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Conceptual framework for behavioral and social science in HIV vaccine clinical research

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Abstract

HIV vaccine clinical research occurs within a context where biomedical science and social issues are interlinked. Previous HIV vaccine research has considered behavioral and social issues, but often treated them as independent of clinical research processes. Systematic attention to the intersection of behavioral and social issues within a defined clinical research framework is needed to address gaps, such as those related to participation in trials, completion of trials, and the overall research experience. Rigorous attention to these issues at project inception can inform trial design and conduct by matching research approaches to the context in which trials are to be conducted. Conducting behavioral and social sciences research concurrent with vaccine clinical research is important because it can help identify potential barriers to trial implementation, as well as ultimate acceptance and dissemination of trial results. We therefore propose a conceptual framework for behavioral and social science in HIV vaccine clinical research and use examples from the behavioral and social science literature to demonstrate how the model can facilitate identification

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of significant areas meriting additional exploration. Standardized use of the conceptual framework could improve HIV vaccine clinical research efficiency and relevance.

Introduction

Preventive HIV vaccines are intended for HIV uninfected individuals. Ideally they will prevent new infections, but may also work by attenuating the course of HIV if the vaccine recipient becomes infected due to exposure to the virus. Current investigational preventive vaccines cannot cause HIV infection.

HIV vaccine evaluation interfaces with behavioral and social science research (BSSR) in many ways. For example, behavioral-social factors can facilitate or impede trial conduct and eventual vaccine uptake, even if the vaccine candidate is effective. These factors include underlying perceptions about HIV, misconceptions about HIV vaccine research and its volunteers, effects of experimental vaccines on trial participants, socio-cultural and ethical-legal contexts in which trials are conducted, and past clinical trial experience. Vaccine research is a cornerstone of biomedical efforts toward HIV prevention and is inextricably linked with social and behavioral strategies as part of a multilevel approach to prevention [1].

A systematic framework that aims to identify and address issues arising before, during and after an HIV vaccine trial is needed to integrate behavioral-social and HIV vaccine clinical research. In this article, we present an organized framework that HIV vaccine scientists can use when considering which behavioral-social factors to address in their research. Conceptual frameworks have been applied to many behaviors, including HIV vaccines. The framework presented here builds on previous models and frameworks to identify target areas for proactive integration BSSR into future trials. It represents multiple factors whose causal relationships remain to be elucidated through extensive additional research. Our goal is to promote a coordinated approach to the inclusion of behavioral-social factors in HIV vaccine development that will not only enhance research efficiency, but also increase attention to ethical issues, considerations for the relevance of findings, and planning for successful vaccine roll out.

Need for a Behavioral-Social Science Framework in HIV Vaccine Clinical Research

Many of the conceptual/theoretical models that have been developed to understand health-related behaviors are based on existing social and psychological theories. Conceptual frameworks are used to help us understand a specific situation or issue by providing a systematic way to articulate hypothesized relationships among social, behavioral and biological determinants and the outcome of interest. They provide a structure for identifying strategic points where intervention is likely to have its greatest impact. Typically, models are grounded in multiple theories, and in the context of health promotion/disease prevention the theories have often been adapted from the psychosocial sciences [2]. BSSR about HIV prevention has evolved from predominantly psychological models that focus on individual behavior to models that view more broadly the dynamics of couples, networks, communities and societies that contribute to the epidemic [3, 4]. Several models that acknowledge population and societal influences have applications to HIV prevention research.

Exploration of theory-based approaches to health behavior informs the development of a comprehensive framework for HIV vaccine trials. For example, Rhodes, Stein, Fishbein, Goldstein et al [5] used the Integrative model of Behavioral Prediction to understand how

prevention interventions work. Their study provided strong evidence that enhanced interventions significantly influence male and female condom use with main and casual partners. Enhanced counseling appears to systematically change self-efficacy and negative behavioral beliefs as well as influence normative beliefs [5]. Galea, Ahern & Vlahov [6] discussed a theoretical framework incorporating key contextual variables that may be determinants of drug use behavior and related HIV risks. The framework was based on the premise that social policy and regulation affect contextual, mediating, and individual-level factors [6].

The above models incorporate critical concepts from well-established theories. While they do apply to health behaviors, it is questionable whether trial participation, particularly HIV vaccine trial participation, is necessarily a health seeking or health promoting (or neither) behavior. Kafaar, Kagee, Lesch and Swartz [7] point out that whether or not HIV vaccine trial participation is a health promoting behavior depends on whether one views it from the investigator perspective or from the participant perspective. Researchers may be tempted to fall back on the most well-known theories of health behavior, even though their applicability to HIV vaccine trials is untested and at best partial.

Limited attempts have been made to develop BSSR models of HIV vaccine trial participation. The South African AIDS Vaccine Initiative (SAAVI) Socio-behavioral Group conducted a qualitative investigation into factors that enable or inhibit participation in HIV vaccine trials, and developed an Enabler-Inhibitor quadrant model [8]. Both enablers and inhibitors can be considered as existing at multiple levels: individual, family, community and societal levels [8]. The model unfortunately does not hypothesize relationships between factors needed to inform interventions. The International AIDS Vaccine Initiative (IAVI), International Center for Research on Women (ICRW) and University of Nairobi diagrammed the interaction between vaccine and social science research to inform a study on gender related barriers and facilitators to women's participation in HIV vaccine trials in Kenya [9, 10]. The framework illustrates the intersection between the states of the clinical process, volunteer experience and the structural, socio-cultural context that influences these processes [9]. The AIDS Vaccine Advocacy Coalition (AVAC) formulated Good Participatory Practice (GPP) Guidelines to set global standards for stakeholder engagement for biomedical HIV prevention trials. These guidelines review the complexities of biomedical HIV prevention research, enumerate guiding principles and establish standards of GPP to facilitate meaningful research [11].

Social and Individual Behavior in the HIV Epidemic and Prevention Research

Realization has grown about the ways that social, ethical, behavioral, economic, and cultural factors reciprocally impact the HIV epidemic. Social research has illuminated the epidemic's effect on demographic trends, household structure and function, care giving, gender dynamics, education, economy and governance [12]. Friedman, Kippax, Phaswana-Mafuya et al identify six major themes ranging from war and economic dislocation to unintended social consequences from treatment failures that are emerging bases for HIV research [13]. We briefly take up three areas of social scientists' long-term engagement with the HIV/AIDS epidemic that suggest how BSSR on different levels can inform HIV vaccine trials: social determinants (drivers), social and behavioral interventions, and social impact.

Because determinants of HIV risk are multi-level, HIV prevention strategies need multiple components to address them. In addition to the immediate behavioral predictors of infection, fundamental social mechanisms underlie the spread of an infectious disease like HIV [14, 15]. For instance, unprotected sexual intercourse and the sharing of injection equipment, two

known drivers of the epidemic, may be motivated by individual reproductive goals, pleasure, peer pressure, love, coercion, habit, or reflect cultural practice. Risk reduction approaches, such as condom distribution, harm reduction in the form of needle exchange or counseling are types of behavioral intervention that mitigate risky behaviors or try to change underlying motivations. However, an ‘upstream’ driver of the epidemic can be lack of education, the effect of which varies by demographics [16, 17]. Since level of education influences how uptake and integration of prevention strategies occurs, the UNAIDS Interagency Task Team on Education advocates more and better schooling [18].

Contemporary behavioral interventions to mitigate HIV transmission now draw on this fundamental insight that individuals are embedded in and often subject to contexts of family, community and society, enmeshed in cultural norms and perceptions. Behavioral prevention strategies may include attempts to delay onset of first intercourse and/or decrease the number of partners where epidemics have become generalized [19-21], sometimes referred to as primary behavior change [22]. In a broader view, behavioral interventions aim to increase the proportion of protected sex acts [23, 24], provide counseling and testing [25, 26], encourage adherence to antiretroviral therapy [27, 28], and decrease substance use or mitigate its risks [29-31]. Strategies may attempt to motivate behavioral change within individuals through education, motivational activities, skills building and community normative approaches. Theory-based behavioral interventions have been tested with mixed results [32-42]. Behavioral strategies are best combined strategically with biomedical and structural approaches to address local epidemics, focusing on the specifics of individuals, couples, families, groups or networks, institutions or communities.

Behavioral programs have been contrasted with structural interventions that seek to change the social, political or economic context contributing to risk [1, 17], although some authors include more proximal approaches under the category of structural [cf. 43]. Structural strategies may be combined with biomedical interventions including microbicides, vaccines and antiretroviral treatment of HIV-infected persons. Well-executed policies can have multiple benefits. For example, expanded access to treatment not only decreases HIV related morbidity, but also decreases viral load and thus may impact rates of transmission. Parker and Aggleton [44] discuss development of structural interventions that address HIV related stigmatization and discrimination. The approach emphasizes community mobilization aimed at “unleashing resistance to stigmatization and discrimination” that transforms the character of social discussion and supports outcomes such as civil rights legislation.

Another issue that benefits from behavioral and social science inquiry is assessment, monitoring and mitigation of the social impact of HIV and related research [45]. Social impact studies identify both positive and negative aspects and highlight a variety of issues including attitudes to trial participation, job-related problems, difficulties obtaining health and/or life insurance and vaccine-induced seropositivity [46]. Historically the assessment of social impact has been secondary or exploratory. However, more current trials in the HIV Vaccine Trials Network have incorporated social impact assessment as a standard procedure, and the network intends to analyze social impact across trials to determine how to address negative social impact [45].

Many BSS considerations in HIV prevention research are related to ethico-legal considerations and individual behaviors and motivations. These include standard of care, culturally relevant and appropriate informed consent, confidentiality, stigma, community consultation, protection of vulnerable groups, international collaborations, epidemiological and socio-behavioral studies as well as considerations of accessibility, post-trial benefits, and equity and sustainability of interventions [47]. Effective management of ethical issues is critical to the success of all research, particularly that pertaining to the sensitive topic of

HIV. Despite the apparently broad exploration of behavioral and social factors in HIV prevention, there are significant gaps in relation to HIV vaccine clinical research. The literature suggests the need for a systematic approach to addressing those gaps as part of a clinical research agenda [46]. Considerations of the changing ethico-legal and policy landscapes; understanding how high-level statements by institutions, officials and scientific opinion leaders might shape the research agenda; and examinations of the influence of economic concerns on trial roll-out and conduct will be of continuing value.

Studies on behavioral-social determinants of HIV vaccine clinical trial participation are sparse. At the individual level very little research has been conducted on decision-making processes related to enrolling and participating in HIV vaccine trials. Reasons for qualified persons refusing to participate extend to the social, psychological and emotional dimensions (48). Fear of negative biological outcomes, resistance from significant others, anticipated stigma and discrimination, concerns about behavioral disinhibition, and uncertainty about researcher intentions have been cited as reasons for declining participation in actual HIV vaccine trials [48-50]. A qualitative study among HIV vaccine research participants in Kenya highlighted the different factors men and women weigh in deciding upon study participation as well as the differing approaches to decision making. For example, women were more likely to seek multiple consultations with partners, peers and even research staff. They were also expected to seek permission from partners and/or family members. In contrast, men's decision-making processes revealed more autonomy and independence, reflecting the cultural norm [10]. Systematic reviews of vaccine preparedness studies reveal that willingness to participate has a large range (23%-100%) and varies with demographics and environment [51-52].

Barriers and motivators to participation, willingness to participate, knowledge of HIV, vaccine perceptions, retention of participants in trials, mistrust of researchers, sexual risk reporting during the trials, and sero-conversion during participation in a trial are relevant to trial conduct [53-55,10]. One systematic review found that safety concerns, mistrust of those involved in clinical research and risk of discrimination constituted major barriers to HIV vaccine trial participation and highlighted the importance of a well coordinated research plan that includes education, active participation of the local community and development of local expertise and infrastructure [56]. In addition, there are a number of studies on strategies for recruitment, retention/attrition, social harms, sexual risk monitoring, and risk compensation [57], a range of ethical and human rights issues including employment or insurance discrimination related to vaccine induced seropositivity, social discrimination due to trial participation, and potential unblinding through outside testing [53,58].

HIV vaccine preparedness studies indicate that motivators for participation have included altruism, monetary incentives, care/services, testing/counseling, expected protection from HIV infection, as well as support for avoidance of risk behavior [59-60, 55, 10]. If participants have the erroneous expectation that the experimental vaccine provides protection from HIV infection, this may also act as a motivator [7]. Alternatively, concerns about side effects, vaccine induced seropositivity and false positive tests as well as trial-related discrimination have all been documented as being associated with lower willingness to participate [10, 60-61]. Strauss, Sengupta, Kegeles & McLellan et al [62] noted similar benefits and concerns from in-depth interviews with high-risk groups. Self-benefit, helping to stop the spread of AIDS, altruism, increasing social networks, small number of side effects, and an effective vaccine were reported as benefits. In the same cohort, perceived risks included negative side effects, contracting HIV from the vaccine, negative social consequences of trial participation, unpleasant experiences, concern that the vaccine may not work, testing HIV positive, and inconvenience of trial participation.

Determinants that impact clinical trials and trial participants beyond the individual and research realms, such as community related and macro environment factors, have received less attention. While impact of previous clinical trials on current trial participation has been explored [54], little research has been conducted on communities' scientific literacy or how such information diffuses in communities. Although this type of research has been conducted in broader HIV prevention programs [63], there are few HIV vaccine-specific studies that do so [10]. A workshop in South Africa, conducted with a range of stakeholders from principal investigators and social scientists to community outreach workers underscored this issue and identified a set of priority research questions to address it [57, 64].

Lastly, future HIV vaccine uptake should be optimized via investigation of contributing factors in parallel with HIV vaccine development. Use of the health belief model, which focuses on the attitudes and beliefs of individuals, facilitates consideration of psychological factors contributing to HIV vaccine acceptance (65). Future HIV vaccine acceptability is differentially affected by various factors, with efficacy and non risk group membership contributing more than pragmatic obstacles, cost, perceived HIV susceptibility, safety concerns, fear of vaccines, perceived benefits, duration of protection and efficacy (66). HIV vaccine trials present an opportunity to evaluate and manage factors impacting future vaccine uptake (67).

Toward a systematic integration of BSS in clinical research

A comprehensive conceptual framework that broadly maps the terrain of behavioral and social science research in all phases of clinical vaccine development will aid in addressing key gaps in understanding factors important to trial success, including trial participation and eventual vaccine uptake. While models have been applied, none is comprehensive or has been systematically applied by groups conducting HIV vaccine clinical research. The framework presented in Figure 1 emphasizes the intersection between broader social and contextual factors with the science driven process experienced by individual trial participants and researchers. In doing so, it brings attention to key junctures where BSSR contributes to the overall success in vaccine development and eventual roll-out.

Components of the framework are categorized into macro-environment, community, individual, and research [Figure 1]. While participation in an HIV vaccine trial occurs at an individual level, there are multiple levels of influence that impact the volunteer's enrollment and completion of the trial, the final output in this framework. These influences are important for a potential volunteer who may consider not only participation in a trial, but will also need to comply with trial requirements, complete the trial, and accept trial results. From the perspective of the clinical researchers and their teams, understanding the nature of these influences will help inform and refine strategies of engagement thereby facilitating efficient, effective and ethical conduct of the trial. The conceptual framework proposed here attempts to capture the levels of analysis and their significant points of intersection, while specifying the factors by which participation may be affected at each level. Understanding and studying these intersections will help in achieving a number of intermediate and final outcomes of interest including recruiting and retaining eligible volunteers in the trial and reducing risk behaviors.

The Macro environment takes into account the considerations of the changing policy climate, how institutional officials and scientific opinion leaders may influence the research agenda, shifting power dynamics amongst individual and institutional stakeholders, cultural factors, as well as the influence of economic concerns on trial conduct. The research considerations focus on clinical trial recruitment, retention/attrition, social harms, sexual risk

monitoring and risk compensation as well as a range of ethical and human rights issues (employment, insurance, social discrimination), but can also take into account the cultural competency of the investigators and the clinical site staff. The Community related aspects take into consideration social norms and networks, but also attempt to address community interactions and their integration; few studies have been conducted on community dynamics, the impact of previous clinical trials on current trial participation, community literacy or how information diffuses in communities. Individual factors considered in this model include motivators and barriers to clinical trial participation, recruitment and retention as well as participant experience and trial completion, all of which influence trial participation. The proposed conceptual model provides a guide to address considerations of multiple components and contexts of research trials and a map to potentially guide the integration of behavioral and social science research with HIV vaccine trials.

Positioning of the framework components reflects their impact on a potential volunteer's trial participation. By identifying, describing, operationalizing and measuring the influences of different components, researchers will be able to discern the type and intensity of that influence on the outcome of interest as well as the interaction of those influences with others. Framework components provide concepts for causal models that will help explain and predict individual participation, community acceptance and ultimately enhance the confidence we can place in the internal validity of HIV vaccine trials. For example, when working with vulnerable and marginalized groups the legal and institutional conditions at the macro level as well as community norms (and those in the immediate peer network) will influence where and how these groups congregate, access information and health services, experience social impact, and make decisions related to health and sexual behaviors. In addition, individual understanding and behavioral intentions will determine who among them will participate and who will not, how study processes will enhance or deter participation, and so on. Identifying and understanding these factors within the broader context of a trial embedded in a community will further inform how to better reach those who are eligible for participation. Finally, modeling influences within the conceptual framework will provide insights and possible explanations for why certain results or patterns are seen in the clinical results.

Discussion

In this paper we have presented a broad conceptual framework that builds on existing work and advances the discussion by highlighting the multilevel contexts in which a trial is carried out. Informed by the literature and several authors' experiences, the framework highlights gaps and maps a comprehensive view of the domains of BSSR applicable to HIV vaccine trials. Previous BSSR related to HIV vaccine trials has largely focused on the individual volunteer in the vaccine trial, specifically individual-level factors that influence HIV vaccine trial participation and experience, and the impact of vaccine trial conduct on individual behaviors. Review of the literature reveals instances where the value of applying a conceptual framework in identifying the multiple levels of influence would be helpful.

Examples of HIV Vaccine clinical trials related research that integrate concepts from our framework are shown in Table 1. Relevant topics for future study are proposed.

Investigators will benefit from locating social and behavioral factors related to HIV vaccine clinical research in a comprehensive contextual framework. For example, what is the effect of vaccine trial conduct on local health system function (e.g. staff requirements, introduction of new technologies) and how do these health systems influence vaccine trial conduct (e.g. standard of care, perception of research) [81]? A comprehensive framework such as the one proposed here will enable researchers to identify which behavioral-social factors have been

adequately addressed (e.g. individual barriers and facilitators) and where additional investigations are merited (e.g. how non-aligned health policies at different tiers of government may hamper HIV vaccine trial conduct). Also, assessment of risk behavior and understanding by trial volunteers, including behavioral disinhibition, risk behavior/profile assessment, and the Hawthorne effect of participating in research (trial participants may modify their behavior just in response to participating in a trial), could be incorporated into planned research. Researchers could use the proposed framework to tease out causal pathways of behaviors that impact vaccine evaluation. It is unlikely that any one study could address the behavioral social issues comprehensively. For research addressing behavioral issues, attention to methods and methodology will be critical. A rigorous approach should be established a priori to ensure integrity of the research.

While our framework is helpful for systematic exploration of behavioral-social factors related to HIV Vaccine clinical trial participation, it does have limitations. First, the framework is not predictive, but rather hypothesis generating. While a predictive model would be extremely helpful, it would ultimately require the components in this conceptual framework be operationalized, measured and tested across a wide range of trial settings. Also, relative contributions of different components are not represented in the framework. Some components will carry more weight in particular situations and less in others. Furthermore, the framework does not distinguish between developed and developing country settings. We have attempted to design a framework flexible enough to be applied in diverse settings, but cannot be certain that every nuance is captured. The framework is general and will likely need to be tailored for specific circumstances. Lastly, the framework makes certain assumptions about the relationships of its components. While these are logical relationships reflected in the literature, it is not clear that they are universal. Despite these caveats, the framework provides a structured paradigm in which to consider behavioral-social aspects of HIV vaccine clinical research.

Conclusion

Addressing BSSR issues throughout clinical vaccine development is important for ensuring scientific validity and relevance to target populations, as well as identifying factors that contribute to an observed pattern or association. Further along the development path, HIV vaccine roll-out will likely be challenging, especially in light of emerging biomedical preventions, partially effective HIV vaccines in development, HIV associated stigma, and the influence of research findings on community perceptions of vaccines in general [60]. Multifaceted community mobilization employing mass media, social marketing, community engagement and targeted policy may be beneficial [47]. Use of the proposed conceptual framework will help to ensure consideration of behavioral-social factors that are central to a comprehensive approach to HIV vaccine clinical research.

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Figure 1.

Conceptual framework for behavioral-social science in HIV Vaccine Clinical Research

The framework shows factors that contribute to the participant's experience and finally trial completion. The framework represents a dynamic process with constant interactions amongst the components. Compartment size is not reflective of relative contribution of the components.

Table 1

Select completed studies and future research topics to which the conceptual framework applies

Model Component	Examples of Completed Studies	Relevant Topics for Future Study
Macro Environment	<ul style="list-style-type: none"> Sayles et al (2010) Future HIV vaccine acceptability among young adults in South Africa [68]. Johnson et al (2009) The effect of educational attainment and other factors on HIV risk in South African women: results from antenatal surveillance, 2000- 2005 [17]. Hargreaves et al (2008) Systematic review exploring time trends in the association between educational attainment and risk of HIV infection in sub-Saharan Africa [16]. Kakinami et al (2008) Differences in HIV vaccine acceptability between genders (USA) [69]. 	<ul style="list-style-type: none"> How is the epidemic evolving in the region? How do national and institutional policies and practices impact risk, access to health care and AIDS vulnerability among those most at risk (e.g. MSM)? How do national and institutional policies and practices impact engagement, recruitment and participation in trials among those at highest risk? How are power dynamics likely to influence vaccine roll-out and access? Drawing lessons from HPV vaccine as a proxy for a future HIV vaccine, assess the impact of policy and economic issues on uptake after licensure.
Community	<ul style="list-style-type: none"> Sengupta et al (2010) A conceptual model exploring the relationship between HIV stigma and implementing HIV clinical trials in rural communities of North Carolina [70]. Newman et al (2009) A small dose of HIV? HIV vaccine mental models and risk communications (USA) [71]. Mills et al (2006) Enrolling women into HIV preventive vaccine trials: An ethical imperative but a logistical challenge (Africa) [72]. Roberts et al (2005) HIV vaccine knowledge and beliefs among communities at elevated risk: conspiracies, questions and confusion (USA) [73]. 	<ul style="list-style-type: none"> Evaluation of community engagement practices across groups conducting HIV vaccine trials. Assess experience (or non-experience) of community members, enrolled volunteers, and non-enrolled screeners with CAB members and site staff. What are community perceptions, norms and expectations related to understanding of HIV, HIV vaccines, and trial site activities? How are power dynamics likely to influence participation and engagement in research? How are community advisory board members identified and chosen? How do we translate participation in research dialogue into actual enrolment in trials?
Research Related	<ul style="list-style-type: none"> Frew et al (2009) In "Step" with HIV vaccines? A content analysis of local recruitment campaigns for an international HIV vaccine study (US and Canada) [74]. Lindegger et al (2006) Beyond the checklist: Assessing understanding for HIV vaccine trial participation in South Africa [56]. Djomand et al (2008) The HVTN Protocol 903 Vaccine Preparedness Study: Lessons learned in preparation for HIV vaccine efficacy trials (Caribbean, Southern Africa, Latin America) [75]. Russell et al (2005) A pilot study of the quality of informed consent materials for Aboriginal participants in clinical trials (Australia) [76]. De Bruyn et al (2008) Knowledge and attitudes towards HIV vaccines among Soweto adolescents (South Africa) [77]. 	<ul style="list-style-type: none"> Obtain information from community members and trial screeners about their understanding of HIV prevention research. Develop and test more accurate tools to measure HIV risk. Evaluate screening and enrollment data collection processes across networks. Assess impact of site services and staff on trial participation and perception. How do we engage vulnerable populations (e.g. MSM, adolescents, CSWs)? What impact do results from other HIV prevention trials have on vaccine trials? What are the experiences of sero-converters in phase II B HIV vaccine trials?

Model Component	Examples of Completed Studies	Relevant Topics for Future Study
		<ul style="list-style-type: none"> Are current informed consent processes effective? What is the social impact of participation in HIV vaccine research?
Individual	<ul style="list-style-type: none"> Sayles et al (2010) Future HIV vaccine acceptability among young adults in South Africa [68]. Gray et al (2008) Participation in two phase II prophylactic HIV vaccine trials in UK [78]. Newman et al (2010) "Once Bitten, Twice Shy": Participant perspectives in the aftermath of an early HIV vaccine trial termination (Canada) [79]. Frew et al (2009) Understanding differences in enrollment outcomes among high-risk populations recruited to a Phase IIb HIV vaccine trial (USA) [80]. 	<ul style="list-style-type: none"> How do we identify and address evolving barriers and facilitators to trial participation? Survey community and screeners on how they obtain and process and information. Evaluate tools used to assess understanding of information. Determine ratios of people who sought information, screened, qualified, enrolled and completed the study vs. number who had contact with site staff. Amongst participants who have been screened and are qualified, why do some not enroll? How does individual experience feedback onto one's own participation, participation of others and on research conduct? What are participant's perceptions and experiences from the trial once completed?