOUT HIV/AIDS □ GET SMALL REIMBURSEMENT EVERY TIME I COME TO A STUDY VISIT □ BE TESTED FOR SEXUALLY TRANSMITTED INFECTION □ RECEIVE REGULAR HEALTH CARE RELATED TO RESEARCH □ GET FREE PREGNANCY TEST EVERY 3 MONTHS □ OTHER (SPECIFY) _____ □ REFUSED TO ANSWER □ DO NOT KNOW
3.4	How likely or unlikely would you be to enroll in a new experimental HIV vaccine if: **Read** *(Use these responses to fill the question **below**)* NOT APPLICABLE 77 REFUSED TO ANSWER 88 DO NOT KNOW 99 ☐☐ a. YOU WERE REQUIRED TO COME TO THE CENTER ON A SPECIFIC DAY EVERY THREE MONTHS FOR TWO YEARS ☐☐ b. YOU WERE REQUIRED TO TALK TO A NURSE ABOUT YOUR EXPERIENCES IN THE STUDY ☐☐ c. YOU WERE REQUIRED TO BE TESTED FOR HIV EVERY THREE MONTHS ☐☐ d. YOU WERE REQUIRED TO BE INJECTED WITH A VACCINE CANDIDATE A FEW TIMES ☐☐ e. YOU WERE REQUIRED TO GIVE BLOOD SAMPLES EVERY TIME YOU CAME FOR A STUDY VISIT ☐☐ f. THE RESEARCH CENTER WERE OPEN ON THE WEEKEND (E.G. SATURDAYS) ☐☐ g. IF FEMALE: YOU WERE REQUIRED TO USE A CONTRACEPTIVE METHOD SUCH AS HORMONAL CONTRACEPTION WHILE YOU ARE IN THE STUDY	VERY UNLIKELY 00 SOMEWHAT UNLIKELY 01 SOMEWHAT LIKELY 02 LIKELY 03 VERY

Site: ☐1 ***CISPOC*** ☐2 ***CIDI*** **Subject Number** ___ ___ ___ ___ ___ ___ **Visit:** _____

3.5	How important are the following factors in making a decision about participating in a research study of an experimental HIV vaccine? SOMEWHAT IMPORTANT 02 *(Use these responses to fill the question **below**)* **Read** NOT IMPORTANT AT ALL 00 IMPORTANT 01 VERY IMPORTANT 03 REFUSED TO ANSWER 88 DO NOT KNOW 99 ☐☐ a. I MAY BE HELPING FIND AN HIV VACCINE THAT WORKS ☐☐ b. I WOULD BE HELPING STOP THE HIV/AIDS EPIDEMIC ☐☐ c. MY FRIENDS AND FAMILY WOULD SUPPORT ME ☐☐ d. I WOULD MEET NEW PEOPLE ☐☐ e. I WOULD BE HELPING MY COMMUNITY ☐☐ f. I WOULD BE HELPING MY COUNTRY ☐☐ g. I WOULD BE HELPING ADVANCE HIV PREVENTION RESEARCH ☐☐ h. PEOPLE MAY THINK I HAVE HIV/AIDS ☐☐ i. PEOPLE MAY THINK THAT I AM AT RISK FOR HIV/AIDS ☐☐ j. PEOPLE MAY NOT WANT TO HAVE SEX WITH ME ☐☐ k. PEOPLE MAY REFUSE CONTACT WITH ME	
3.6	Do you think a preventive HIV vaccine would be useful in controlling HIV infection? ☐☐	NO 00 YES 01 REFUSED TO ANSWER 88 DO NOT KNOW 99
A s	**the question below only at 'Exit Visit'**	
3.7	Can we contact you for future HIV vaccine studies? ☐☐	NO 00 YES 01

CLOSING REMARKS

**** BEFORE YOU RELEASE THE VOLUNTEER, CHECK THAT ALL QUESTIONS ARE ANSWERED.**

1st Data Entry Initials/Date_____ 2nd Data Entry Initials/Date_____

10.3.2 Annex 2 – Study II_Questionnaire

Nº do Participant: |__|-|__|__| **Data:** |__|__|-|__|__|-|__|__|__|__|

Dear Participant

Thank you for being a part of our study. The aim of this study is to help us understand better your experience of having participated in a previous study of a candidate vaccine against HIV, the TaMoVac II in order to better prepare future trials of HIV vaccine.

For taking part of TaMoVac II, we would like to understand how your participation in the study, has affected your life. This information is important, in order to develop strategies aimed at meeting the needs of potential volunteers for future studies of HIV vaccines candidates in Mozambique. It is important to know if the information that was transmitted to the volunteers in regards to the study procedures, was simple and clear, and if the volunteers, understood the essence of the message.

While participating in this study, we'll ask about the knowledge you acquired during the study, about your sex life, and the impact of your participation in the study in your personal and social life.

We would like to remind you that your participation is voluntary, and that all responses will be kept private and confidential. Your link to the study is made by your study number, and not by your name. You do not have to answer any question that makes you feel uncomfortable. But the responses to these questions will help us understand, if the participation in a previous phase II clinical trial of a HIV-1 vaccine candidate, TaMoVac II, affected, and if so, your perceptions and knowledge in relation to the studies of HIV vaccines, your sexual behavior, and if your participation in the study had any impact on your personal and social life.

A supervisor can participate during the interviews to ensure its quality. Before he can join in, we will ask you, for your permission. The supervisor will keep all matters private and confidential.

Knowledge and Perceptions

In this section, we will ask you about your thoughts and knowledge with regards to your participation in the study of a candidate vaccine against HIV. Much of the information that we will discuss, it was provided to you, during yours participating in the study. Some of the questions may seem very personal. Please remember that all your answers will be kept private and confidential. Your link to the study is made by your study number, and not by your name. You do not have to answer any question that makes you feel uncomfortable. Your honesty will help us better prepare the content of our messages.

1. In generally, vaccines are used to protect against infection? *(Only one answer)*
   a) [ ] Yes
   b) [ ] No
   c) [ ] Don't know

2. Phase I and II of candidate preventive vaccine studies against HIV, can include people who are HIV-negative? *(Only one answer)*
   a) [ ] Yes
   b) [ ] No
   c) [ ] Don't know

3. Phase I and II of candidate preventive vaccine studies against HIV, can include people who are HIV – HIV negative, but at risk of getting infected with HIV? *(Only one answer)*
   a) [ ] Yes
   b) [ ] No
   c) [ ] Both
   d) [ ] Don't know

4. Phase III (efficacy) of candidate preventive vaccine studies against HIV, can include people who are HIV negative, but at risk of getting infected with HIV. *(Only one answer)*
   a) [ ] Yes
   b) [ ] No
   c) [ ] Both
   d) [ ] Don't know

5. Phase III of candidate preventive vaccine studies against HIV can include people who are HIV-negative and HIV -positive? *(Only one answer)*

a) [ ] Yes

b) [ ] No

c) [ ] Both

d) [ ] Don't know

6. The aim of candidate preventive vaccine studies against HIV, is to find a HIV vaccine that can protect against infection caused by HIV in the future? *(Only one answer)*

a) [ ] Yes

b) [ ] No

c) [ ] Don't know

7. A preventive vaccine against HIV, can be used to cure people infected with HIV? *(Only one answer*)

d) [ ] Yes

e) [ ] No

f) [ ] Don't know

8. Would you like to be vaccinated against HIV, if it was found a vaccine that protects against the HIV? *(Only one answer)*

a) [ ] Yes

b) [ ] No

c) [ ] Don't know

Because:

9. In clinical trials, the research products used are: *(more than one answer possible)*

a) [ ] Placebo

b) [ ] Vaccine

c) [ ] Both

d) [ ] Don't know

10. Is there any chance of becoming infected with HIV, because you received the candidate vaccine? *(Only one answer)*

e) [ ] Yes

f) [ ] No

g) [ ] Don’t know

11. Is there a probability that the vaccine candidate can cause you health problems in the future? *(Only one answer)*
    a) [ ] Yes
    b) [ ] No
    c) [ ] Don’t know

12. A person who received the vaccine may have an HIV-positive result in the rapid tests, even if not infected? *(Only one answer)*
    a) [ ] Yes
    b) [ ] No
    c) [ ] Don’t know

13. If you have a HIV-positive test result, induced by the vaccine candidate, this means that you are protected against HIV infection? *(Only one answer)*
    a) [ ] Yes
    b) [ ] No
    c) [ ] Don’t know

14. If you have a HIV-positive test result, induced by the vaccine candidate, this means that you are HIV infection? *(Only one answer)*
    a) [ ] Yes
    b) [ ] No
    c) [ ] Don’t know

15. Is it possible, that the HIV-positive test result induced by the HIV vaccine candidate can last for more than 5 years, in a volunteer who received a HIV vaccine candidate in a clinical trial? *(Only one answer)*
    a) [ ] Yes
    b) [ ] No
    c) [ ] Don’t know

16. Your partner will be protected if you have a HIV-positive test result induced by the vaccine candidate? *(Only one answer)*
    a) [ ] Yes
    b) [ ] No

c) [ ] Don’t know

17. Your children will be protected against HIV infection because of your HIV-positive test result induced by the vaccine candidate? *(Only one answer)*
    a) [ ] Yes
    b) [ ] No
    c) [ ] Don’t know

18. Is there a possibility that, your children may have malformations at birth because of your HIV-positive test result induced by the vaccine candidate? *(Only one answer)*
    a) [ ] Yes
    b) [ ] No
    c) [ ] Don’t know

Form Completed By: _____ _____ | __ | __ | - | __ | __ | - | __ | __ | __ | __ |

Name Signature Date (dd / mm / yyyy)

Sexual behavior

In this section, we will ask you about your sex life and the possible use of alcohol and drugs. Some of the questions may seem very personal. Please remember that all your answers will be kept private and confidential. Your link to the study is made by your study number, not by name. You do not have to answer question that makes you feel uncomfortable. But your responses to these questions will help us understand if the participation in a previous phase II clinical trial of HIV-1 vaccine candidate, TaMoVac II, affected, and if so, the sexual behavior of our participants. Your honesty will help us understand this change in behavior.

The issues addressed refer to the three months before this interview. We will not judge your sex life, the possible use of alcohol or drugs.

Before we continue it is important to define some terms:

Sexual Relationships: By sex, we are talking about sex with vaginal penetration (When the penis it's placed within the vagina) or sex with anal penetration (when the penis it's placed within the anus, for anus we mean the orifice which pass the stool).

Receptive: the person to whom the penis was inserted; **penetrative:** the person who placed the penis.

Sexual partner: the person with whom we had or have sex.

Condom use: It is considered condom use (male or female) when the condom was used all the time the penis was inserted, or when the condom is not broken, not torn or slipped.

1. In the last three (3) months, did you have vaginal or anal sex? *(Only one answer)*
   a) [ ] Yes.
   b) [ ] No (Jump to question 15).
   c) [ ] Refused to answer

2. In the last three (3) months, did you have sex with more than one sexual partner? *(Only one answer)*
   a) [ ] Yes.
   b) [ ] No.
   c) [ ] Refused to answer.

3. Your main sexual partner *is (more than one answer possible)*
   a) [ ] Someone for whom, you have a special feeling?
   b) [ ] Someone on whom, you depend financially?
   c) [ ] Someone who depends financially on you?
   d) [ ] Someone with whom you lived, but currently live no more?
   e) [ ] Someone with whom, you live now?
   f) [ ] Someone with whom, you have or had a commitment?

   Who ( ) boyfriend; ( ) Groom; ( ) Husband; ( ) Lover; outro_____

4. Your secondary partner, who is not your primary sexual partner, *is (more than one answer possible)*
   a) [ ] Someone for whom, you have a special feeling?
   b) [ ] Someone on whom, you depend financially?
   c) [ ] Someone who depends financially on you?
   d) [ ] Someone with whom you lived, but currently live no more?
   e) [ ] Someone with whom, you live now?
   f) [ ] Someone with whom, you have or had a commitment?

   Who ( ) boyfriend; ( ) Groom; ( ) Husband; ( ) Lover; outro_____

5. In the last three (3) months, what was the gender of your sexual partner? *(More than one answer)*
   a) [ ] Man
   b) [ ] Female
   c) [ ] Both

6. In the last three (3) months, did you have receptive vaginal sex?? *(Only one answer)*
   a) [ ] Yes. How many? _____
   b) [ ] No

7. In the last three (3) months, did you have receptive anal sex? *(Only one answer)*
   a) [ ] Yes. How many? _____
   b) [ ]

8. In the last three (3) months, did you have penetrative vaginal sex? *(Only one answer)*
   a) [ ] Yes. How many? _____
   b) [ ] No

9. In the last three (3) months, did you have penetrative anal sex? *(Only one answer)*
   a) [ ] Yes. How many? _____
   b) [ ] No

10. In the last three (3) months, did you used a condom during sex? *(Only one answer)*
    a) [ ] Always (all sex)
    b) [ ] Sometimes (half of sex)
    c) [ ] Rarely (less than half of sex)
    d) [ ] No

11. In the last three (3) months, with whom you did not use a condom *(only one answer)*
    a) [ ] Main partner
    b) [ ] Occasional Partner (s)
    c) [ ] Both

12. The reason that made you not to use condoms: (more than one answer)
    a) [ ] Because you think you are protected, for having participated in the study?
    b) [ ] Your sexual partners did not want to use condoms?
    c) [ ] You do not believe in HIV?
    d) [ ] Because you trust your partner?
    e) [ ] Don't know?
    f) [ ] Others: _____

13. In the last three (3) months, among the people with whom you had sex, there was someone who was HIV positive or whom you suspected it was? *(Only one answer)*
    a) [ ] Yes.
    b) [ ] No.
    c) [ ] Don't know?

14. In the last three (3) months, one of your sexual partners did HIV testing? *(Only one answer)*
    a) [ ] Yes. Who? _____
    b) [ ] No.
    c) [ ] Don't know?

15. In the last three (3) months, you had sex in exchange for money, goods or services? *(Only one answer)*
    a) [ ] Yes.
    b) [ ] No.

16. In the last three (3) months, you were diagnosed with any sexually transmitted disease? *(Answer)*
    a) [ ] Yes
    b) [ ] No

17. Do you regularly drink alcohol (defined as more than 35 units a week for men or 14 units per week for women. 1unit = 1 cup beer or wine or a strong alcohol measure). *(only one answer)*
    a) [ ] Yes
    b) [ ] No

18. In the last three (3) months, you used intravenous drugs or consume chronically any other drugs (e.g. marijuana, cocaine)? *(Only one answer)*
    a) [ ] Yes, which one? _____
    b) [ ] No

19. In the last three (3) months, you shared syringes? *(Only one answer)*
    a) [ ] Yes. Why? _____
    b) [ ] No

20. In the last three (3) months you had sex, while on the effect(s) of ? *(more than one an answer)*
    a) [ ] of alcohol?
    b) [ ] of drugs?
    c) Specify: _____

21. In the last three (3) months you had sex with a partner who: *(more than one answer)*
    a) [ ] Had sex with someone else, during the same period?
    b) [ ] is a drug user?
    c) [ ] Regularly consume alcohol?

d) [ ] Was under the effect of drug?

e) [ ] Was under the effect of alcohol?

22. In the last three (3) months, how would you rate your risk for acquiring HIV infection? *(Only one answer)*

a) [ ] High

b) [ ] Moderate

c) [ ] Low

Because:

23. Do you think that because you participated in a HIV-1 vaccine candidate test, influenced in your sexual behavior? *(Only one answer)*

a) [ ] Yes

b) [ ] No

Because:

Form Completed By: _____ _____ | __ | __ | - | __ | __ | - | __ | __ | __ | __ |
Name Signature Date (dd / mm / yyyy)

Social Harm

In this section, we will ask you about your personal and social life. It is important to know, whether if during your participation in the study, and/or after your participation in the study, if you received some support, and/or suffered some sort of negative comment, or any other negative experience due to your participation in the study. Please remember that all your answers will be kept private and confidential. Your link to the study is made by your study number, not by your name. You do not have to answer any question that makes you feel uncomfortable. Your honesty will help us understand the impact, that participating in a HIV vaccine candidate study have in the personal and social life of volunteers.

The questions that follow refer to the period during which stemmed activities in the study (from start to end of study).

1. Have you ever told anyone about your participation in the study of candidates for HIV vaccine? *(Only one answer)*

   a) [ ] Yes
   b) [ ] No
   c) [ ] Don't you remember
   d) [ ] Refused to answer

2. The person you told is: *(more than one answer)*

	Yes	**No**
Father/Mother		
Brother(s) / Sister(s)		
Cousins		
Close relative with whom you live: _____		
Boyfriend		
Husband		
Another sexual partner: _____		
Classmate		

Work colleague		
Your boss / direct supervisor		
Doctor		
Nurse		
Personalize church / religion / cult		
Other: _____		

3. Did you receive support from the person to whom you told? *(only one answer)*
   a) [ ] Yes: Whose _____?
   b) [ ] No
   c) [ ] you Don't know
   d) [ ] Refuses to answer

4. There was someone whom you did not tell about your participation in the study, but you would like to have told? *(only one answer)*
   a) [ ] Yes: Who _____?
   b) [ ] No.
   c) [ ] You don't remember (jump to 5)
   d) [ ] Refuses to answer (skip to 5)

   4.1. For fear that the person (people) could: *(more than one answer)*

	Yes	**No**
Think that you were infected with HIV/AIDS, because you participated in a HIV vaccine candidate study.		
Think that you have think promiscuous behaviors such as exchange of goods, money or services, for sex, because you participated in a HIV vaccine candidate study.		
Think that you have multiple partners.		
Demonstrate negative attitudes toward the HIV vaccine candidate study, for thinking that it could infect		

Demonstrate negative attitudes toward the HIV vaccine candidate study, for thinking that could cause other problems		
Think that I'm being a "guinea pig" in an experiment with foreign scientists.		
I would not be able to explain that it can have an HIV-positive result, and not be infected		
It is a personal matter that does not concern anyone else.		
Others: _____ _____ _____		

4.2. You think that if you had revealed about your participation in the study, the consequences could be?*(More than one answer)*

	Yes	**No**
Be rejected by your family		
Be rejected by your boyfriend, husband or other partner: _____		
Be unable to establish a new relationship		
Be discriminated at work or losing your job		
You might not get a job in a public institution:		
Be discriminated at school		
Be discriminated by religion / church staff		
Be discriminated by health workers		
Cannot donate blood		
Not be able to travel because the results of physical fitness, may be abnormal		
Unable to get a bank loan, because of a vaccine induced HIV-positive result		
Others: _____ _____ _____		

4.3. While participating in the study suffered negative comment or feedback, as? *(more than one answer)*

	Yes	No
Being infected, because you have participated in a HIV vaccine candidate study		
Lack of support from your family when you were sick, because you have participated in a HIV vaccine candidate study		
Be considered a person who has promiscuous behaviors such as, exchange of goods, money or services for sex because you have participated in a HIV vaccine candidate study		
About the fact that you might have multiple sexual partners		
Your main partner left you because you have participated in a HIV vaccine candidate study		
You cannot have a new partner, because of your involvement in a HIV vaccine candidate study		
Polls related to the fact of being a "test subject" in an experiment		
Be discriminated in your job or lose your job, your colleagues do not want to engage in activities with you, because of your involvement in a HIV vaccine candidate study		
Community comments on the negative effects of HIV vaccine candidate study		
Others: _____ _____ _____		

4.4. For whom did you suffered the comments or negative reactions? *(only one answer)*

Father/mother		
Brother(s) / Sister(s)		
Close relative with whom you live: _____		
Boyfriend		
Husband		
Another sexual partner _____		

Classmate		
Work colleague		
Your boss / direct supervisor		
Health care staff, who? _____		
vv		
Church / religion / cult staff		
Other: _____		

B. The following questions cover the period from the end of the study at the time of interview.

5. Upon completion of the study, you told anyone about your participation in a HIV – vaccine candidate study? *(Only one answer)*

   a) [ ] Yes

   b) [ ] No

   c) [ ] Don't remember

   d) [ ] Refused to answer

   5.1. The person you told was your(s): *(more than one answer)*

	Yes	**No**
Father/mother		
Brother(s) / Sister(s)		
Close relative with whom you live:_____		
Boyfriend		
Husband		
Another sexual partner: _____		
Classmate		
Work colleague		
Your boss / direct supervisor		
Doctor		
Nurse		

Church / religion / cult staff		
Other: _____		

6. In your opinion the reaction was: *(only one answer)*
   a) [ ] Positive (approval or other positive comment)
   b) [ ] Neutral (manifested no feeling or opinion)
   c) [ ] Negative (reproved, made a negative comment)
   d) [ ] Don't Know

7. Upon completion of the study, you told anyone that by having participated in the study and received the candidate vaccine against HIV, your HIV test result **can be positive,** without this necessarily means that you are infected? *(Only one answer)*
   a) [ ] Yes
   b) [ ] No
   c) [ ] You Don't remember
   d) [ ] Refused to answer

   7.1. The person you told was: *(more than one answer)*

	Yes	**No**
Father/mother		
Brother(s) / Sister(s)		
Close relative with whom you live: _____		
Boyfriend		
Husband		
Another sexual partner: _____		
Classmate		
Work colleague		
Your boss / direct supervisor		
Doctor		
Nurse		
Church / religion / cult staff		

Other: _____		

7.2. Upon completion of the study , you suffered a negative comment or feedback, because you can have / had a false-positive HIV result, as:

	Yes	No
Being infected with HIV, because you have participated in a HIV vaccine candidate study		
Lack of support from your family, when you was sick, because you have participated in a HIV vaccine candidate study		
Be considered a person who has promiscuous behaviors such as, exchange of goods, money or services for sex because of the possibility of having a false-positive HIV result		
About the possibility/fact of you having multiple sex partners		
Your main partner left you, because of the possibility of you having a false-positive HIV result		
You cannot have a new partner because of the possibility of you having a false-positive HIV result		
Polls related to the fact of being a "test subject" in an experiment		
Be discriminated in your job or lose your job, your colleagues do not want to engage in activities with you, because of the possibility of you having a false-positive HIV result		
Community on the negative effects of candidate HIV vaccine, due to the possibility of having a false positive for HIV		
Others: _____ _____		

Thank you for your participation in the study!

Form Completed By: _____ _____ | __ | __ | - | __ | __ | - | __ | __ | __ | __ |

Name Signature Date (dd / mm / yyyy)

10.3.3 Annex 3 – Study II_In-Depth Interview

Study II – In-Depth Interviews

Perceived Susceptibility

Topics to be explored:

- What is HIV? How is it transmitted? Who can be infect by HIV?
- How the participant assesses himself regarding his risk of HIV acquisition? High or Low risk? The motives why he assesses himself as high, moderate or low risk for HIV acquisition?
- If his participation in a HIV vaccine clinical trial has influenced is perceived risk for HIV acquisition?

Perceived Seriousness

Topics to be explored:

- Is HIV infection serious? Why? The reasons why they think HIV infection is serious or not? Who is more likely to develop the disease – AIDS stage?
- If they think that because they participated in a HIV Vaccine clinical trial they think they will not develop AIDS?

Perceived Benefits of Taking Action

Topics to be explored:

- If the volunteers view any benefit in complying with the current HIV prevention interventions (for examples condoms)?
- Which interventions they believe to be most efficacious, and which they would adopt?
- What should be done for people at risk, to accept HIV preventive interventions, including condom use or the change of their sexual behavior?

Barriers to Taking Action

Topics to be explored:

- In the volunteers perspective, the reasons why people, especially young adults from Mozambique, continue to get infected?
- If the volunteers think that people from their community, would support HIV preventive interventions, and the motives?
- If the volunteers think that people from their community, would support HIV preventive research, including HIV vaccine research, and the motives?

Cues to Action

Topics to be explored:

- If they, at all times, use HIV preventive interventions? Does counseling and information regarding HIV really helps, or are there any other factors associated?
- If they think young people from their community, would be willing to accept HIV preventive interventions, including a HIV vaccine, if they received more and better counseling? Why?
- If they think the community would support, that people from their community, would be vaccinated with a HIV vaccine, if one becomes available?

10.3.4 Annex 4 – Study II_Focus Group Discussion

Research Participation

Topics to be explored:

- What is research? What is the purpose/objective of the study? What is experiment?
- What is the participants perception regarding signing the informed consent, and what does it mean? Is it necessary? Why Participants have duties and rights?
- What is the participant's perception in regards to research? What is their perception regarding their participation in a clinical trial? Was it a good or bad experience?

Sexual Behavior

Topics to be explored:

- Participant's perception regarding counseling?
- Why even with counseling, some the participants acquired an STI?
- If a participants partners, may have any kind of influence, at a participant using or not protection? Is it easy to negotiate the use of protection with their partners? Why?
- What they do think regarding, trading sex for money, goods or others? Is it common? Why?

Social Harm

Topics to be explored:

- How people from their community view their participation in a HIV Vaccine? Their parents? Friends?
- What could be the negative comments towards the clinical trial participants? Based on what?
- If they think people from their community would support the conduct of HIV research?
- If the community would support participation of people from their own community in HIV research?

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Dean's Office
Medical Faculty

MMRS MUNICH MEDICAL RESEARCH SCHOOL

Affidavit

Capitine, Igor

Surname, first name

Street

Zip code, town

Country

I hereby declare, that the submitted thesis entitled

Socio-Behavioral aspects regarding participation to HIV Vaccine Clinical Trials among young people in Maputo, Mozambique (SoBeVacH)

is my own work. I have only used the sources indicated and have not made unauthorised use of services of a third party. Where the work of others has been quoted or reproduced, the source is always given.

I further declare that the submitted thesis or parts thereof have not been presented as part of an examination degree to any other university.

Maputo, 09/05/2022

Place, date

Igor Paulo Ubisse Capitine

Signature doctoral candidate

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Confirmation of congruency between printed and electronic version of the doctoral thesis

Capitine, Igor

Surname, first name

Street

Zip code, town

Country

I hereby declare that the electronic version of the submitted thesis, entitled

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Maputo, 09/05/2022

Place, date

Igor Paulo Ubisse Capitine

Signature doctoral candidate