An update on human immunodeficiency virus vaccine preparedness studies

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Human immunodeficiency virus (HIV) vaccine preparedness studies (VPSs) have taken place in both the Organisation for Economic Co-operation and Development (OECD) countries and the non-OECD countries. HIV VPSs are conducted to assess the feasibility of phase 3 HIV vaccine trials. This descriptive review is an update of HIV VPSs in the non-OECD countries, and examines the willingness to participate (WTP) in hypothetical HIV vaccine trials, as well as retention. Few VPSs have been published in the OECD countries since the discontinuation of the STEP/Phambili HIV vaccine trials. Barriers to participation in the non-OECD countries after the STEP/Phambili studies include safety issues and side effects, vaccine-induced seropositivity (VISP) and mistrust among key informants (KIs). HIV VPSs indicate that HIV vaccine trials are still feasible in the non-OECD countries, but barriers must be overcome to improve feasibility. Hypothetical WTP in a VPS may not translate into actual WTP in an HIV vaccine trial.

INTRODUCTION

Human immunodeficiency virus (HIV) vaccine preparedness studies (VPSs) have taken place in both the Organisation for Economic Co-operation and Development (OECD) countries (Dhalla et al., 2007) and non-OECD countries (Dhalla et al., 2009). HIV VPSs are conducted to evaluate the willingness to participate (WTP), recruitment and retention rates with regard to hypothetical HIV vaccine trials, and to assess the feasibility of an actual HIV vaccine trial (Dhalla et al., 2009). A VPS that assesses the practicability of a vaccine trial should ideally be a precursor of a vaccine study (Seage et al., 2001).

Retention refers to completion of study visits in an HIV VPS for follow-up interviews, counselling and HIV antibody testing. In a preventative trial, high-risk individuals need to be recruited as they are more likely to seroconvert; otherwise, the sample size required for an HIV vaccine study would be too large or require follow-up for too long. Conducting a trial when the HIV seroincidence is too low (<2 %) would also make it impossible to detect a real difference between the vaccine and placebo (Rida et al., 1997).

The OECD is an international organization of 34 generally high-income countries that accept the principles of representative democracy and a free market economy (OECD, 2011). The non-OECD countries are generally lower-income countries, often with a higher prevalence and incidence of HIV than the OECD countries.

The HIV/AIDS epidemic continues to affect sub-Saharan Africa disproportionately, with 70 % of all new HIV infections in 2012 (UNAIDS, 2013). A recent article reviewed the inclusion of South African adolescents in HIV vaccine trials, and discussed strategies for successful recruitment and retention of adolescents in HIV vaccine trials (Adler, 2012). The strategies outlined included education of trial participants and their parents/guardians, community outreach and social messaging, issues surrounding privacy and consent, compliance with the law, compensation and health service access (Adler, 2012).

HIV VPSs

HIV VPSs in the OECD countries up to 2006 (Dhalla et al., 2007) and non-OECD countries up to 2007 (Dhalla et al., 2009) have been reviewed previously.

WTP (willingness to participate) (in the USA, Canada, Europe and Australia) ranged in injection drug users (IDUs) from 41 to 86 % (eight studies) and in men who have sex with men (MSM) from 23 to 94 % (11 studies); in women at heterosexual risk (WAHR), it was 81 % in one study (Dhalla et al., 2007). For retention (USA only) at 12 months, IDUs overall were found to be retained at a range of 67–98 % (two studies) and WAHR at 67–92 % (two studies). In two studies, 12-month retention in

Abbreviations: Ad5, adenovirus 5; AOR, adjusted odds ratio; HIV, human immunodeficiency virus; HR, hazard ratio; IDU, injection drug users; KI, key informant; MSM, men who have sex with men; OECD, Organisation for Economic Co-operation and Development; VISP, vaccine-induced seropositivity; VPS, vaccine preparedness study; WAHR, women at heterosexual risk; WTP, willingness to participate.

Two supplementary tables are available with the online Supplementary Material.
MSM was 81–84 % (two studies). In one study in MSM, 87 % of older MSM (≥25 years) and 71 % of younger MSM (<25 years) were retained at 12 months (Scheer et al., 1999).

In the non-OECD countries, the lowest WTP was 23 % in community residents in Cape Town, South Africa, whilst the highest was 100 % in women in Tamil Nadu, India and in female commercial sex workers in Mombasa, Kenya (Dhalla et al., 2009). The 12-month retention ranged from 77 to 85 % in the populations described.

Preventative HIV vaccine trials in the OECD countries

Completed phase 3 HIV vaccine trials include the VaxGen (AIDSVAX B/B) study in MSM and WAHR, which took place in Canada, the USA and Puerto Rico and was completed in 2003 (Francis et al., 2003). This clinical trial tested the rgp120 HIV vaccine, and found that the vaccine was ineffective.

The STEP study was a phase 2B multi-centre preventative HIV vaccine trial with sites in the USA, Canada, Australia, the Dominican Republic, Haiti and Peru (NIH US National Library of Medicine, 2007). The STEP study tested the adenovirus 5 (Ad5) vector in MSM and found it to be ineffective. This clinical trial was stopped in September 2007, as there was a statistically significant increase in HIV acquisition in the vaccinated group, compared with the placebo group, in those who were uncircumcised (Buchbinder et al., 2008). The two factors responsible for the higher rate of HIV acquisition in the vaccinated group compared with the placebo group were circumcision status in male participants and exposure to the Ad5 vector used in the STEP study (Buchbinder et al., 2008). The unadjusted hazard ratio (HR) for risk of HIV-1 acquisition was highest in men who were uncircumcised and who were Ad5 seropositive [HR 3.3, 95 % confidence interval (CI) 1.3–11.9]. Risk was intermediate in men who were uncircumcised and Ad5 seronegative (HR 3.3, 95 % CI 0.7–15.8) and in men who were circumcised and Ad5 seropositive (HR 1.6, 95 % CI 0.7–3.8). Risk did not seem to be increased in men who were both circumcised and Ad5 seronegative (HR 0.7, 95 % CI 0.3–1.4). These results did not found that the rgp120 vaccine (AIDSVAX B/E) was ineffective (Pitisuttithum et al., 2006). Due to the results of the STEP study, the Phambili study in South Africa, which used the same vaccine as the STEP study, was stopped in 2007 (Gray et al., 2014). The RV144 vaccine trial in Thailand in lower-risk heterosexuals utilized the HIV vaccines ALVAC HIV (vCP1521) and AIDSVAX B/E (Rerks-Ngarm et al., 2009). This vaccination regimen was found to be moderately effective (30 %) in reducing HIV acquisition.

The main objective of this review was to provide an update of HIV VPSs that have taken place in the non-OECD countries, following a previous review on HIV VPSs published in 2009 (Dhalla et al., 2009). Data on non-OECD countries as opposed to OECD countries were used in this review of VPSs, as much of the current literature on VPSs refers to resource-limited settings. A further objective was to compare WTP in HIV vaccine trials and retention rates using South African data from before and after the STEP/Phambili studies.

METHODS

In 2014, the Cochrane Database for Systematic Reviews, Medline, Pubmed, Embase, and Google Scholar were searched and the relevant articles were selected. The search terms used were ‘HIV’, ‘vaccine preparedness’, ‘HIV vaccine’, ‘developing country’ and ‘non-OECD’. The search terms also included authors in the subject area. Journals publishing HIV/AIDS topics were also searched. Additional articles were retrieved from bibliographic references. The literature review focused on articles from 2007 onwards, as a previous review on HIV VPSs in non-OECD countries reviewed articles prior to and including 2007 (Dhalla et al., 2007). Articles were included if they were: (i) published in a peer-reviewed journal; (ii) took place in non-OECD areas; and (iii) were in English.

Where the type of questionnaire (i.e. interviewer or self-administered) or times of data collection were not available from the individual articles, investigators were contacted to obtain this information. Information on the study population, location and sample size was extracted from the text and tables of the articles, and then tabulated in our review to describe WTP and the retention rates of VPS participants. Any predictors found to be associated with WTP are included in Table S1 (available in the online Supplementary Material). Adjusted odds ratios (AORs), HRs and prevalence proportion ratios (PPRs), and p-values are presented, if available, for any variables found to be associated with WTP and retention.

RESULTS

Fig. 1 shows the literature review flow diagram. With the search strategy used, 260 articles were identified from the literature. Sixteen articles that were relevant to this review were retrieved in total. Table S1 describes the WTP and Table S2 describes the retention rates of participants in the individual VPSs in the non-OECD countries. The types of questionnaires utilized with regards to WTP were mainly interviewer-administered questionnaires, found in nine studies (Asiki et al., 2013; Deschamps
et al., 2013; Kiwanuka et al., 2013; Middelkoop et al., 2008; Newman et al., 2014; Olanrewaju et al., 2014; Otwombe et al., 2011; Ruzagira et al., 2009; Suhadev et al., 2009) (Table S1). Two studies utilized a self-administered questionnaire (Chariyalertsak et al., 2011; de Bruyn et al., 2008; C. Beyrer, personal communication) and one study in South Africa utilized a self-administered visual analogue scale (VAS) (Giocos et al., 2008). One study conducted in China utilized computer-assisted self-interviewing (CASI) (Chu et al., 2013).

Both ‘adults’ and ‘adolescents’ were examined in these studies (Tables S1 and S2). Although adults were defined as ≥18 years of age in some studies, this was not the case in all studies. For example, in one study in South Africa, adolescents were defined as those aged 16–20 years (Middelkoop et al., 2008). Two studies examined high school students, with age ranges from 10 to 25 years (de Bruyn et al., 2008) and 14–21 years (Giocos et al., 2008). In addition, in the study by Middelkoop et al. (2008), 71% of adolescents were also in high school (K. Middelkoop, personal communication).

WTP

Thirteen retrieved studies in the non-OECD countries examined WTP in a hypothetical HIV vaccine trial and predictors of WTP (Table S1). These studies were those subsequent to the studies cited in our previous review of WTP (Dhalla et al., 2009).

The non-OECD countries examined in the present article included South Africa, India, Uganda, Thailand, China, Nigeria and the Dominican Republic, Haiti and Puerto Rico.

In adults, WTP in these studies ranged from 40 to 99.4% (Table S1). WTP was highest in adults from fishing communities in Uganda (99.4% at baseline), where an interviewer-administered questionnaire was administered (Asiki et al., 2013). It was lowest in itinerant female hairdressers in Nigeria (35%), in which an interviewer-administered questionnaire was also utilized (Olanrewaju et al., 2014). In the latter study, some participants were between 16 and 17 years of age. In the nine studies utilizing interviews, WTP ranged from 35 to 99.4% (Table S1).

In the two studies utilizing self-administered questionnaires (Chariyalertsak et al., 2011; de Bruyn et al., 2008), WTP in a hypothetical HIV vaccine trial ranged from 69.7 to 88.2% (Table S1). In the one study that utilized a self-administered VAS, 79.5% of participants were WTP (Giocos et al., 2008).

The types of population examined in the individual studies on WTP are shown in Table S1. Four studies examined adults and adolescents in South Africa. Besides adults (Middelkoop et al., 2008), populations examined in South Africa included adolescents (Middelkoop et al., 2008; Otwombe et al., 2011) and high school students (de Bruyn et al., 2008; Giocos et al., 2008). Including
data from our previous review of VPSs in the non-OECD countries, WTP in the South African studies ranged from 13 to 93 % in adolescents (Jaspan et al., 2006; Lindeger et al., 2007; Middelkoop et al., 2008) and 79.3–88.2 % in high school students as presented in the individual articles (de Bruyn et al., 2008; Giocos et al., 2008). Furthermore, in the study by Middelkoop et al. (2008), 71 % of adolescents were in high school (K. Middelkoop). In the same study in adults, baseline WTP was at 40 % (Middelkoop et al., 2008). In a previous, interview-based study by Lindeger et al. (2007) in South Africa published in 2007, older members of the sample expressed more WTP in HIV vaccine trials, whilst younger participants (particularly in the 21–30 years age group) were more likely to be unsure about participation in a hypothetical HIV vaccine trial.

In our previous review of HIV VPSs in the non-OECD countries, three studies in South Africa were identified that examined WTP in a hypothetical HIV vaccine trial and examined predictors of WTP (Jaspan et al., 2006; Lindeger et al., 2007; Smit et al., 2006). Data in the study by Smit et al. (2006) were collected in 2003. WTP in an HIV vaccine trial was only 23 % in this setting in participants aged 16–40 years (Smit et al., 2006). In the study by Middelkoop et al. (2008), in which data were collected between 2003 and 2005, baseline WTP was 13 % in adolescents (16–20 years) and 40 % in adults (21–39 years). The dates of data collection and the age range of participants in the study by Lindeger et al. (2007) were not stated and the information was not available from the trial investigators.

In the study by Smit et al. (2006), in community residents (16–40 years), knowledge of HIV vaccines was associated with an increased WTP in an HIV vaccine trial. In the study by Middelkoop et al. (2008) between 2003 and 2005, increasing HIV vaccine knowledge was significantly associated with a greater WTP as reported at both the start and end of the study ($P<0.001$ for both adults (21–39 years) and adolescents (16–20 years) at baseline and 12-month follow-up).

**Consent to participate**

Consent to participate in adolescents ($<18$ years of age) was studied in several studies in South Africa. In a study by Jaspan et al. (2006) in South Africa, consent was obtained by adolescents and parents in their homes, and WTP using a self-administered questionnaire was 79 %. In the study by de Bruyn et al. (2008), which utilized a facilitated self-administered questionnaire, WTP in a hypothetical HIV vaccine trial by high-school students was 88.2 %. In this study, both parental and child consent was required for participation for those $<18$ years of age. In the study by Middelkoop et al. (2008), the enrolment of adolescents was simplified by the fact that parental consent was waived for those aged 16–20 years; the WTP in this study was only 13 % at baseline. In the study by Giocos et al. (2008), the investigators obtained passive consent (A. Kagee, personal communication): the students were given an informed consent form to take home, and it was assumed that when the forms were not brought back, the parents consented to participation by the students. The WTP in this study was 79.3 % (G. Giocos, personal communication). However, this type of passive consent is no longer allowed or sufficient in studies (A. Kagee, personal communication). For instance, in a more recent study conducted after the STEP/Phambili trial in South African, for adolescents aged 16–18 years, both parental and participant consent were required for study participation; WTP was high at 89 % in males and 96 % in females prior to giving information on the STEP/Phambili trial (Otwombe et al., 2011).

**WTP before and after the STEP/Phambili trial**

The data collection times for the individual WTP studies are shown in Table S1. Other than the study by Otwombe et al. (2011) in South African adolescents, it is not clear from other VPSs after the STEP/Phambili trial whether participants were aware of the results of the STEP/Phambili study. Therefore, in the present article, a comparison before and after the STEP/Phambili trial was made specifically using South African data. In a study in Cape Town, South Africa, in adolescents between 2004 and 2005, 79 % of adolescents were either definitely or probably WTP in an HIV vaccine trial (Jaspan et al., 2006). In another Cape Town study prior to public dissemination of the STEP/Phambili results, WTP ranged from 13 % in adolescents to 40 % in adults in South Africa, in a study in which data were collected between 2003 and 2005 (Middelkoop et al., 2008). In a 2011 study, Otwombe et al. (2011) in South Africa compared WTP (very willing, somewhat willing or willing) in adolescents before and after information was given on the STEP/Phambili trial. In males, WTP was 89.3 % before and 72.6 % after being given information on the STEP/Phambili trial. In females, WTP was 95.6 % before and 77.1 % after being given the information (Otwombe et al., 2011).

**Retention**

Retention was examined in five studies in African countries including South Africa (Middelkoop et al., 2008; Price et al., 2012), Kenya (Price et al., 2012), Tanzania (Geis et al., 2011) and Uganda (Ruzagira et al., 2011; Kiwanuka et al., 2013) (Table S2). The types of population enrolled in these VPSs included heterosexuals (including both adults and adolescents) (Geis et al., 2011; Middelkoop et al., 2008; Price et al., 2012), HIV discordant couples (Ruzagira et al., 2011), MSM (Price et al., 2012) and general fisher-folk communities (Kiwanuka et al., 2013). The follow-up times varied depending on the VPS (Table S2). In a previous review of retention rates in HIV VPSs in the non-OECD countries, the 12-month retention rates ranged from 77 to 85 % (Dhalla et al., 2009). In one study on heterosexuals in Tanzania, the 6-month follow-up was 94.7 % and the 4-year follow-up (or at seroconversion) was 68.9 % (Geis et al., 2011). In another...
study in HIV discordant couples in Uganda, the 2-year follow-up was 80.2 % (Ruzagira et al., 2011) (Table S2). In a further study, the retention rate was 76.9 % overall in a general fisher-folk population in Uganda at 12 months (Kiwanuka et al., 2013) (Table S2). With regard to factors associated with retention in these African countries, higher retention was associated with being female (Middelkoop et al., 2008; Geis et al., 2011) and being of older age (Geis et al., 2011; Ruzagira et al., 2011).

In studies that examined retention, it is again unclear whether participants of the respective studies were aware of the results of the STEP/Phambili and RV144 HIV vaccine trials. Prior to the studies by Middelkoop et al. (2008) and Price et al. (2012), no previous VPS had examined retention rates in South African populations (Dhalla et al., 2009). In the study by Middelkoop et al. (2008) before the STEP/Phambili trial, in which data were collected between 2003 and 2005, there was no significant difference in retention rates at 12 months between adults (83 %) and adolescents (87 %). Price et al. (2012) examined retention in a Cape Town study, in which participants were enrolled between 2005 and 2008. Participants were followed monthly for 1 year in Cape Town, and the loss to follow-up rate was 21.8 per 100 person-years in volunteers. In summary, the length and time demands of a specific study may have impacted retention numbers more so than the STEP/Phambili trial data.

The HIV seroincidence rate in the study by Price et al. (2012) was 2.7 per 100 person-years in women in Kilifi (Kenya) and Cape Town (South Africa), an incidence sufficient for a phase 3 HIV vaccine trial. The HIV seroincidence in women was significantly lower than the incidence rate observed in MSM (6.8 cases per 100 person-years) in the same study.

Barriers to participation in hypothetical HIV vaccine trials before and after the STEP/Phambili trial

Besides WTP, barriers and motivators were assessed both prior to and after the STEP/Phambili studies. The author has previously published a manuscript outlining barriers to participation in a hypothetical HIV vaccine trial in 2011 (Dhalla & Poole, 2011). The study by Otowmbe et al. (2011), which examined WTP after the STEP/Phambili trial, did not examine barriers to participation.

In one study in India, focus groups were held among MSM and interviews were held among key informants (KIs) to explore barriers associated with WTP in a hypothetical HIV vaccine trial (data collection between June 2010 and June 2011) (Chakrapani et al., 2012). Key informants (KIs) were more educated than other participants (all KIs had a college degree), and also tended to occupy leadership roles (Chakrapani et al., 2012). Barriers to participation included stigma/discrimination, issues of confidentiality/privacy, vaccine-induced seropositivity (VISP), concerns about trust in government, financial concerns and excessive compensation, having dependent family members and disclosure of sexuality to family members, possible increases in unprotected sex, and safety and side effects. Once the results of the STEP study were disclosed to potential volunteers, some MSM reported that trialists should disclose everything about the STEP study prior to conducting an HIV vaccine trial (Chakrapani et al., 2012). Mistrust regarding volunteers being treated as guinea pigs by foreign trialists was also reported by KIs, although not by most MSM.

The STEP study also enrolled some high-risk women from the Caribbean (Buchbinder et al., 2008). Between 2009 and 2010, Deschamps et al. (2013) reviewed barriers to participation in female commercial sex workers in the Caribbean using interviews. Permanent injury or death was of most concern (70 % being very concerned), followed by VISP (48 % very and 27 % somewhat concerned). Side effects were also of concern to participants.

DISCUSSION

In this review, WTP in a hypothetical HIV vaccine trial, retention and barriers to participation were examined in the non-OECD countries. In South Africa, data were examined before and after the STEP/Phambili studies with regard to WTP in only one study (Otowmbe et al., 2011). It should be noted that few VPSs have been published in the OECD countries since the discontinuation of the STEP/Phambili studies (Etcheverry et al., 2013; Ma et al., 2014).

An important issue in the non-OECD countries surrounds socially desirable reporting on the part of adolescents and/or their parents in the reported studies. For example, socially desirable reporting can pertain to the type of questionnaire used in the individual VPS. In the studies cited in this review, WTP did not appear to be modified by the type of questionnaire. In the South African study by Jaspan et al. (2006) in adolescents (aged 11–19 years) using a self-administered questionnaire, the percentage of participants who were WTP (79.5 %) was similar to the percentage WTP in another South African study by Otowmbe et al. (2011) using interviews in adolescents 16–18 years of age. In the latter study, overall WTP was 75 % after information was given regarding the STEP/Phambili results. In addition to the type of questionnaire used, WTP may also be modified by parental consent in studies involving adolescents. Data obtained from investigators showed that when parental consent was obtained, WTP was higher than when it was not obtained. This was further exemplified in a study by Giocos et al. (2008) in which subjective norms were significantly associated with participation in an HIV vaccine trial [AOR = 1.19 (1.07–1.34)].

In the study by Otowmbe et al. (2011), WTP was 17 % lower in males (89.3 % before and 72.6 % after) and 19 % lower in females (95.6 % before and 77.1 % after) after...
being given information on the STEP/Phambili trial. However, with reference to participant knowledge of the results of the STEP/Phambili trial, potential participants such as MSM who are familiar with research and researchers may still participate in HIV vaccine trials and other clinical trials. Furthermore, participants may also not disclose their HIV status or being on antiretroviral treatment.

For most of the studies cited, other than that by Otwombe et al. (2011), it was unclear whether the participants were aware of the results of the STEP/Phambili and RV144 HIV vaccine trials. However, even with the results of the South African study by Otwombe et al. (2011), hypothetical WTP in a VPS may not translate into WTP in an actual HIV vaccine trial. For example, in a study in high-risk HIV-uninfected individuals in the USA, only 20% who stated hypothetical WTP in a VPS actually enrolled in a phase 2 trial (Buchbinder et al., 2004). Currently, there is no valid data tool available that can be used to distinguish hypothetical from actual WTP.

Barriers to participation in HIV vaccine trials are important to examine as predictors of participation before and after the STEP/Phambili trial. However, in future HIV vaccine trials in the non-OECD countries, concerns about participation in an HIV vaccine trial should be addressed (Deschamps et al., 2013), including safety concerns such as physical harm concerns and side effects, VISP, social stigmatization and mistrust in potential volunteers. For example, in a VPS by Deschamps et al. (2013), concern about participation in an HIV vaccine trial in commercial sex workers was inversely related to WTP in a hypothetical HIV vaccine trial. Dealing with participant stressors such as separation from family and having a family member with HIV may also improve participation in an HIV vaccine trial (Otwombe et al., 2011).

Limitations

There are several limitations to the present review. First, this is a descriptive review and does not follow Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The lack of any intervention studies or of meta-analysis of the results across studies is also an important limitation. As the regression models in the studies cited in this review were not consistent among studies and the author did not have access to raw data, AORs could not be combined in a formal meta-analysis. Another limitation to this review was that there was only one reviewer, and this may introduce bias. Finally, a limitation would be that hypothetical WTP may not translate into actual WTP in an HIV vaccine trial.

Future research

Studies in the non-OECD countries could be designed to help understand gaps in our understanding of WTP. More studies in South Africa could be designed to examine the difference in WTP after participants are given information on the STEP/Phambili trial. Barriers and motivators in South Africa can also be assessed after the results of the STEP/Phambili trial. As has been done in the OECD countries (Buchbinder et al. 2004), VPSs could be conducted to determine whether hypothetical WTP translates into actual WTP. In future VPSs, regression models should be kept consistent among studies such that AORs between predictor variables and the outcome could be combined in a formal meta-analysis. For example, knowledge of HIV vaccine trials and HIV vaccine trial concepts could be measured more consistently. Other cognitive factors such as self-efficacy and optimism about HIV vaccines/vaccine trials could also be measured consistently. The cognitive factors of knowledge, self-efficacy and HIV treatment optimism have been evaluated previously in relation to WTP in a hypothetical HIV vaccine trial in IDUs in Vancouver, Canada (Dhalla et al., 2009). Future HIV vaccine preparedness research should utilize self-administered questionnaires or audio-computer self-assisted interviews (ACASI) to avoid social desirability bias.

CONCLUSION

Few articles have been published in the OECD countries since the discontinuation of the STEP/Phambili studies. Therefore, this article updates HIV VPSs following a previously published article in the non-OECD countries in 2009 (Dhalla et al., 2009). In one South African study, the overall WTP rate was 93% before participants were given information on the STEP/Phambili trial and 75% after they were given such information. As the study by Otwombe et al. (2011) in South Africa is the only one to specifically make this comparison on WTP, the finding of the difference in WTP is not a very robust review finding. Barriers to participation post-STEP/Phambili trial studies include safety issues and side effects, VISP and mistrust among KIs. The results on HIV VPSs indicate that HIV vaccine trials are still feasible in non-OECD countries and South Africa, but barriers must still be overcome to improve feasibility. However, it should be noted that hypothetical WTP may not translate into actual WTP in an HIV vaccine trial.

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