Population-level Impact and Cost-effectiveness of an HIV Vaccine in South Africa

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Introduction

RV144 is to date the only HIV vaccine trial to show efficacy (1), albeit rapidly waning over time (2). It was shown that high levels of antibodies directed at conserved regions of the V1V2 loop correlated with reduced HIV acquisition in the RV144 trial population (3). The HVTN702 trial (4) plans to deploy a similar vaccine formulation to that of RV144 for subtype C HIV with an additional 12 month booster to achieve a goal of 50% efficacy at month 24. In addition to the trial setup, we also model two-yearly boosters starting at month 36 to maintain durability over a period of 10 years.

Methods

The **individual-based network model** EMOD v2.6, calibrated to prevalence and incidence estimates from recent national surveys in South Africa (5,6), was used to evaluate population-level impact of a vaccine available in 2027. An impulse and exponential decay model of time-dependent vaccine efficacy was optimized such that a goal of **50% efficacy** is met. We consider **age cohort vaccination** at 80% coverage at age 10 and 15 with or without age off-set between gender and varying sequential attrition levels for two-yearly boosters. Uncertainty in incidence decline between 2017 and 2027 was modeled by **three distinct scenarios of treatment scale-up** implementations: maintaining Status Quo, with additional oral PrEP for high risk populations, and achieving 90-90-90 (including high-risk oral PrEP). Population-level effectiveness was assessed by incidence decrease and number of infections prevented per 1000 vaccinated over 20 years of vaccination. Maximum cost-effective prices of 10-year vaccination and booster series were calculated from the ratio of the net budget impact to DALYs averted.

Results

Modeling time-dependent vaccine efficacy for the **HVTN702 regimen with additional booster series** shows that without attrition, an average efficacy of 30% could be maintained over 10 years of immunization (Figure 1). If two-yearly boosters were not maintained, average efficacy would be at residual levels of 15% at the 10 year endpoint (dotted green lines in Figure 1).

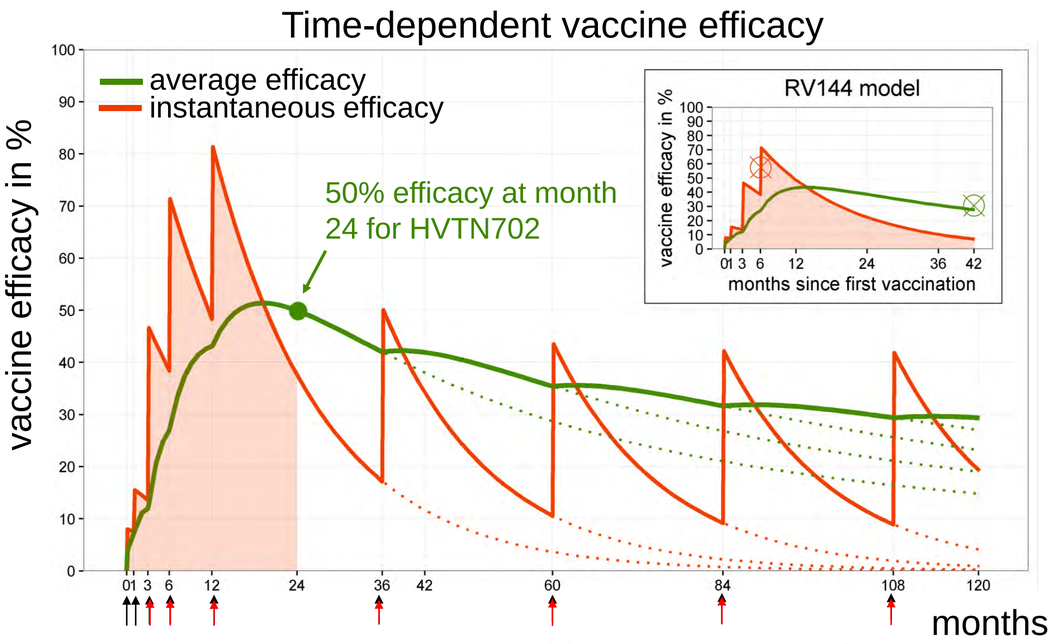

Figure 1. The instantaneous vaccine efficacy curve (red) is parameterized such that the average efficacy (green) achieves a goal of 50% at the 24 month endpoint. The subpanel (upper right) shows the same model fit to point estimates from RV144 (59% instantaneous efficacy after 6 months, 31.2% average efficacy at the month 42 endpoint).

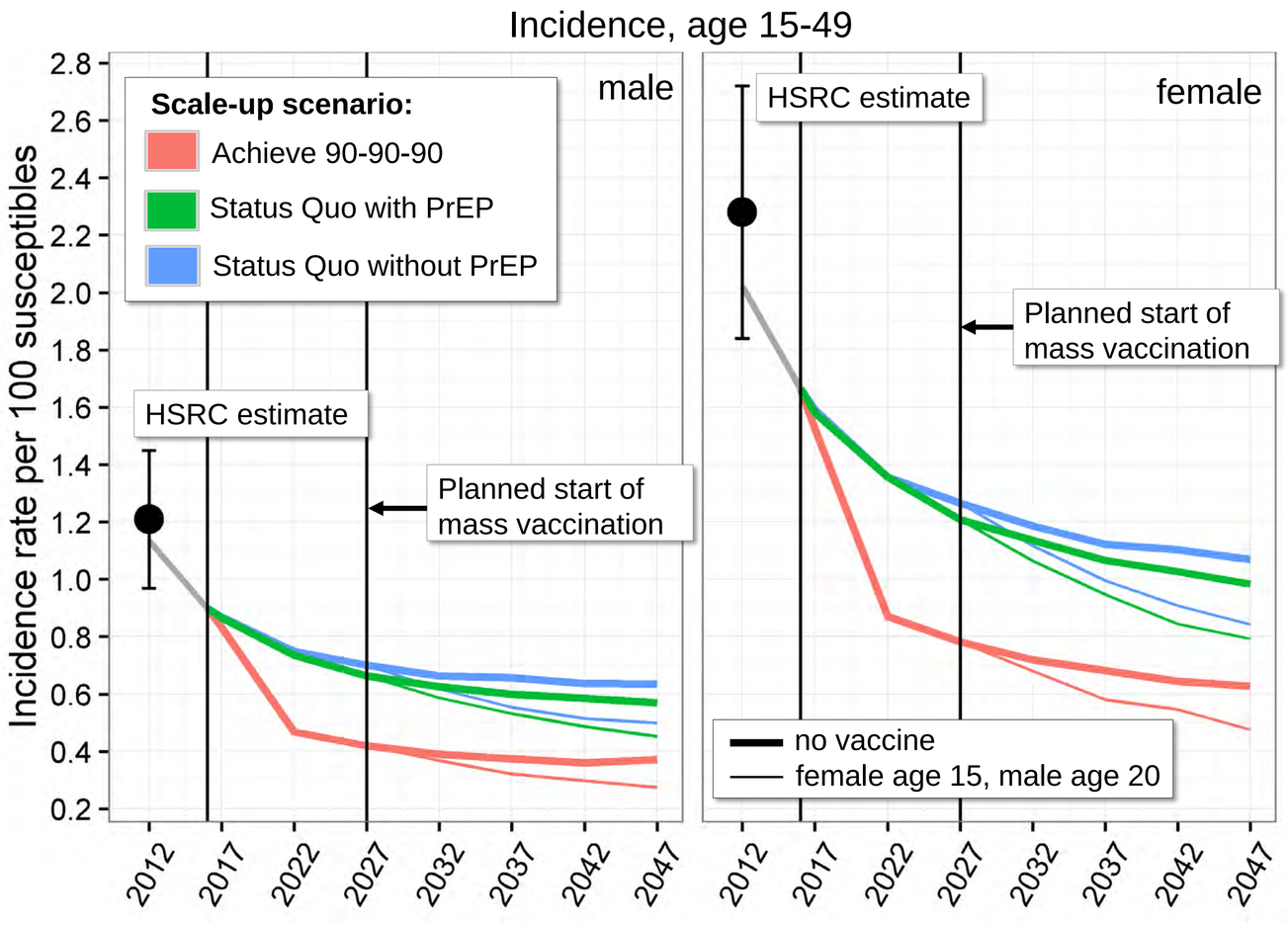

Figure 2. Model fit and projected average incidence for three different treatment scale-up scenarios. Gender differences in incidence persist despite scale-up. Vaccinating 15 year old women and 20 year old men could reduce HIV incidence by up to 18% and 24% for men and women respectively.

At 80% coverage, a partially effective vaccine could **reduce HIV incidence in South Africa by up to 18% and 24% for men and women** respectively. Starting immunization at age 15 in women and age 20 in men would prevent 14-30 HIV infections averted per 1000 individuals vaccinated (Figure 3). If gender differences in vaccination age were impractical to implement, then vaccinating age 15 would prevent 9-22 HIV infections per 1000 vaccinated, a result **sensitive to concurrent scale-up of ART and booster attrition**. In contrast, combining HIV vaccination with the current HPV vaccine program by vaccinating at 10 years of age would result in 0.1-5 HIV infection prevented per 1000 vaccinated due to waning immunity.

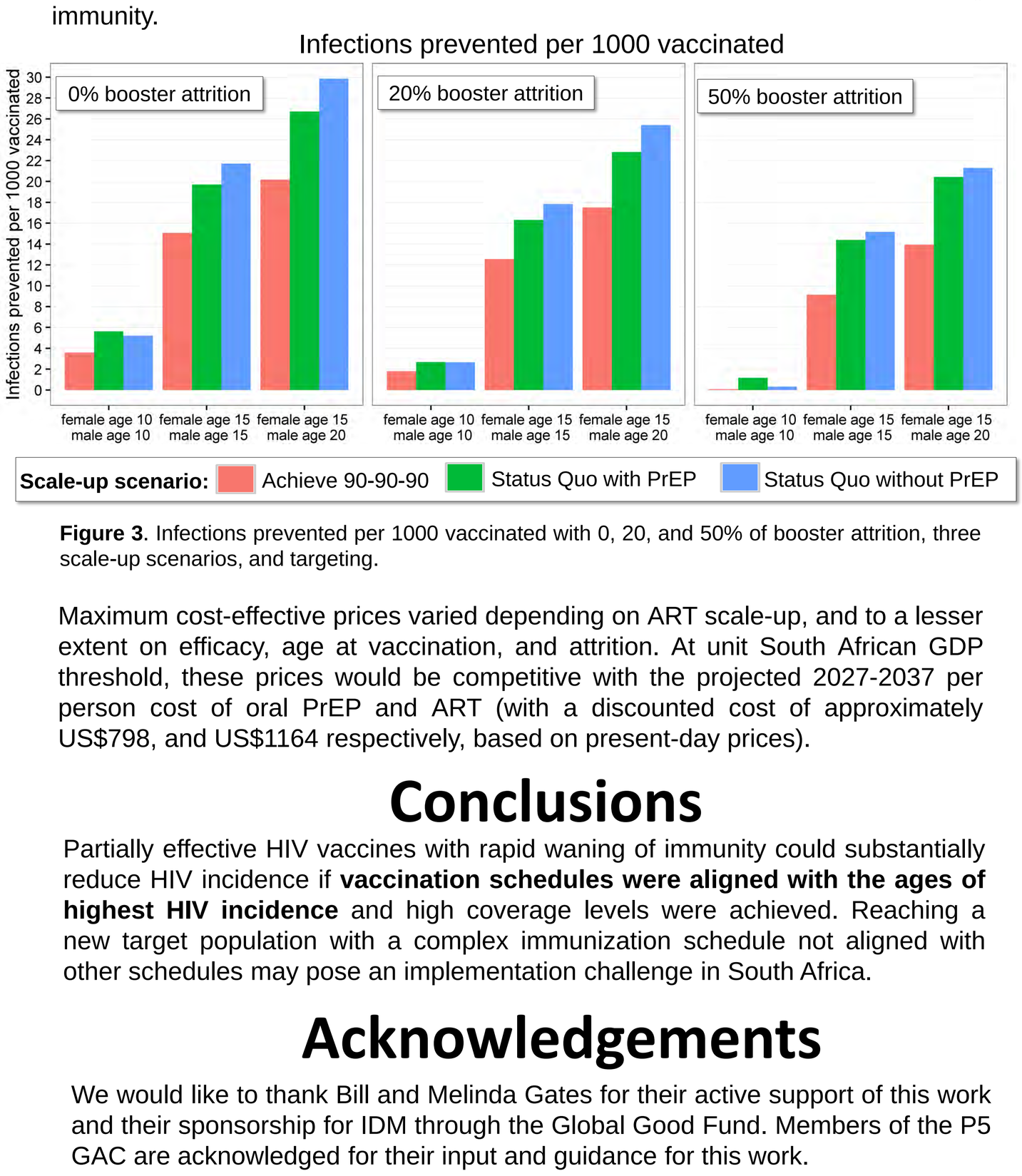

Figure 3. Infections prevented per 1000 vaccinated with 0, 20, and 50% of booster attrition, three scale-up scenarios, and targeting.

Maximum cost-effective prices varied depending on ART scale-up, and to a lesser extent on efficacy, age at vaccination, and attrition. At unit South African GDP threshold, these prices would be competitive with the projected 2027-2037 per person cost of oral PrEP and ART (with a discounted cost of approximately US$798, and US$1164 respectively, based on present-day prices).

Conclusions

Partially effective HIV vaccines with rapid waning of immunity could substantially reduce HIV incidence if **vaccination schedules were aligned with the ages of highest HIV incidence** and high coverage levels were achieved. Reaching a new target population with a complex immunization schedule not aligned with other schedules may pose an implementation challenge in South Africa.

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