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Presentation to:  
The IOM Committee on Methodological  
Challenges in HIV Prevention Trials

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## Research is...

Research is four things: brains with which to think, eyes with which to see, machines with which to measure and, fourth, money.

*Albert Szent-Györgyi, 1937 Nobel Laureate in Medicine*

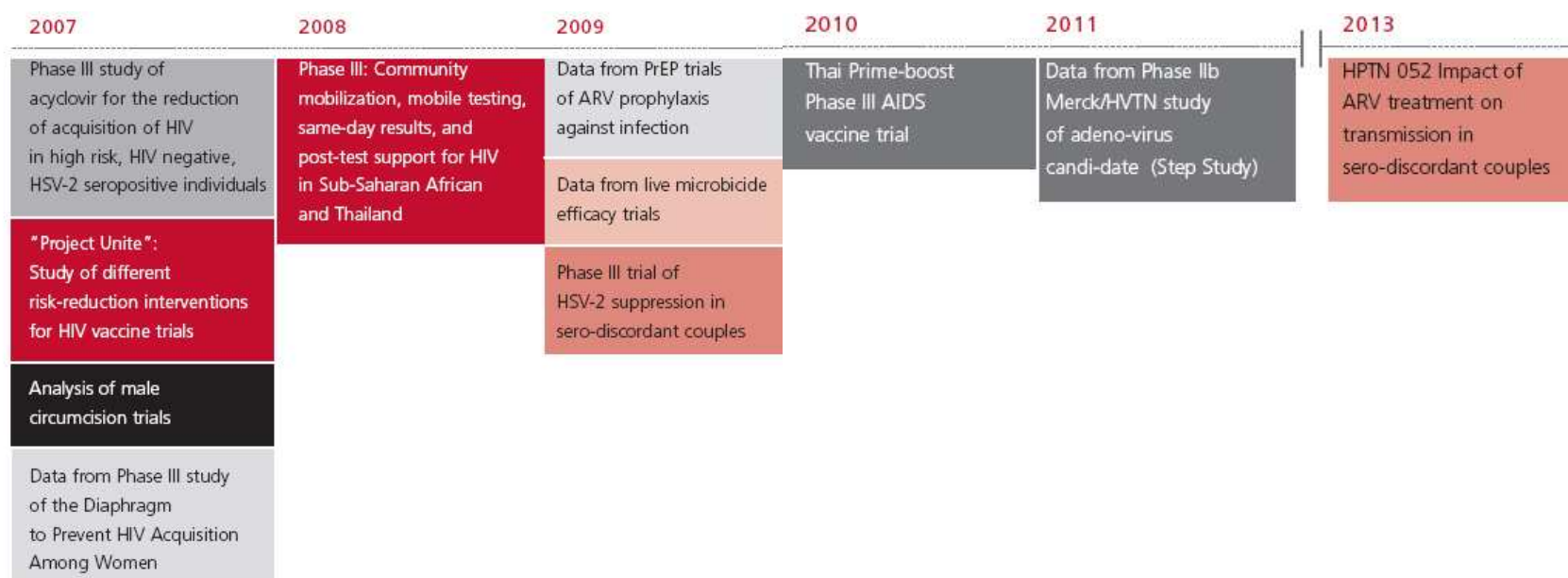
## Prevention research needs...

Increases in:

- Transparency
- Diversity of populations
- Literacy
- Rapid integration of results
- Readiness

# Research that Could Re-define Prevention

## Timeline Of Anticipated Results



<http://www.avac.org/timeline-website/>

## Prevention research science

- “Guns don’t kill people; people do.” *National Rifle Association*
- As we develop new prevention technologies, we need social and behavioural science to guide, influence and contextualize.
- Need to understand how these products are actually used.

## **Trials – names and sequence**

- Nomenclature matters: I, II, IIB/“Test of Concept”, III
- Trial sequencing – both within the product development process for a product and among different approaches
- “Test of Concept” trials can be an important part of product development, but they are not necessarily faster and cheaper
- What each of these trials can (and cannot) do needs to be clearly articulated
- Operations research

## People power

Need to answer questions about safety and effectiveness in a range of populations who need and will use these products.

- Adolescents
- Women (especially in PrEP)
- MSM (especially in microbicides)

## Readiness

- Capacity to do all that needs to be done – need to measure and monitor this on a routine basis.
- Fourteen ***correlates of readiness*** established as a checklist of specific, quantifiable goals that trial networks, advocates and communities can use to determine whether the field is ready to conduct multiple large-scale AIDS prevention trials in developing countries.

## Reality (and perception) check

- “We know communities can understand complicated topics, but we need to invest in research literacy, and that hasn’t happened yet.” *Activist*
- Researchers seem to believe that “Science is a cult of the learned, and *they* have the answers which the community must receive.” *Community representative and activist*
- “You have come here with the ball and all the rules of the game, and asked us to kick the ball.” *Researcher and advocate*

## **Towards a new GCP/GPP**

- Measure and monitor “Good Community/ Participatory Practice”
- Community involvement beyond CABs (which are necessary, but not sufficient)
- Link Prevention, Testing, Treatment and Trials – opportunity to recognize the many potential links between prevention research and broader efforts to build health care infrastructure and civil society capacity

## Issues for prevention trials

- Right now all of the prevention trials that are being conducted ask more or less the same question:

***Does this strategy decrease the risk of HIV infection more than the standard prevention package provided by the study (condoms, clean needles – sometimes!, risk reduction counseling)?***

## Issues for prevention trials

### *But*

As we learn more about new, additional strategies, we will have to decide when to add these to the “standard of care” provided to trial volunteers.

### *And*

We will need to develop even better ways to talk about partial efficacy (since none of these strategies is likely to be 100%)

## **Issues for prevention trials**

The world needs combination HIV therapy and combination HIV prevention. When/if any of these new strategies is found effective, it will become a powerful tool, but it will need to be delivered alongside expanded behavioral interventions, male and female condoms, clean needles, HIV testing, and access to HIV treatment.



## Readiness for recruitment into Phase 1 and 2 trials

- **Correlate #1:** VCT centers linked to treatment, care and clinical trials.
- **Correlate #2:** VCT counselors educated about HIV vaccine research and trained to incorporate referrals to vaccine trials into post-test counseling for all HIV negative individuals.

## Readiness for recruitment into large-scale trials

- **Correlate #3:** New cohorts developed with an inter-network plan for collecting and sharing prevalence and incidence data.
- **Correlate #4:** Shared documentation of site assessment and readiness protocols used to collect epidemiological data with a coordinated effort to translate experience to date into concrete estimates of sample size, capacity needed for future trials.

## Readiness for recruitment into large-scale trials

- **Correlate #5:** Epidemiological studies and cohorts in populations that have proven hard to reach—women at heterosexual risk in clade B countries; intravenous drug users; young gay men of color.
- **Correlate #6:** Funding and supplies for cohort building infrastructure—including steady supplies of HIV rapid test kits; outreach teams equipped with cars and bikes to follow up with cohort members; ongoing vaccine-related staff development for epidemiological study staff.

## Readiness to manufacture & supply candidate vaccines

- **Correlate #7:** Dedicated HIV vaccine production plant capable of manufacturing sufficient quantities of vaccines for small and mid-size trials.
- **Correlate #8:** Financial incentives for more industry experts to conduct translational research for the HIV vaccine field.

## Readiness for long-term relationships with sites & communities

- **Correlate #9:** High percentage of active sites operating with flexible research agendas and minimal “downtime” between projects.

## Readiness for staffing & supporting developing-country trials

- **Correlate #10:** New PhD, RN and MD degrees awarded to people from developing countries each year—who remain in or return to their home countries to participate in research projects.
- **Correlate #11:** Number of developing country regulatory authorities, including ethical and scientific review boards, institutional review boards and data safety and monitoring bodies that have the training, resources and administrative support to review multiple protocols from fields of research—including HIV vaccine trials—each year.

## Readiness for a series of efficacy trials & partial efficacy

- **Correlate #12:** Media stories, political speeches and community dialogues that accurately articulate the nature of the search for an HIV vaccine.

## Readiness for global collaboration

- **Correlate #13:** Community, developing world, and non-US government stakeholders whose substantive input is taken into account during the US National Institutes for Health's recompetition process for its clinical trial networks.
- **Correlate #14:** PEPFAR or GFATM-sponsored ARV programs in communities engaged in vaccine research, and existing vaccine trial sites that share capacity with ARV scale-up programs.