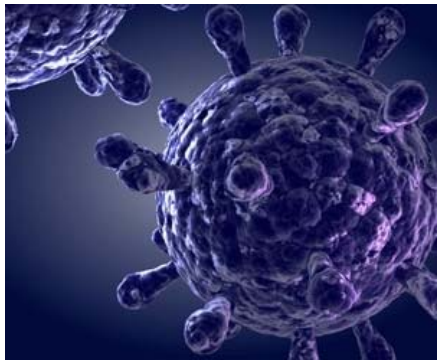
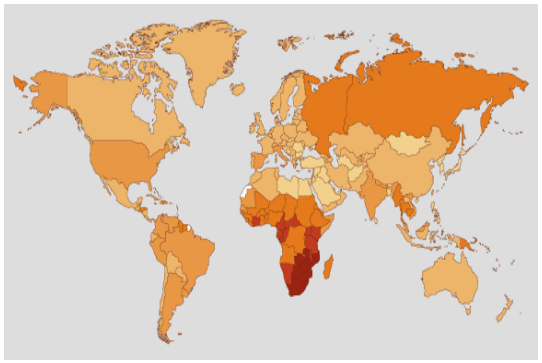
# Potential Impact of an RV144-like HIV Vaccine in Diverse Epidemic Settings



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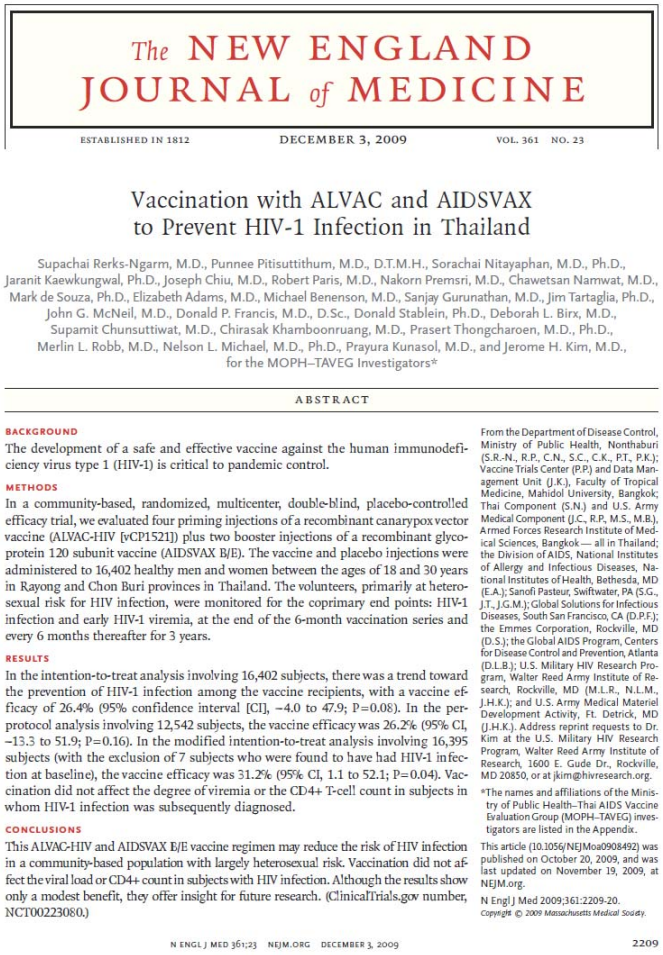
# RV144 trial

- Results published December 2009
- 16,402 participants in Thailand
- Vaccine regimen
  - ALVAC (weeks 0, 4, 12, 24)
  - AIDSVAX B/E (weeks 12, 24)
- Overall efficacy over 42 months
  - Intention to treat: **26.4%** (p=0.08)
  - Per-protocol: **26.2%** (p=0.16)
  - Modified ITT: **31.2%** (p=0.04)
- But trial data suggest that efficacy may decline over time…



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Vaccination with ALVAC and AIDSVAX to Prevent HIV-1 Infection in Thailand

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ABSTRACT

BACKGROUND

The development of a safe and effective vaccine against the human immunodeficiency virus type 1 (HIV-1) is critical to pandemic control.

METHODS

In a community-based, randomized, multicenter, double-blind, placebo-controlled efficacy trial, we evaluated four priming injections of a recombinant canarypox vector vaccine (ALVAC-HIV [vCP1521]) plus two booster injections of a recombinant glycoprotein 120 subunit vaccine (AIDSVAX B/E). The vaccine and placebo injections were administered to 16,402 healthy men and women between the ages of 18 and 30 years in Rayong and Chon Buri provinces in Thailand. The volunteers, primarily at heterosexual risk for HIV infection, were monitored for the coprimary end points: HIV-1 infection and early HIV-1 viremia, at the end of the 6-month vaccination series and every 6 months thereafter for 3 years.

RESULTS

In the intention-to-treat analysis involving 16,402 subjects, there was a trend toward the prevention of HIV-1 infection among the vaccine recipients, with a vaccine efficacy of 26.4% (95% confidence interval [CI], −4.0 to 47.9; P=0.08). In the per-protocol analysis involving 12,542 subjects, the vaccine efficacy was 26.2% (95% CI, −13.3 to 51.9; P=0.16). In the modified intention-to-treat analysis involving 16,395 subjects (with the exclusion of 7 subjects who were found to have had HIV-1 infection at baseline), the vaccine efficacy was 31.2% (95% CI, 1.1 to 52.1; P=0.04). Vaccination did not affect the degree of viremia or the CD4+ T-cell count in subjects in whom HIV-1 infection was subsequently diagnosed.

CONCLUSIONS

This ALVAC-HIV and AIDSVAX B/E vaccine regimen may reduce the risk of HIV infection in a community-based population with largely heterosexual risk. Vaccination did not affect the viral load or CD4+ count in subjects with HIV infection. Although the results show only a modest benefit, they offer insight for future research. (ClinicalTrials.gov number, NCT00223080.)

From the Department of Disease Control, Ministry of Public Health, Nonthaburi (S.R.-N., R.P., C.N., S.C., C.K., P.T., P.K.); Vaccine Trials Center (P.P.) and Data Management Unit (J.K.), Faculty of Tropical Medicine, Mahidol University, Bangkok; Thai Component (S.N.) and U.S. Army Medical Component (J.C., R.P., M.S., M.B.), Armed Forces Research Institute of Medical Sciences, Bangkok — all in Thailand; the Division of AIDS, National Institutes of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD (E.A.); Sanofi Pasteur, Swiftwater, PA (S.G., J.T., J.G.M.); Global Solutions for Infectious Diseases, South San Francisco, CA (D.P.F.); the Emmes Corporation, Rockville, MD (D.S.); the Global AIDS Program, Centers for Disease Control and Prevention, Atlanta (D.L.B.); U.S. Military HIV Research Program, Walter Reed Army Institute of Research, Rockville, MD (M.L.R., N.L.M., J.H.K.); and U.S. Army Medical Materiel Development Activity, Ft. Detrick, MD (J.H.K.). Address reprint requests to Dr. Kim at the U.S. Military HIV Research Program, Walter Reed Army Institute of Research, 1600 E. Gude Dr., Rockville, MD 20850, or at jkim@hivresearch.org.

*The names and affiliations of the Ministry of Public Health–Thai AIDS Vaccine Evaluation Group (MOPH–TAVEG) investigators are listed in the Appendix.

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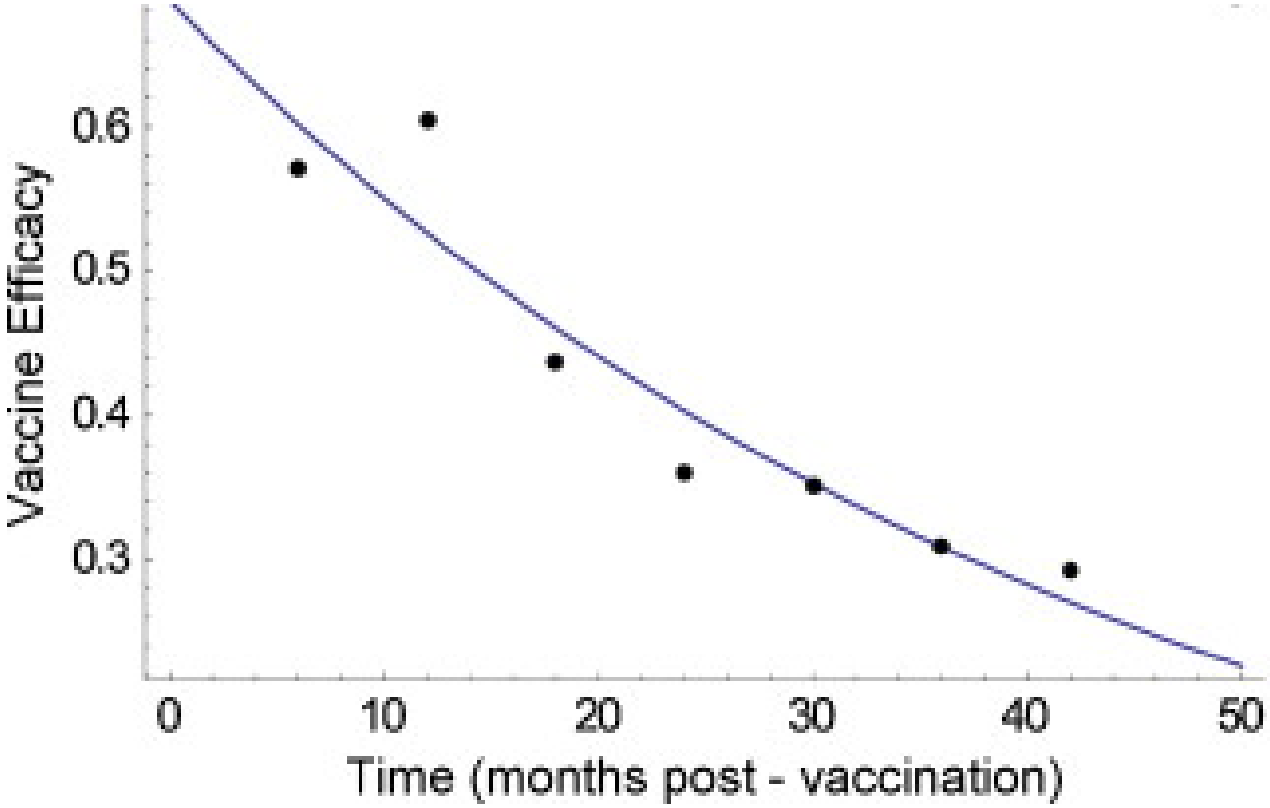
# Curve fit to RV144 trial data

- $Efficacy = 0.78\, e^{-0.06t}$




Hankins CA, Glasser JW, Chen RT. Modeling the impact of RV144-like vaccines on HIV transmission. *Vaccine* 2011; 29(36):6069-71.

# HIV vaccine modeling consortium

- UNAIDS and CDC convened consortium in early 2010
- Invited independent groups of epidemiologists and mathematical modelers
- Research question:

  ***What is the impact of a modestly effective HIV vaccine with waning efficacy (similar to RV144) on the HIV epidemic?***

- Presented preliminary results at AIDS Vaccine Conference in Atlanta (September 2010)
- Published special issue of *Vaccine* (August 2011)

# Reference case

- Modelers identified a clear reference case to facilitate model comparisons
  - Single vaccination campaign with waning efficacy
  - Vaccination of adult population: 30% or 60% coverage
  - Modeled outcome: proportion of HIV infections averted over 10 years
- Additional analyses (optional)
  - Periodic booster vaccinations, ***assuming restoration of immunity***
  - Effect of behavioral risk compensation
  - Cost-effectiveness
- ***All other modeling assumptions and parameters were allowed to vary between groups***

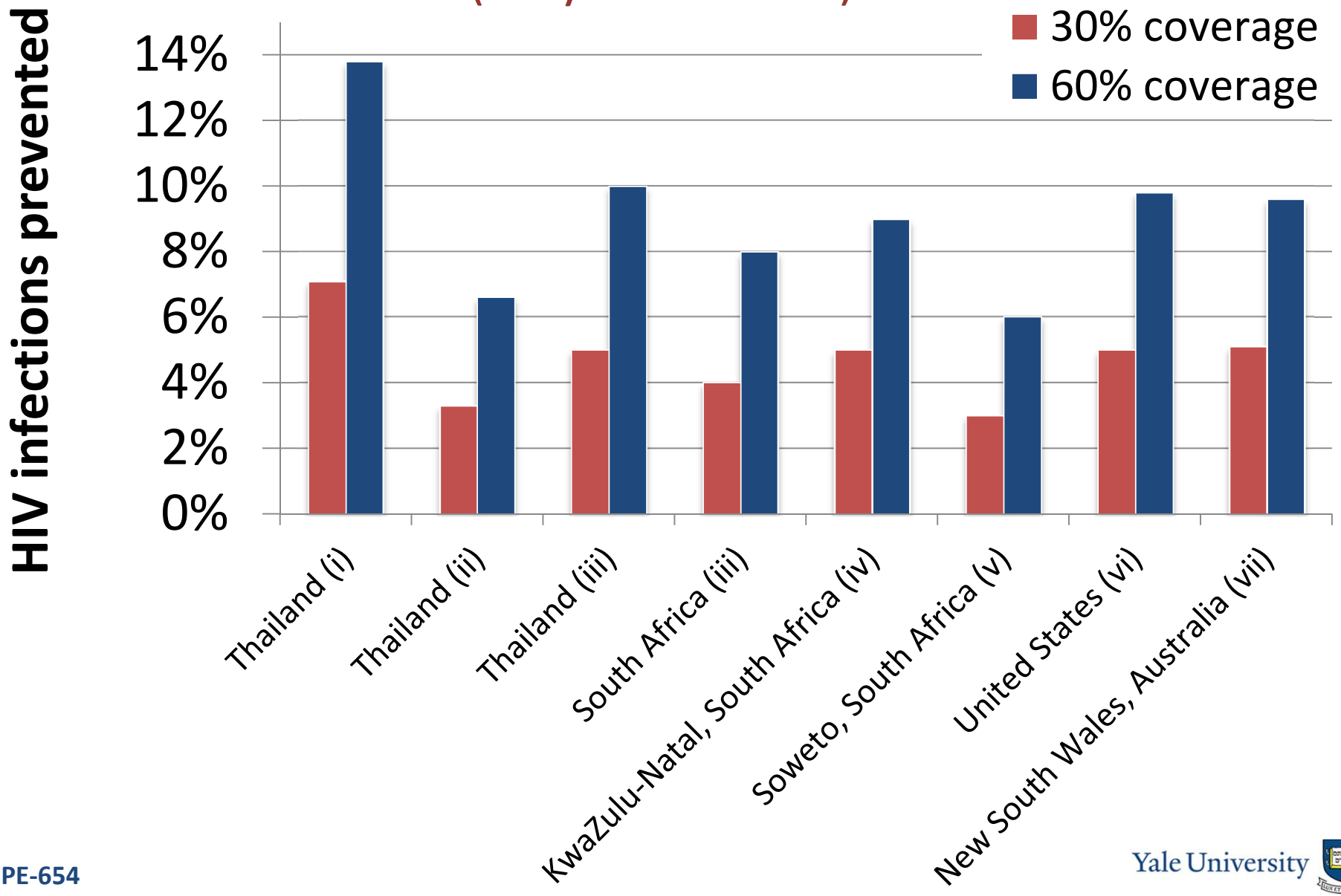
# Results summary

## (10-year horizon; 60% vaccination coverage)

| Authors | Setting | Baseline HIV Prevalence | HIV Infections Averted | With Boosters (frequency) | Vaccinations per Infection Averted |
|---|---|---|---|---|---|
| Nagelkerke et al | Thailand | <2% (all)<br>4% (CSW) | **14%** | 58% (1y) | 1200 |
| Schneider et al | Thailand | 1% (all)<br>25% (MSM)<br>35% (IDU) | **7%** | 25% (2y)<br>38% (1y) | |
| Andersson and Stover | Thailand | 1.4% (all) | **10%** | 35% (1.4y) | 1725 (all)<br>220 (high-risk) |

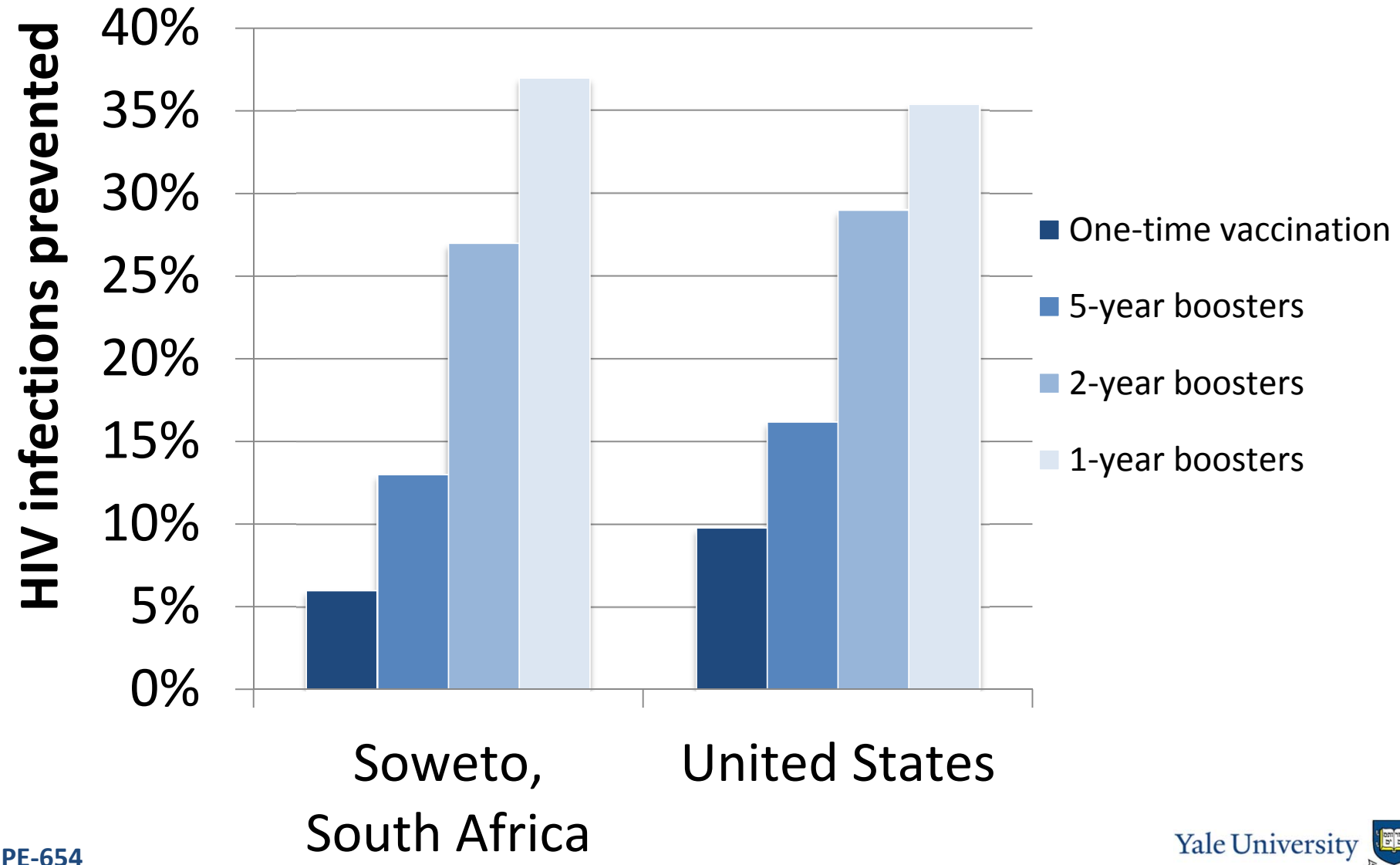
# HIV infections prevented

## (10-year horizon)



# Impact of periodic boosters

## (10-year horizon; *assuming full restoration of immunity*)



# Lessons learned (1)

- Model-based analyses were broadly consistent, despite widely different assumptions.
  - A single vaccination campaign reaching 60% of adults averts approximately **10%** of new HIV cases.
- If effective, periodic booster vaccinations substantially improve infections averted.
  - Bi- or tri-annual boosters prevent **20-27%** of cases.
  - Annual boosters prevent **35-58%** of cases.
- Prioritization to groups at higher risk of HIV improves program efficiency.
  - Can prevent **80%** as many infections, with 10% of required vaccinations, compared to universal adult vaccination.

# Lessons learned (2)

- Vaccination with partially effective HIV vaccines can be cost-effective.
  - At $100 per regimen, vaccination in South Africa costs $2,700/case averted, or $10,000/life-year gained.
  - At $500 per regimen, vaccination in USA costs <$100,000/QALY gained.
- Behavioral risk compensation post-vaccination does not eliminate vaccination benefits.
- Rate of efficacy decline affects short- and long-term epidemic outcomes.

# Key remaining questions

- *What is the rate of efficacy decline and duration of protection?*
- *How does efficacy differ among individuals at higher risk of HIV infection?*
- *What is the role of a vaccine in a portfolio of interventions?*
- *What is the immunological impact of vaccine boosters?*
- *Is there evidence of behavioral risk compensation post-vaccination?*

# Related posters

- Abstract **WEPE-654**

  Elisa Long et al.

  *A model-based consensus on the impact of an RV144-like HIV vaccine in diverse epidemic settings*

- Abstract **TUPE-179**

  Katharine Kripke and Matthew Hamilton

  *Differing models, same results: testing the consistency of seven HIV vaccine impact models across seven populations*

# Acknowledgments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