CAPRISA
CENTRE FOR THE AIDS PROGRAMME OF RESEARCH IN SOUTH AFRICA

HVTN 702: A **pivotal** phase 2b/3 multi-site, randomized, double-blind, placebo-controlled clinical trial to evaluate the safety and efficacy of ALVAC-HIV (vCP2438) and Bivalent Subtype C gp120/MF59 in preventing HIV-1 infection in adults in South Africa

Glenda Gray (Chair)
Linda-Gail Bekker(Co-chair)
Kathy Mngadi (PI for CAPRISA Durban ECRS)

HIV VACCINE
TRIALS NETWORK

WHO ARE WE?

Who is the HVTN?

The HVTN is an international collaboration of scientists, clinical trial sites, and community representatives working with governments and industry in the global search for an HIV vaccine with a goal of speeding the development and testing of HIV vaccine candidates.

We need a vaccine.

...to conquer global *and* local HIV epidemics.

Globally-

- 35 million people are living with HIV/AIDS
- About 7,000 new infections take place each day

Locally- South Africa (as of 2013)

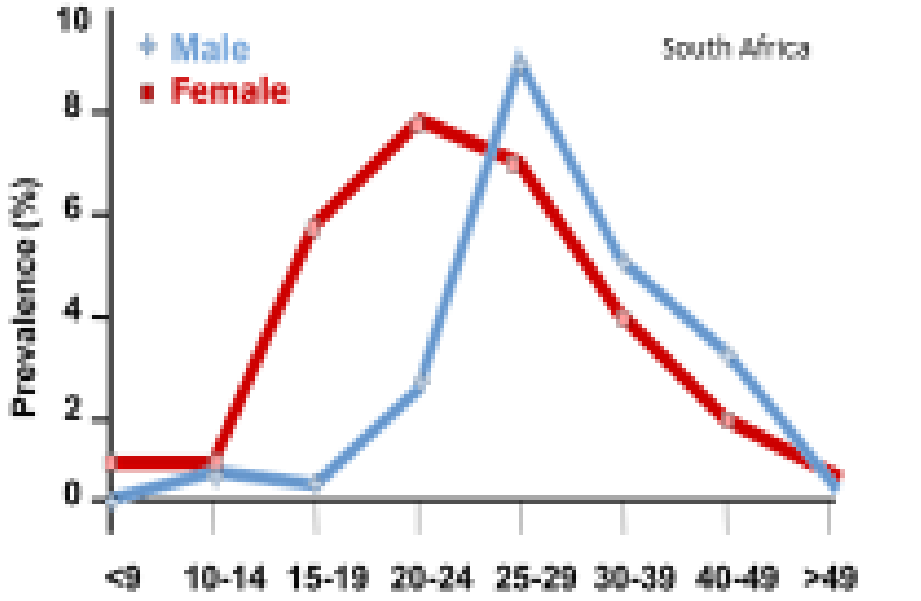
- There are more than 6 million people living with HIV/AIDS
- About 20% of adults aged 15-49 are living with HIV

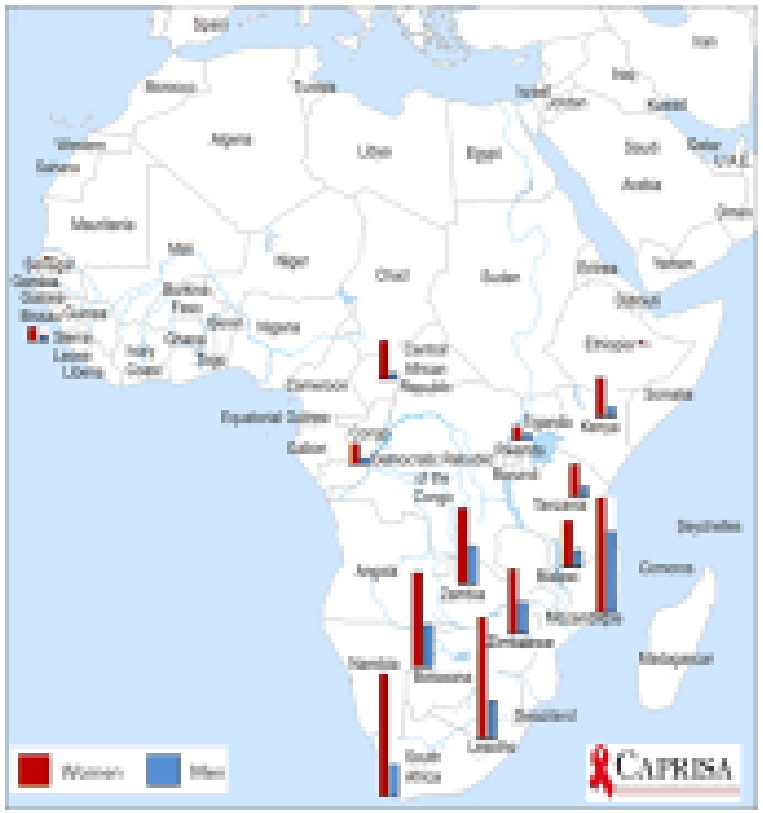
Disproportionate burden of HIV in young women in South Africa

HIV infection and tuberculosis in South Africa: an urgent need to escalate the public health response

THE LANCET

Salim S Abdool Karim, Gavin J Churchyard, Quarraisha Abdool Karim, Stephen D Lawn

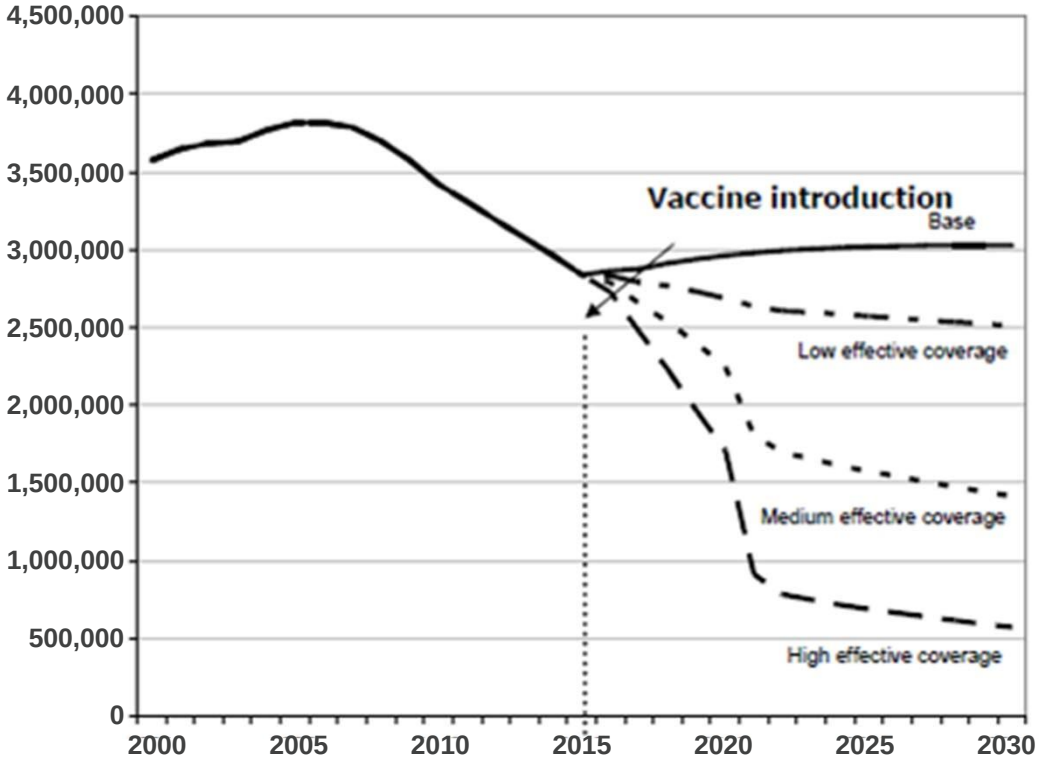




CAPRISA

Potential Impact of a Vaccine

New Adult Infections in Low- and Middle-Income Countries by Year and Vaccine Scenario



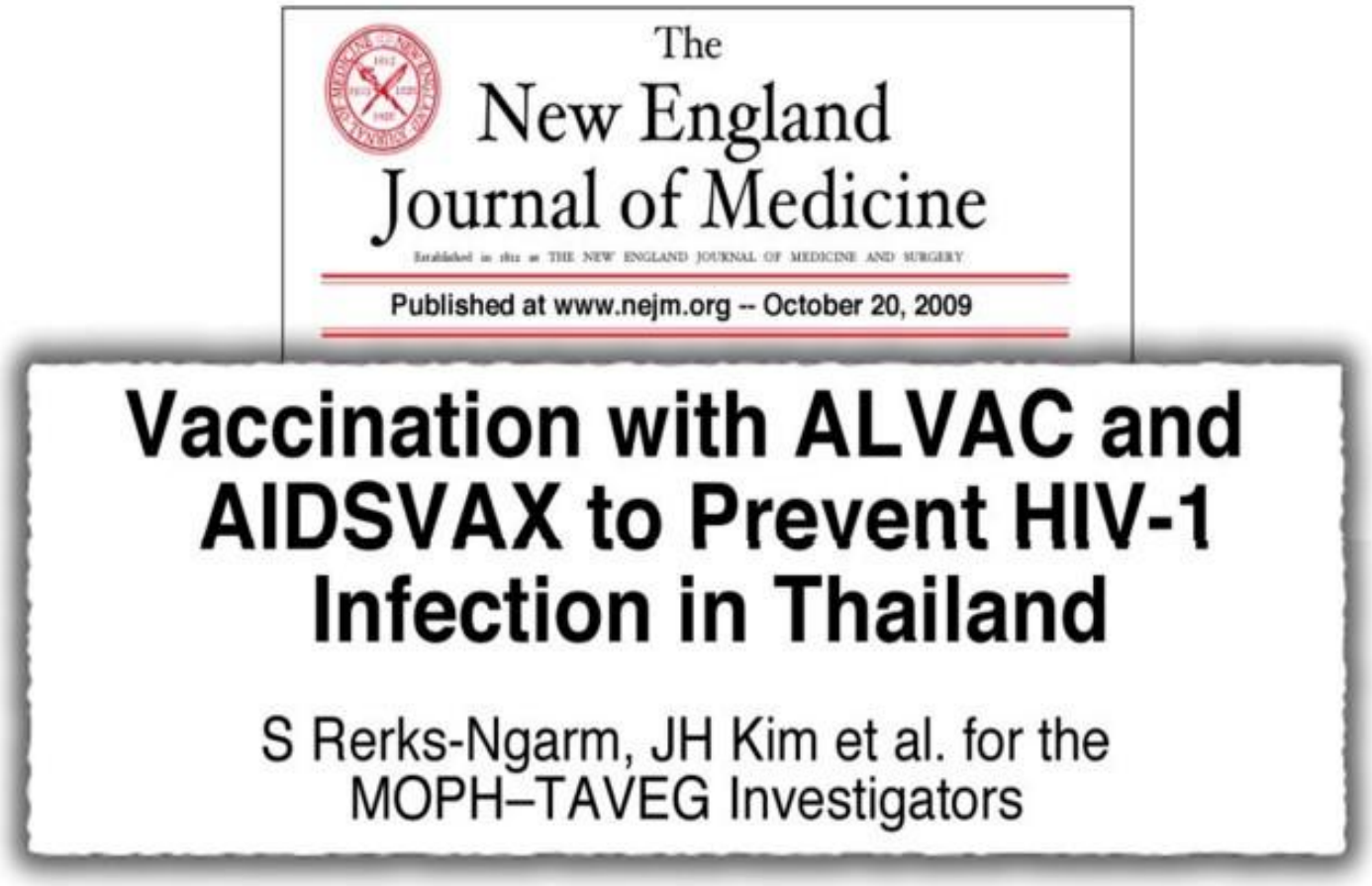
Total new infections averted by an AIDS vaccine between 2015-2030

30% efficacy, 20% coverage	5.5 million
50% efficacy, 30% coverage	17 million
70% efficacy, 40% coverage	28 million

Even a vaccine with low efficacy and limited coverage can impact the epidemic and play a role in preventing future infections

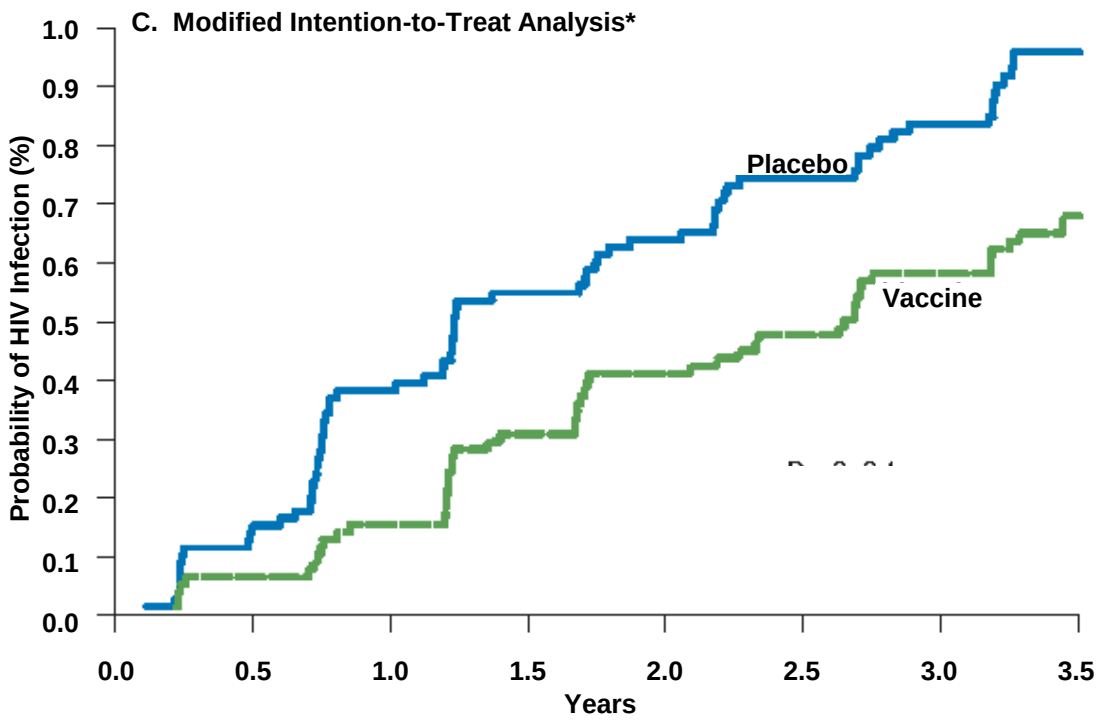
Stover J, et al. The impact of an AIDS Vaccine in Developing Countries: A New Model and Initial Results**. Health Affairs 26(4):1147-1158 (2007)**

First Signal of Efficacy in an HIV Vaccine Clinical Trial



RV144 ALVAC Prime, AIDSVAX B/E Trial

31.2% Estimated Vaccine Efficacy



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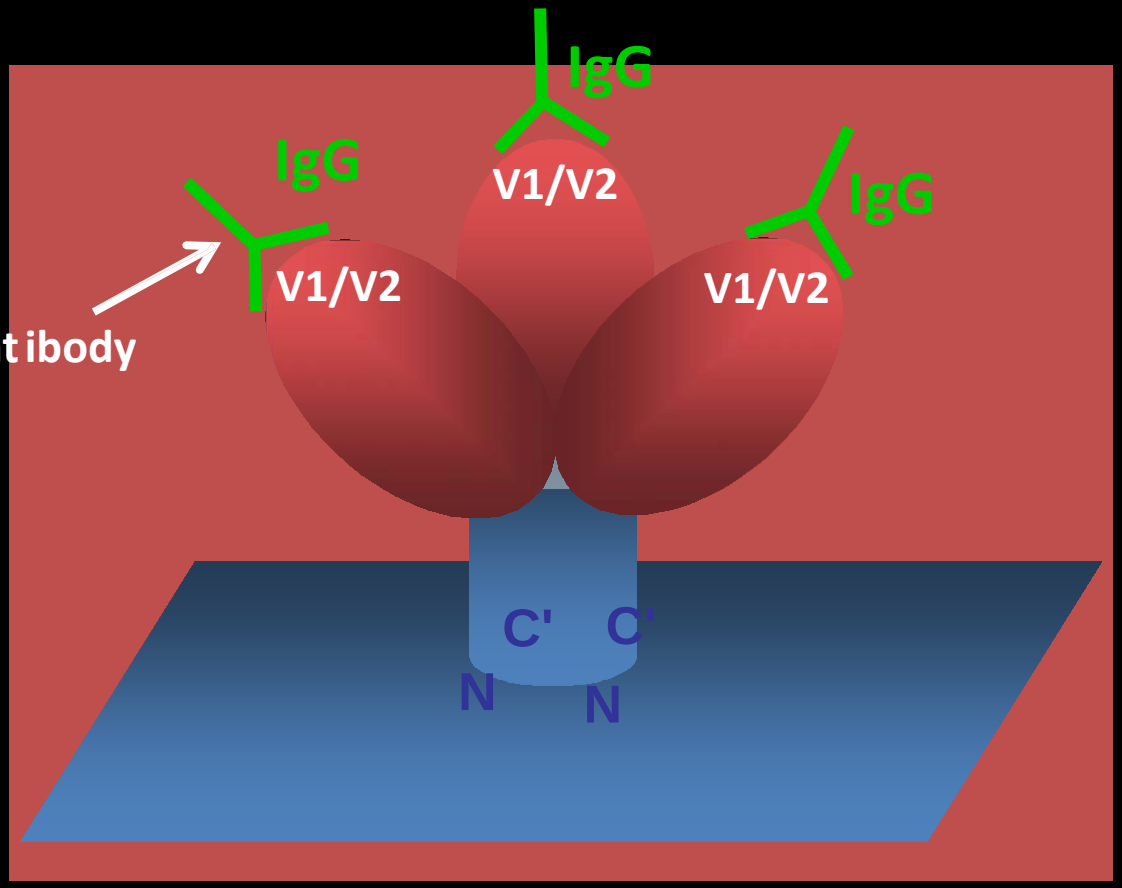
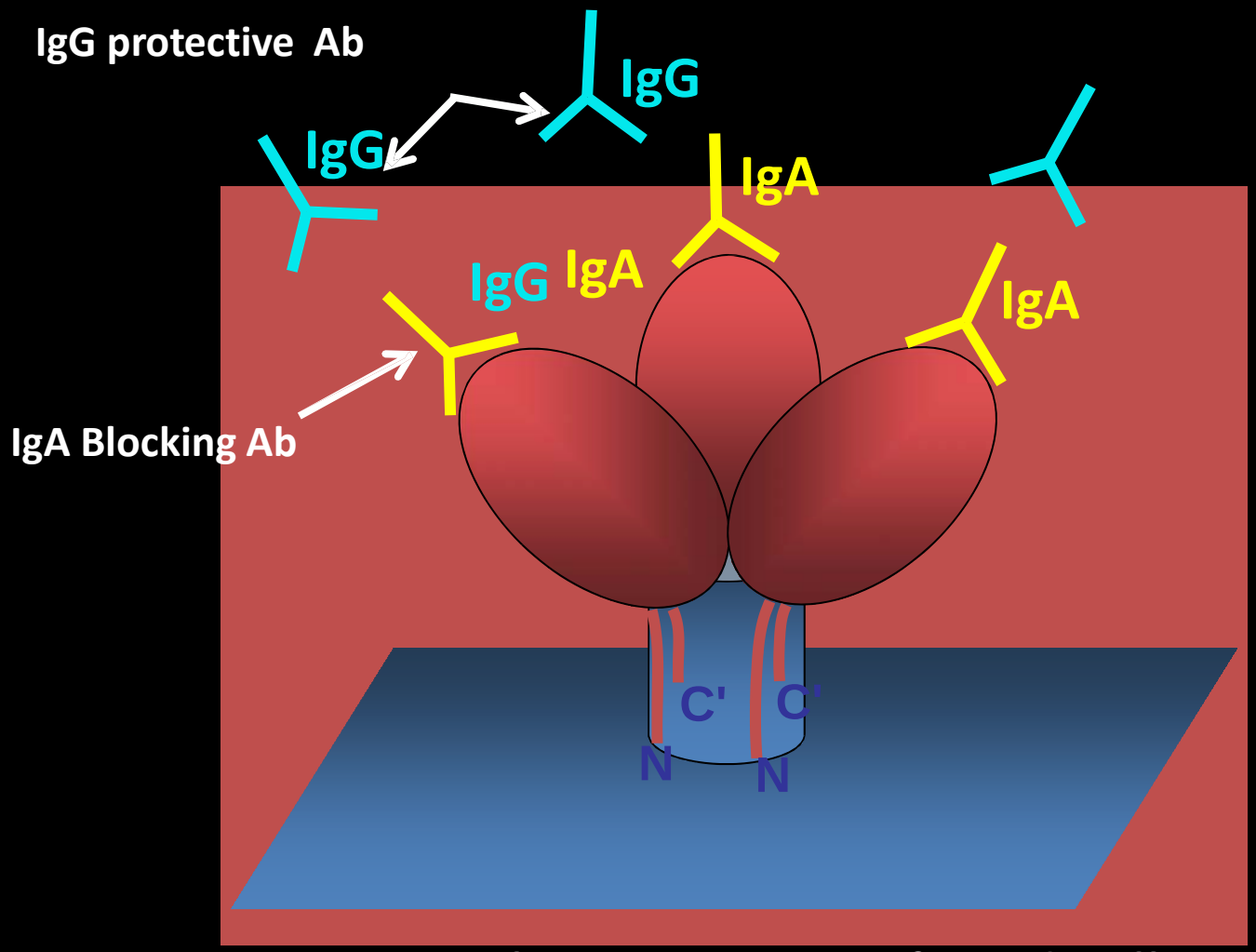
Hypothesis: IgG Antibodies to V1/V2 Can Protect Against HIV-1 Infection



NEJM 366: 1275, 2012

Hypothesis: Monomeric IgA Can Block IgG Binding to HIV-1 Env on Infected Cells and Prevent IgG Protective Functions



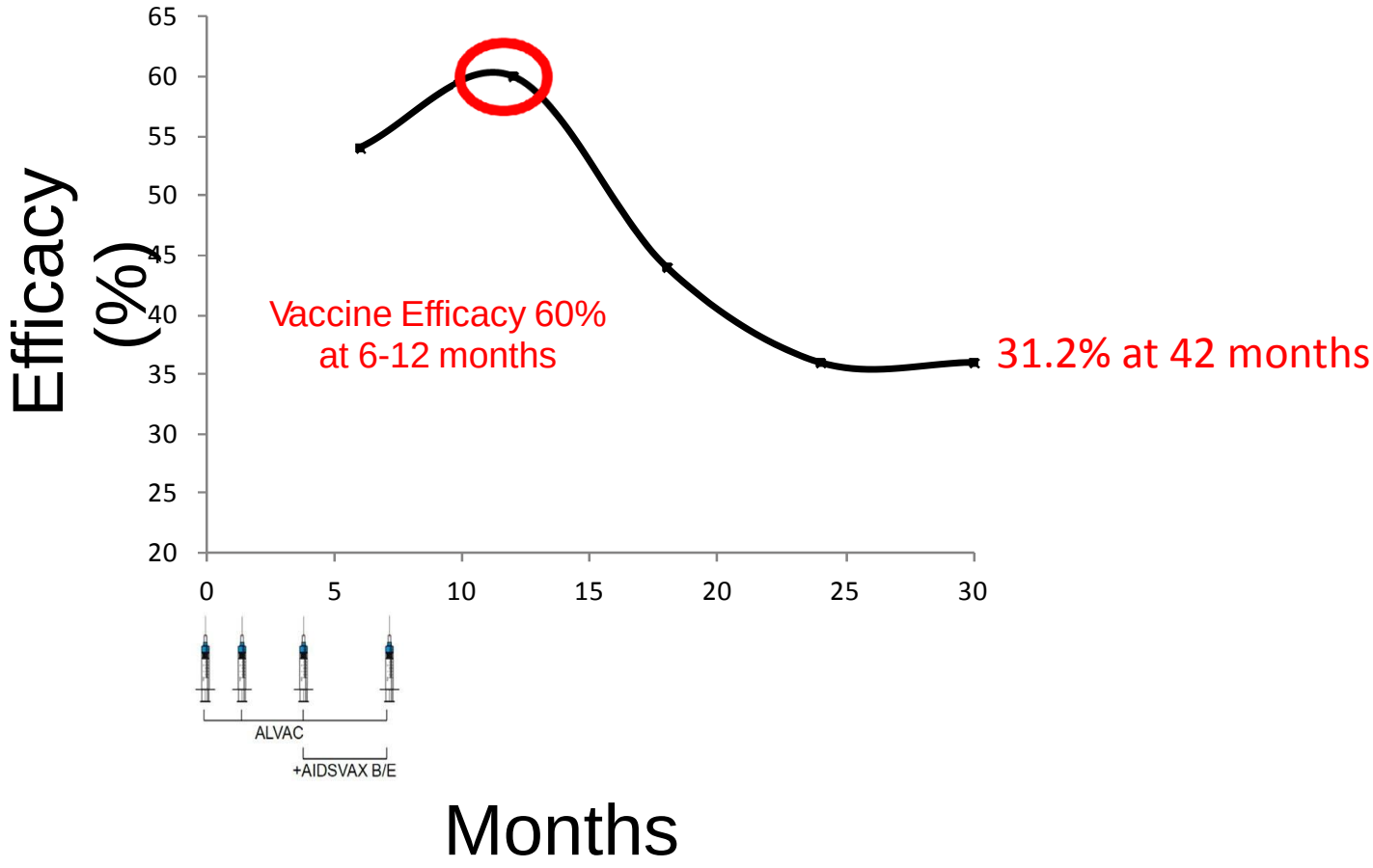
NEJM 366: 1275, 2012

Advancing the findings of RV144 in a clade C region of the world (P5 partnership)

Prime: ALVAC vCP1521

Boost: ALVAC vCP1521 plus VAXGEN env protein (B/E)

Schedule: 0,1,3,6 months; 16,000 volunteers; 1:1 vaccine: placebo; follow-up for 3 years



Although protective efficacy was 31.2% at the primary analysis, 42 months after first vaccination, the highest efficacy was observed at 6-12 months1


uhambo
A JOURNEY OF HOPE TO BE HIV-FREE

Pox-Protein Public-Private Partnership (P5)

P5 is a partnership among Bill & Melinda Gates Foundation, HIV Vaccine Trials Network, NIAID, South African MRC, Novartis, Sanofi Pasteur, and U.S. Military HIV Research Program.

MHRP U.S. MILITARY HIV RESEARCH PROGRAM

HIV VACCINE TRIALS NETWORK

National Institute of Allergy and

SANOFI PASTEUR

MRC SOUTH AFRICA SOUTH AFRICAN MEDICAL RESEARCH COUNCIL

Purpose:

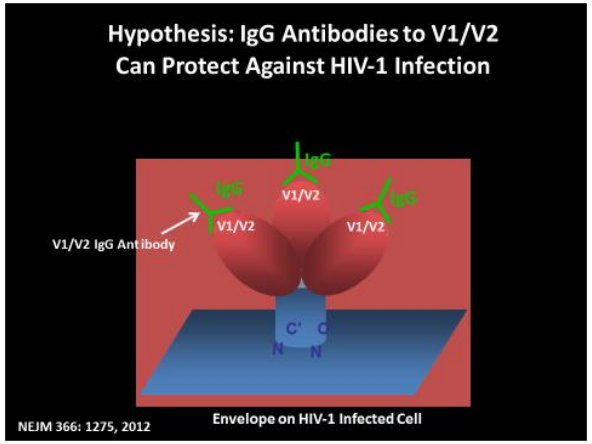
To build on the RV144 result and develop and ultimately license HIV pox-protein vaccines with the potential for broad and timely public health impact.

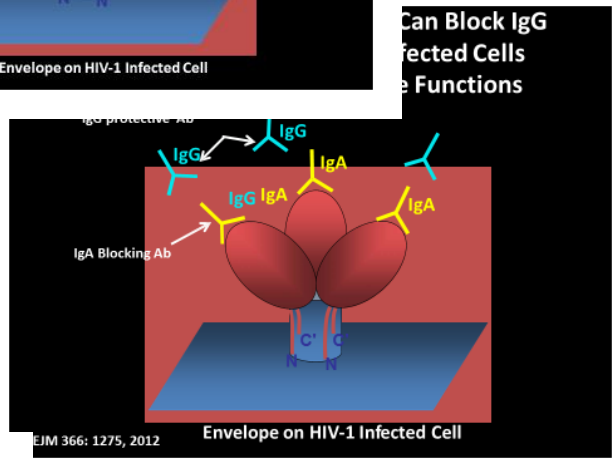
1. Continue to build public-private partnerships critical for success.
2. Work with host countries to support a flexible regulatory strategy in target populations and regions.
3. Generate and incorporate knowledge from the assessment of next-generation vaccine concepts.

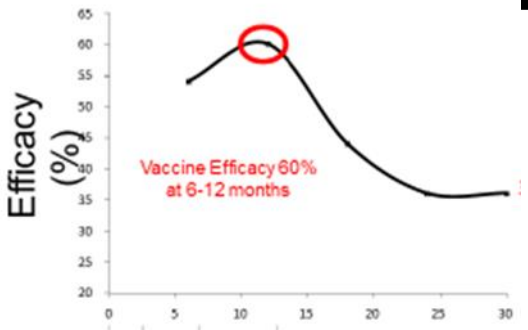
Goals : next generation of HIV vaccines

Same if not better prevention of HIV infection
in South Africa
compared to the RV144

- Correlates of risk consistent across both populations and epidemics ……?
- Better and longer lasting protection –?







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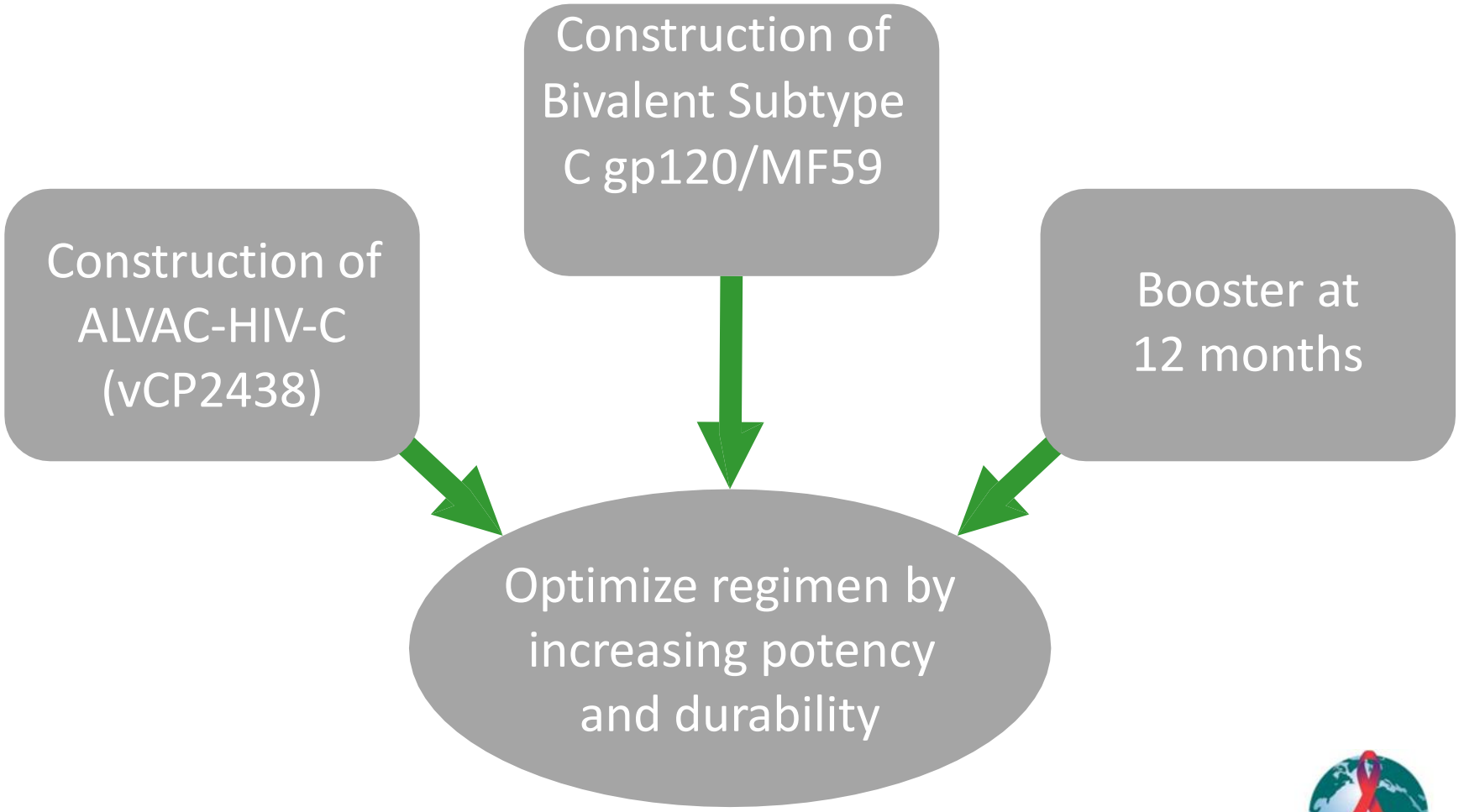
The Strategy for the ALVAC/Protein Phase 3 Program



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HVTN 100: Phase 1-2 Trial

First clinical test of the new products **(HIV –ve, low risk individuals**)

n=252

- Ensure products are safe
- Ensure products illicit an immune response

HVTN 702 : Phase 2b – 3 Trial

n= 5400 **(HIV –ve , high risk individuals)**

- Focus on efficacy
- Extended safety
- Licensure

HIV VACCINE
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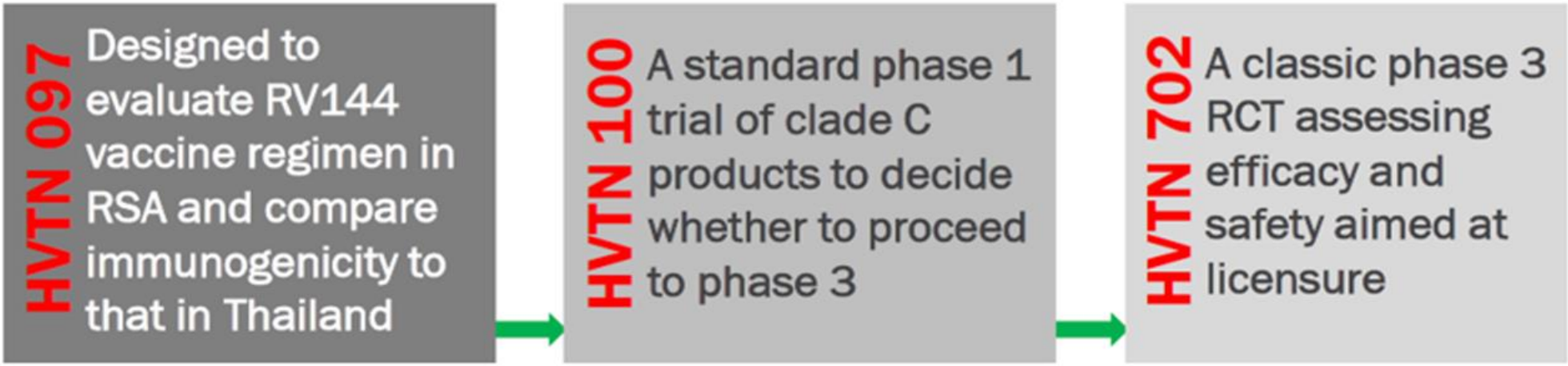
Strategy for the Phase 3 Program



Study Schema: HVTN 100/702

N (total 252)	Primary Vaccine Regimen				Booster
	Month 0	Month 1	Month 3	Month 6	Month 12
210	ALVAC-HIV (vCP2438)	ALVAC-HIV (vCP2438)	ALVAC-HIV+ Bivalent Subtype C gp120/MF59®	ALVAC-HIV+ Bivalent Subtype C gp120/MF59®	ALVAC-HIV+ Bivalent Subtype C gp120/MF59®
42	Placebo	Placebo	Placebo + Placebo	Placebo + Placebo	Placebo + Placebo

Products:

- ALVAC-HIV (vCP2438) expressing HIV-1 env (clade C gp120), clade B (gp41), gag (clade B) & protease (clade B) (Dose: >1 X 10^6 $CCID_{50}$)
- Bivalent subtype C gp120/MF59 containing 100mcg TV1.Cgp120 & 100mcg 1086.Cgp120

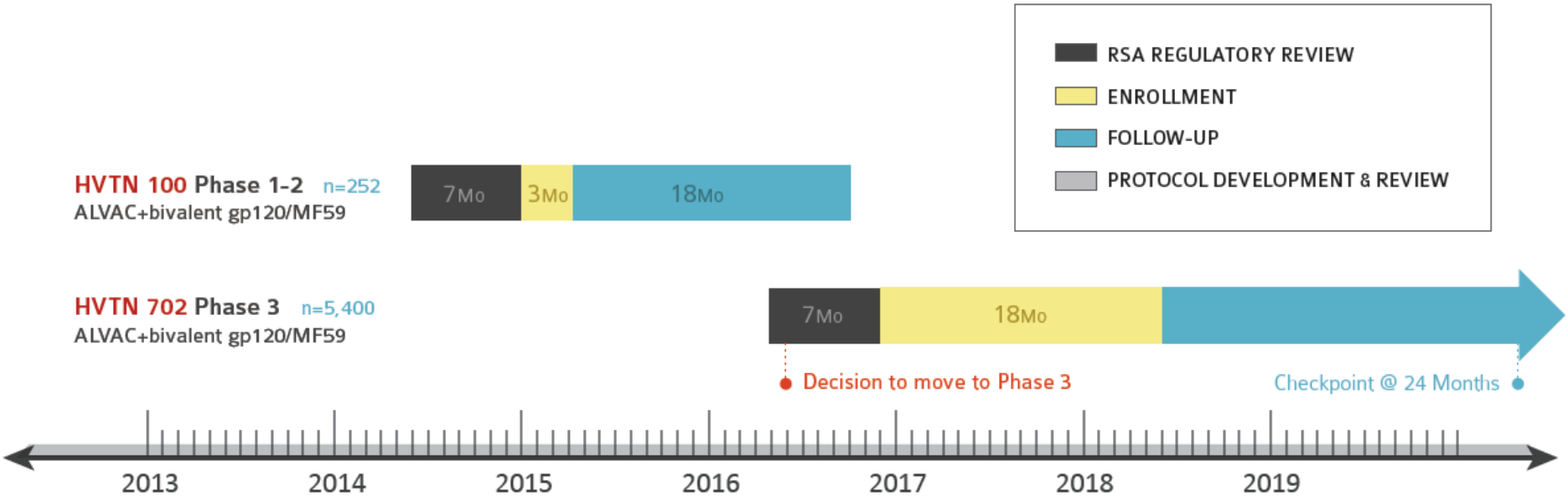
Community Engagement

Figure 2. Layers of Biomedical HIV Prevention Trial Stakeholders

From UNAIDS/AVAC Good Participatory Practice Guidelines for Biomedical HIV Prevention Trials

Various stakeholders may influence or be affected by a biomedical HIV prevention trial. Stakeholders include trial participants and other community stakeholders as well as a broader range of national and international stakeholders.

Timeline for Phase 3 Program



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HIV VACCINES THE WORLD'S BEST HOPE TO END AIDS

Questions??