

Stakeholder engagement in HIV cure research: Lessons learned from other HIV interventions and the way forward

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Introduction

- Increasing understanding of HIV virology and immunology has energized the global scientific community to develop a cure.
- Ongoing research is dominated primarily by concerns regarding the conduct and progress of the current trials aiming at durable drug free viral suppression (functional cure) or as true eradication of HIV (sterilizing cure).
- As of 2014, 54 HIV-cure-related trials were ongoing worldwide, and the number of studies continued to increase. Although a cure seems far in the future, we hypothesize that early, inclusive stakeholder engagement in HIV cure research is essential.
- We define HIV cure research stakeholders as those directly or indirectly involved in organizing HIV cure research studies. Stakeholders include HIV-infected individuals, key affected populations, the scientific community, funding agencies, international agencies, public health and regulatory authorities, pharmaceutical industries, civil society leaders, and media whose understanding and support have been diverse (Table 1). *Stakeholder engagement can shape public perception, contribute research understanding, facilitate volunteer recruitment, and help build multi-sectoral coalitions. Strong stakeholder engagement may also attenuate the risk of research failure and decrease the likelihood of therapeutic misconception.*
- As clinical trials continue to progress, the importance of HIV cure stakeholder engagement only increases and may influence early implementation.

Methods

- We reviewed historical examples of stakeholder engagement in HIV clinical research. We focused on two types of interventions – those which target high-risk, HIV-negative individuals (HIV vaccine trials, antiretroviral pre-exposure prophylaxis (PrEP)) and those targeting HIV-infected individuals (treatment as prevention, prevention of mother-to-child transmission and treatment of acute infection in the context of cure research in Thailand).
- These HIV interventions are clinically important, relatively advanced in clinical development, and at varying stages of program implementation.
- Our objective was to (1) examine the timing, profile and mechanisms of HIV stakeholder engagement, (2) evaluate examples of HIV stakeholder engagement in emerging HIV interventions, and (3) articulate a framework for stakeholder engagement specific to HIV cure clinical research.

Results

- We analyzed five examples of HIV interventions targeted at both high-risk HIV-uninfected and HIV-infected individuals: (1) HIV vaccine trials, (2) pre-exposure prophylaxis (PrEP), (3) treatment as prevention (TasP), (4) prevention of mother-to-child transmission (PMTCT), and (5) treatment of acute infection in the context of cure research (Figure below).
- We examined the historical background, extent of stakeholder engagement and progression over time, and strengths and weaknesses of stakeholder engagement for each of these interventions.
- Examples of stakeholder engagement in HIV clinical research and translation to program implementation were described (Table 1 to right). Based on our analysis of these five HIV interventions, we proposed a five-step process for inclusive stakeholder engagement in HIV cure research (Table 2 to right).

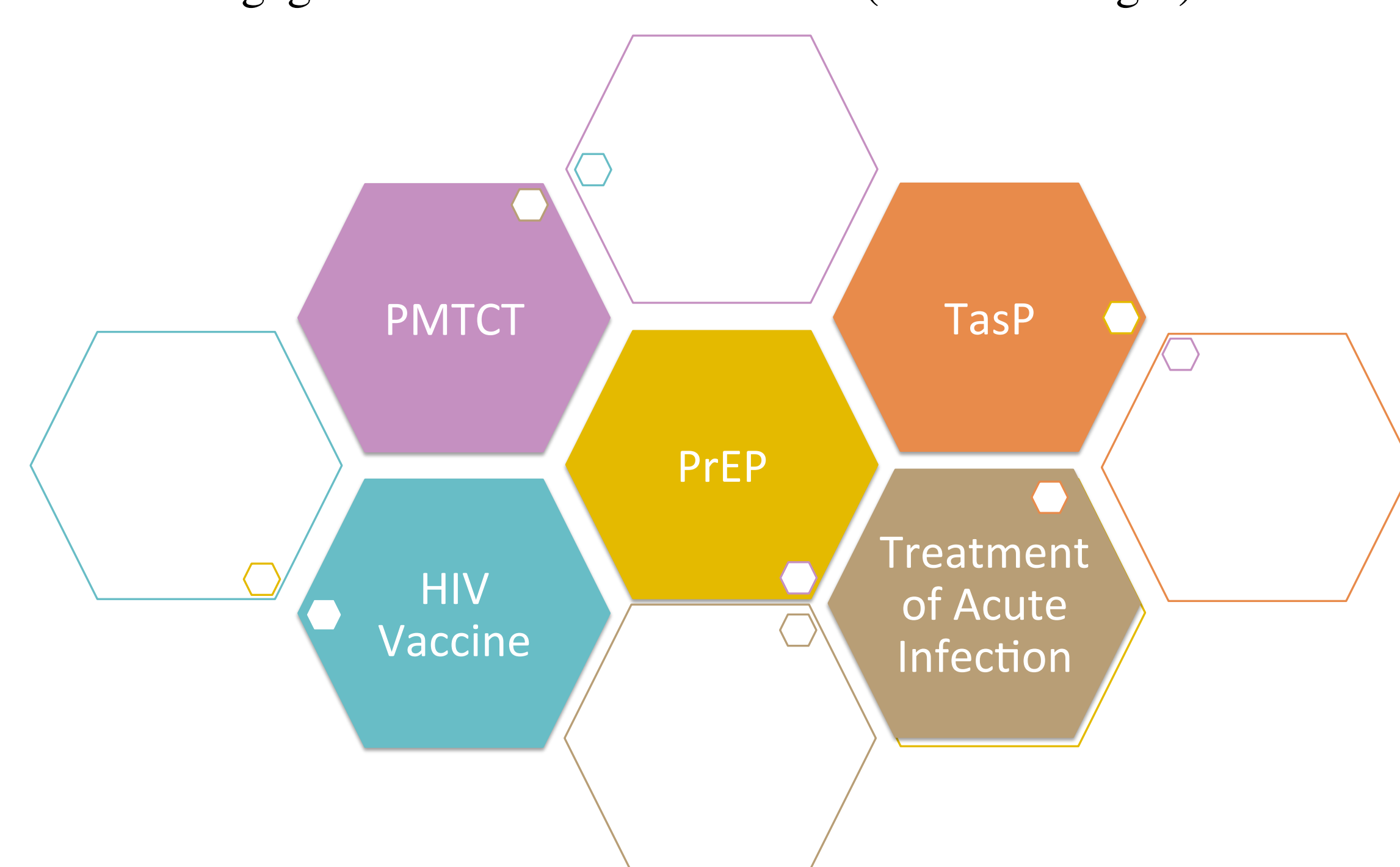


Table 1. History of stakeholder engagement

Intervention	Stakeholder Engagement	Lessons learned
HIV-uninfected individuals		
HIV vaccines	Out of six HIV vaccine efficacy trials conducted since the early 2000s, only RV144 demonstrated efficacy with a 31% reduction in HIV acquisition compared to placebo.	Inclusive stakeholder engagement occurred early. Clinical trials sought political and community support and integrated early planning for future deployment and access.
	Unlike the first trials in resource-limited countries, the implementation of new efficacy trials is now under close scrutiny by communities, scientific and regulatory authorities, and funding agencies.	
PrEP	Early PrEP trials in Cambodia, Cameroon, Malawi and three West African sites failed to launch or were stopped prematurely due to ethical, political, and logistical concerns of civil society leaders. Inclusive stakeholder engagement beyond community advisory boards of individual studies started only in mid to late 2000s.	Trial initiation and implementation challenges later on may reflect inadequate communication between stakeholders and key populations. Earlier engagement of key populations, policy makers, and community leaders may have resulted in better understanding of the social meaning, ethical considerations, and economic consequences of PrEP research.
	A number of efficacy trials started with delay and today, it has been demonstrated that oral PrEP for HIV-negative individuals reduces HIV-1 acquisition in men who have sex with men, serodiscordant couples and people who inject drugs. But implementation has not yet taken off in resource-limited settings.	
HIV-infected individuals		
TasP	The HPTN 052 study went through an 'ethical odyssey' that threatened to jeopardize the trial: People living with HIV demanding access to treatment, the changing threshold of WHO guidelines, the debate about HIV prevention commodities, and the belief of some stakeholders that the biological plausibility of treatment as prevention did not warrant a randomized clinical trial. The study team made use of existing stakeholder platforms for HIV treatment.	This stakeholder engagement process is consistent with the Denver Declaration, in which treatment activists made a call to action and developed community advisory boards. Established channels and platforms for HIV treatment can be used to engage stakeholders.
	Formal mechanisms for stakeholder engagement were established, comprising United Nations agencies and the WHO. The Interagency Task Team on the Prevention and Treatment of HIV Infection in Pregnant Women, Mothers and Children (IATT) supported pilot projects in resource-limited settings and continued until today to review programme progress through regular stakeholder engagement.	
PMTCT	In Thailand the repurposing of HIV vaccine clinical study (RV254/SEARCH 010) to HIV cure research suggest that stakeholder platforms for vaccine development may serve as platforms for HIV cure research.	Wide stakeholder engagement throughout research brought together high-level policy makers, global champions, governments, researchers and communities and helped translate research to implementation. The example from Thailand shows the overlap between research and stakeholder engagement for HIV vaccine development, ART and cure as well as for PMTCT and paediatric care and cure and that HIV cure research can benefit from existing platforms.
	In Thailand, key opinion leaders in the pediatric HIV field engaged PMTCT stakeholders in preparation of a pediatric HIV cure trial. This stakeholder group received support from the Ministry of Public Health (MOPH), and an MOPH advisory board was formed to prioritize pediatric cure research as a national agenda.	
Treatment of Acute Infection		

Table 2. Stakeholder engagement in HIV cure research

Stages of Engagement	Rationale	Technical Tools	Examples
1. Identify/map stakeholders	Essential for subsequent stakeholder engagement	In-person meetings, key informant interviews	Family planning and HIV planning, country-specific plans
2. Critical reflection and repurposing	Core values and processes of engagements often similar	Strategic meetings within CBOs, board meetings at organizations	
3. Identify venues & channels for engagement	Technology rapidly changing and this affords new opportunities for engagement	In-person meetings, key informant interviews, stakeholder analysis	Country-specific stakeholder analysis
4. Engage stakeholders	Multi-sectoral input is critical for research from planning and inception of trials and early implementation	Stakeholder analysis, online forums	Online decision tool
5. Sustain stakeholder engagement	Consistent input from stakeholders is important for programmatic success	Contests, online forums, stakeholder meetings within conferences	Stakeholder analysis to inform program sustainability

Conclusions

While the prospect of HIV cure is perhaps possible in only a subset of HIV-infected individuals, there is cautious optimism that knowledge gained from these selected individuals could lead to better interventions for the general HIV-infected population. The recent history of HIV interventions suggest that a concerted effort for transparent and multi-directional engagement among stakeholders may help address expectations, answer questions, clarify misconceptions, manage failure and prepare for success in a timely manner. Stakeholder engagement is a necessary component of HIV cure research.

Relevant Literature

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