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CONFRONTING INEQUITIES IN STI PREVENTION, DIAGNOSTICS AND CARE

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INTERNATIONAL UNION AGAINST SEXUALLY TRANSMITTED INFECTIONS

The population impact of HSV-2 vaccination on HIV, HSV-2 and genital ulcer disease in South Africa: a mathematical modelling study

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Disclosure

Any circumstances that could give rise to a potential conflict of interest related to the conference or topic under discussion	Name of company, organization or institution
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BACKGROUND

Introduction

- South Africa has one of the highest rates of HSV-2 infection worldwide (~50% prevalence in those aged 15-44 years) and is home to the largest population of people living with HIV globally.

- HIV and HSV-2 infections interact biologically
  - HSV-2 infection increases susceptibility to HIV.[1]
  - HSV-2 co-infection increases HIV viraemia and transmissibility. [2-4]
  - HIV co-infection increases HSV-2 genital shedding and transmissibility. [5-7]

- Previous modelling suggests that HSV-2 infection could contribute 42.1-66.4% of new HIV infections over the next 10 years in the WHO Africa region.[8]

[1] K Looker et al., Lancet Infect Dis 2017; [2] R Gray et al., Lancet 2001; [3] A Latif et al. AIDS 1989
[4] R Barnabas et al. Curr Hiv Res 2012 [5] P Maraud et al. Sex Transmission Infect. 2008;
[6] W Phipps et al. J Infect Dis. 2016; [7] S Phiri et al., Sex Transm Dis, 2013;[8]; R Silhol et al. JAIDS 2021

HSV-2 Vaccine Development

- An HSV-2 vaccine has been identified by the WHO as a key public health goal.
  - Either prophylactic or a therapeutic vaccine

- Mathematical modelling can inform vaccine investment

- In 2015, WHO expert group outlined HSV-2 modelling needs[1]
  - Highlighted the following under-researched areas:
  1. Impact of vaccines in LMICs
  2. Impact of therapeutic vaccines (most developed vaccines but understudied)
  3. Vaccine impact on HIV transmission
  4. Vaccine impact on HSV-2-related disease outcomes

[1] IH Spicknall Vaccine 2018

Objectives

- Evaluate potential impact of HSV-2 vaccines in South Africa
- Investigate how impact differs by uptake/coverage and vaccine characteristics
- Compare impact of prophylactic and therapeutic vaccines

METHODS

Mathematical Model

- Deterministic HIV/HSV-2 transmission model among adults stratified by:
  - Low risk males and females, young (<30 years) and older MSM (>=30 years), FSW and their clients.
- Stratifies HSV-2 infection into 3 levels of symptomatic shedding
- Captures HSV-2 and HIV transmission through varied partnerships.
- Includes cofactor effects:
  - Increased HIV acquisition/transmission risk due to HSV-2 infection
  - HIV infection increases days with HSV-2 shedding.
- Incorporates trends in male circumcision, ART coverage and condom use
  - Including differences by risk groups.
- Model calibrated using approximate Bayesian methods to data on:
  - Key population sizes, HIV prevalence by risk group, HSV-2 prevalence by HIV status and gender, ART coverage by risk group.

Model Analyses

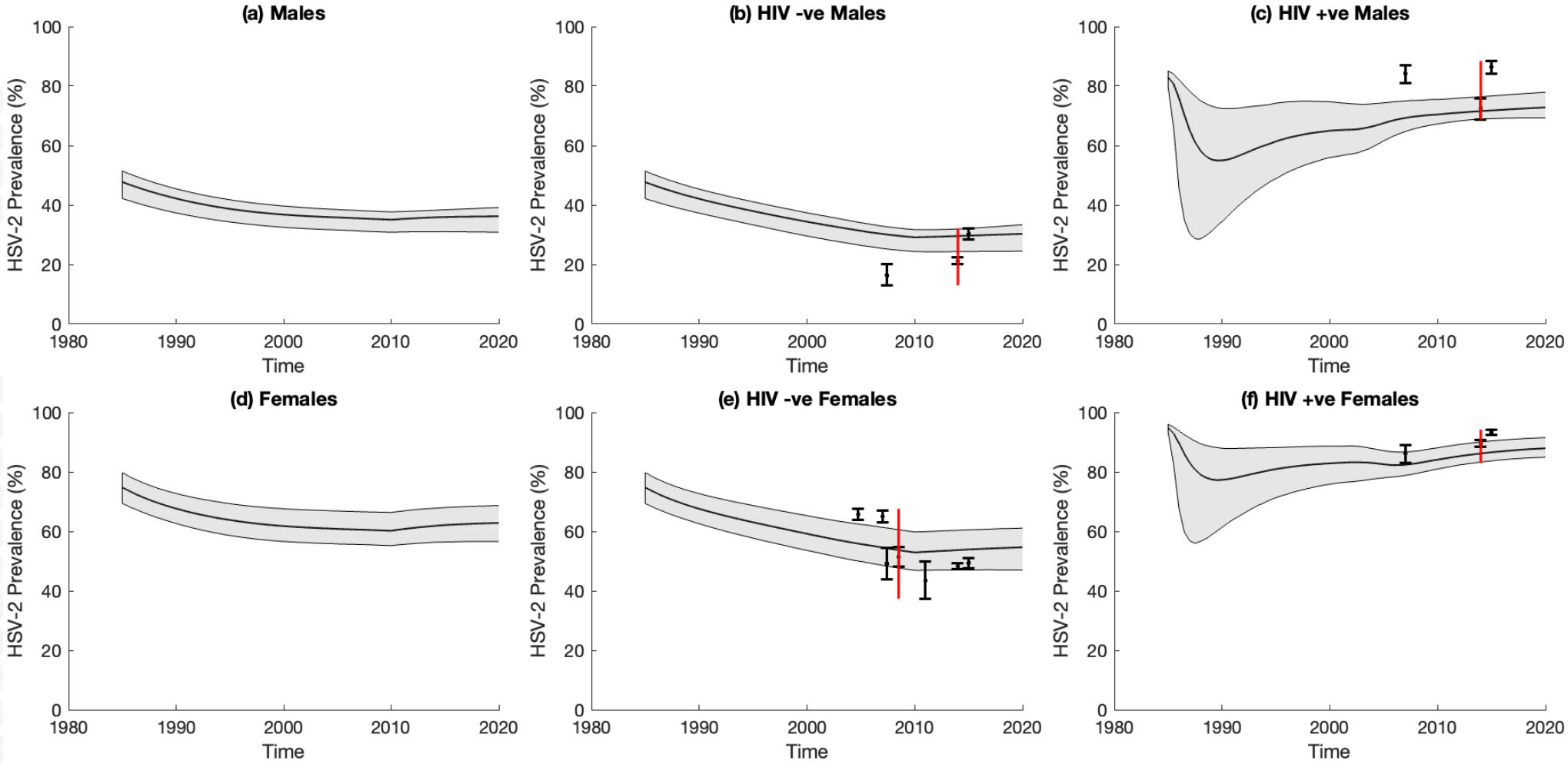
- Estimate the contribution ('tPAF') of HSV-2 infection to HIV transmission over 2020-2029.
  - What proportion of new HIV infections would be averted over 2020-2029 if HSV-2 infection does not elevate HIV transmission or acquisition?

- Assessed impact of different prophylactic or therapeutic vaccination scenarios:
  - Relative reduction in **rate** of new infections or GUD days after 40 years from 2020 vs the status quo

- Estimated number needed to vaccinate (NNV) to avert the following over 2020-2060:
  - one HSV-2 infection,
  - one person-year of GUD,
  - one HIV infection.

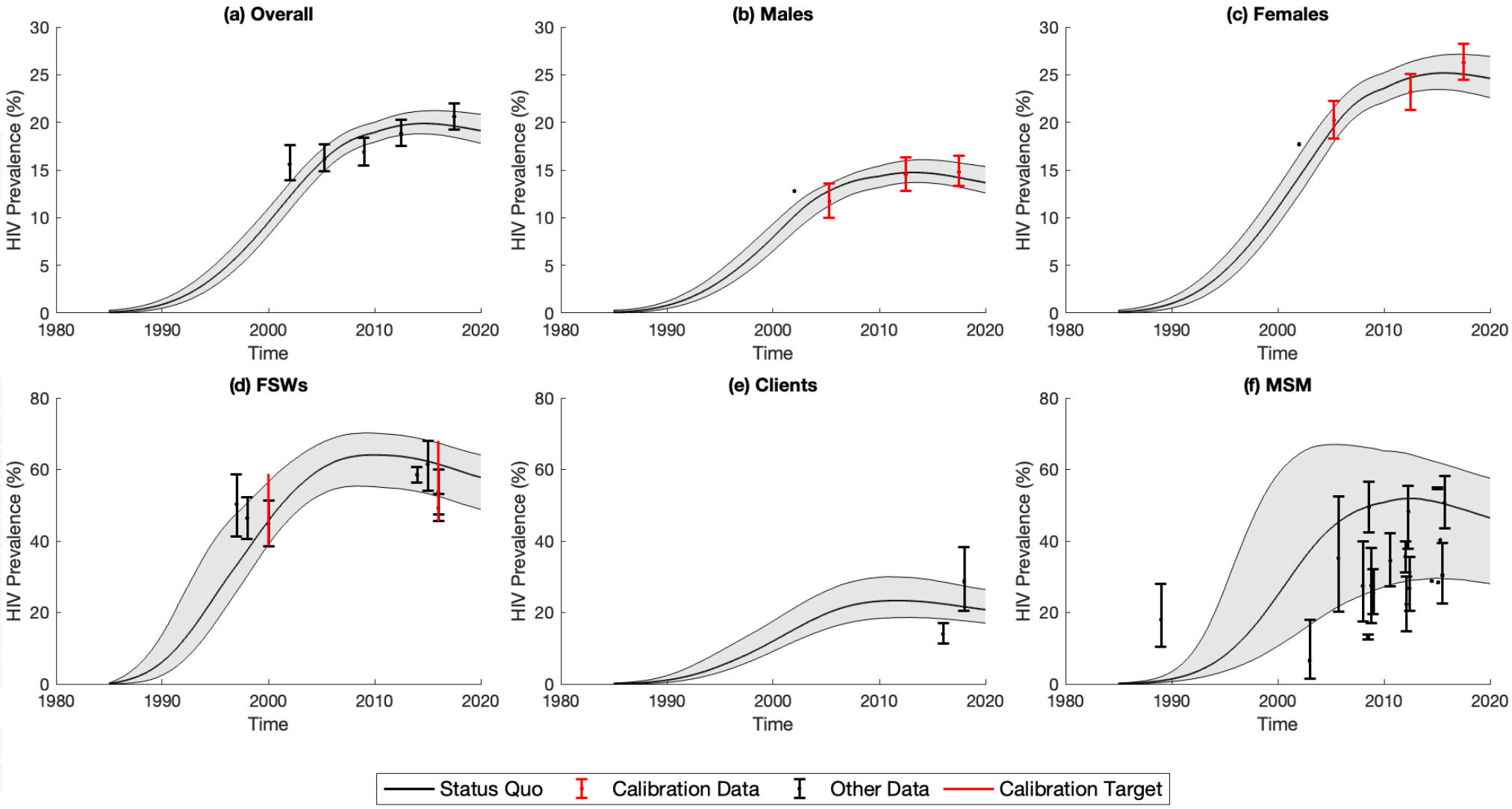
RESULTS

Model Fits: HSV-2 Prevalence



- Stable HSV-2 epidemic, with prevalence of 36% in men and 63% in women in 2020.
- Much higher HSV-2 prevalence among HIV positives.

Model Fits: HIV Prevalence



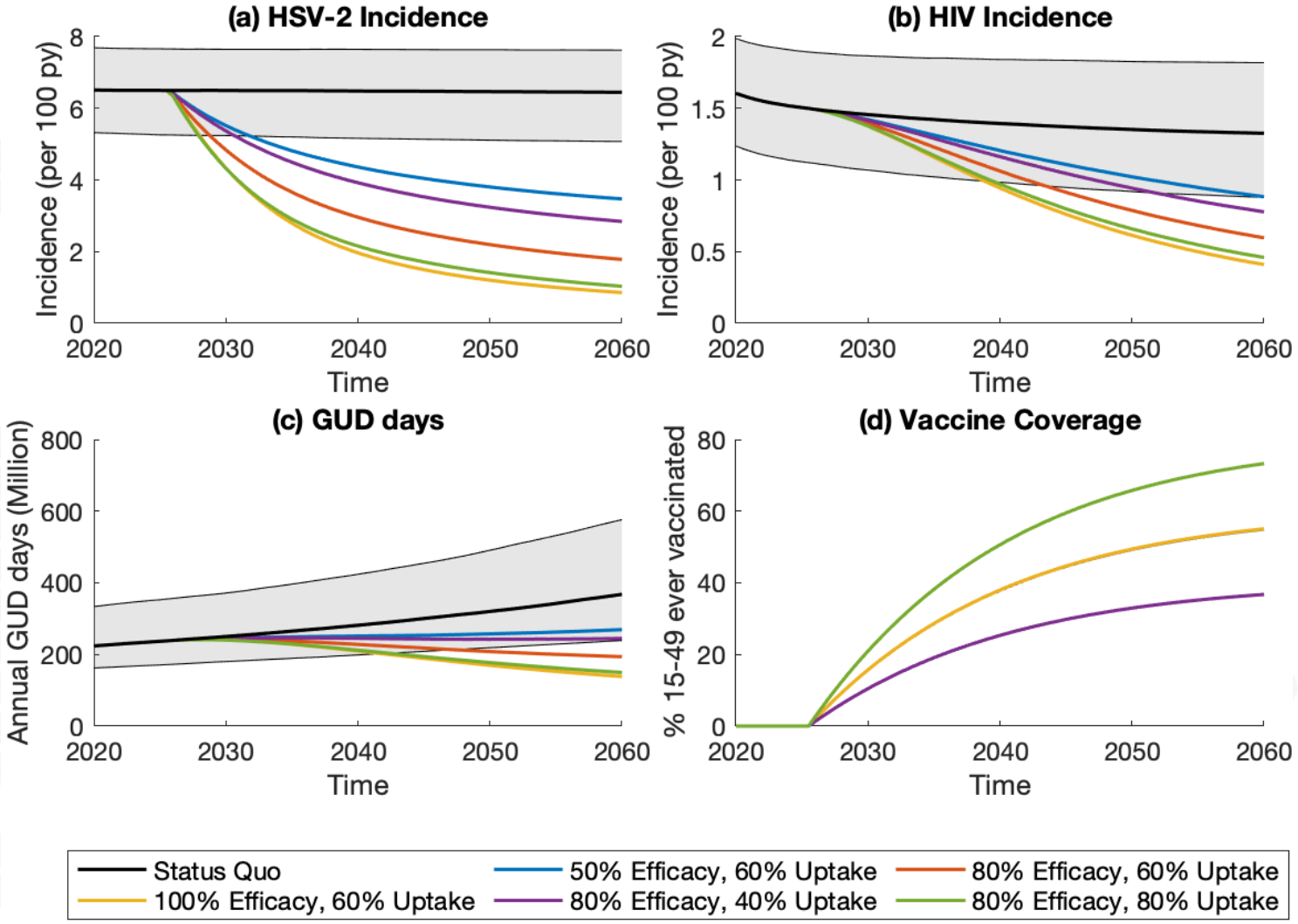
- Slowly decreasing HIV epidemic due to recent scale-up of ART
- HSV-2 is estimated to contribute 70.0% (95%CrI: 62.9-76.1%) of new HIV infections over 2020-2029

PROPHYLACTIC VACCINES

Main Vaccination Scenarios

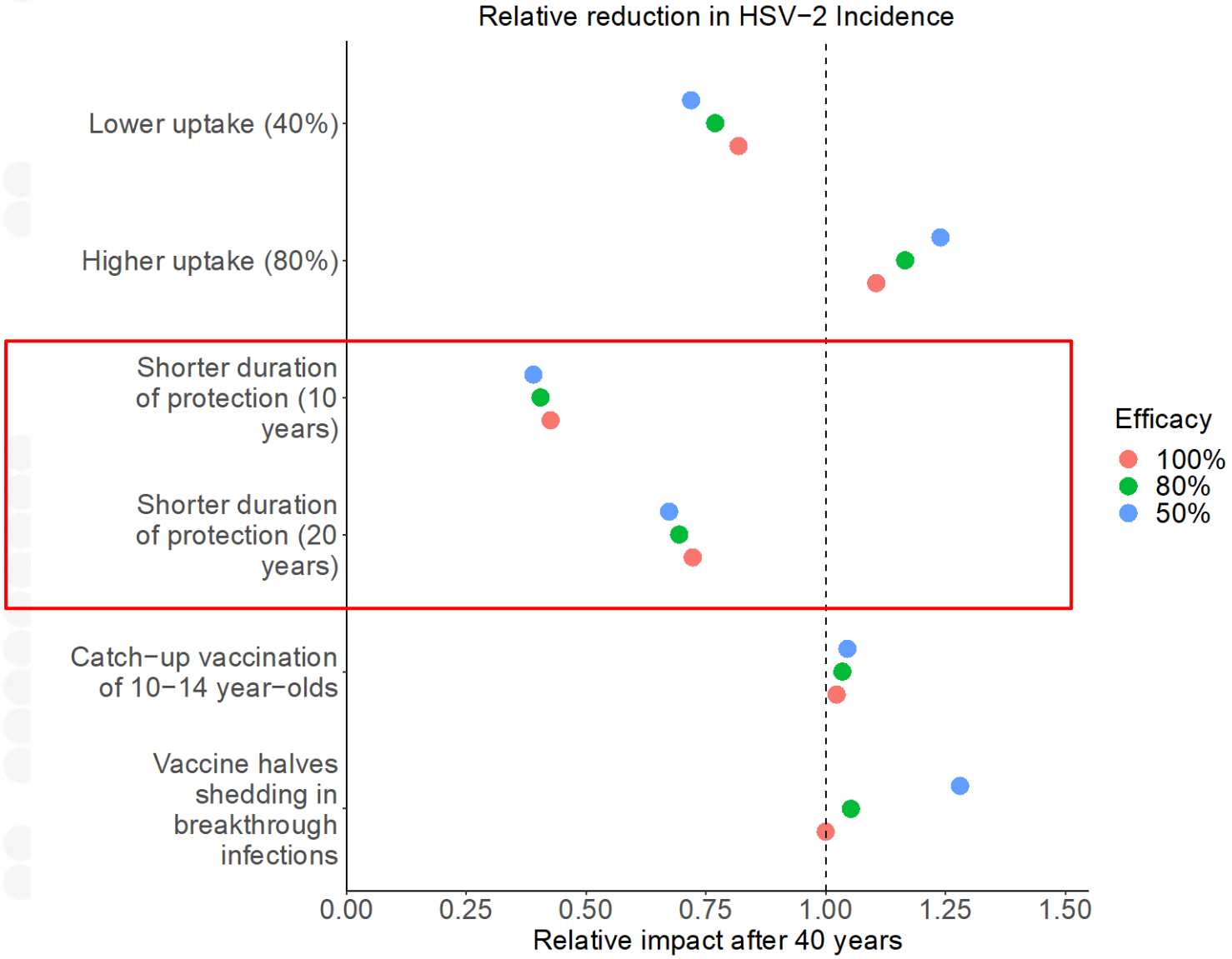
- A proportion (vaccine uptake) of 9-year-olds are vaccinated each year from 2020
- Vaccine provides lifelong protection
- Vaccine reduces risk of HSV-2 acquisition with 50, 80 or 100% efficacy
- Modelled uptakes of 40%, 60% and 80%

Results – Main Scenarios



- Moderate to substantial impact on HSV-2 incidence, depending on efficacy and uptake.
- **50% efficacy and 60% uptake:** reduces HSV-2 incidence by 46% after 40 years.
- **80% efficacy and 80% uptake**: reduces HSV-2 incidence by 84% after 40 years.
- Predicted reductions in HIV incidence and the number of GUD days are similar to each other but smaller than for the impact on HSV-2 incidence.
- **80% efficacy and 80% uptake**: reduces time with GUD by 59% and HIV incidence by 65% after 40 years.

Results – Sensitivity Analyses



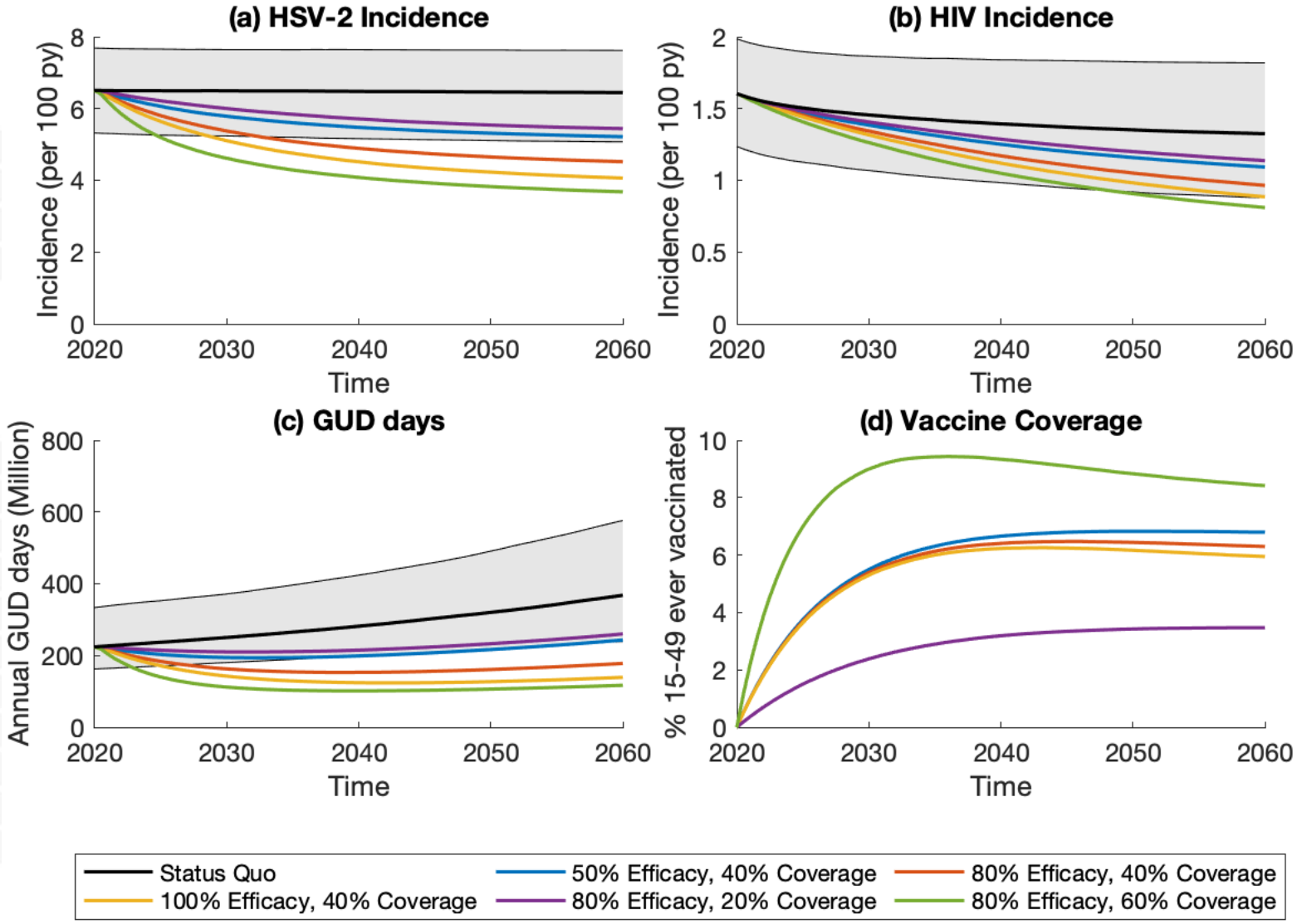
- Impact highly sensitive to varying duration of protection:
  - ~60% lower impact if protection lasts 10 years
  - ~30% lower impact if protection lasts 20 years

THERAPEUTIC VACCINES

Main Vaccination Scenarios

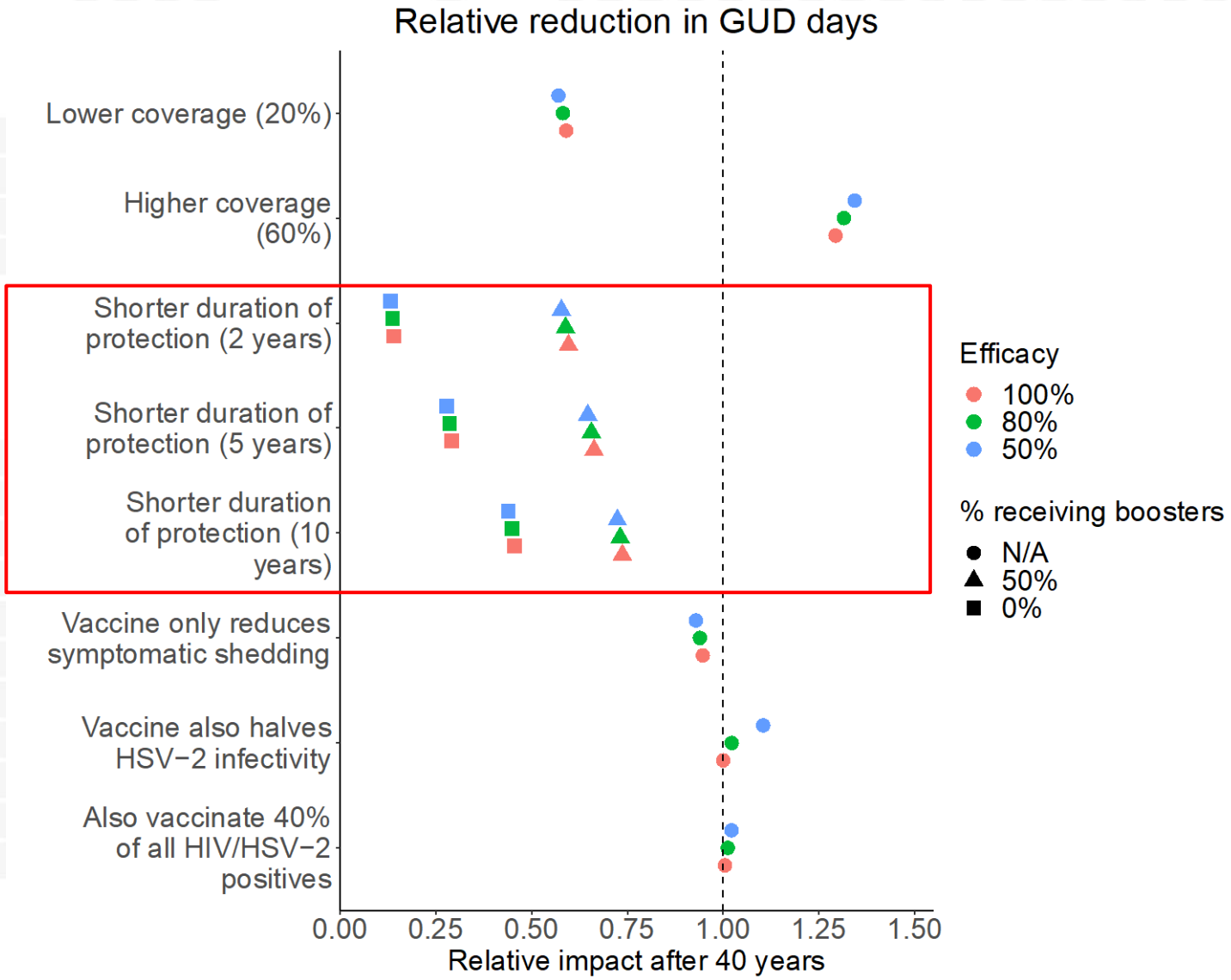
- Model vaccination of individuals with symptomatic HSV-2 infection
- Likelihood of vaccination proportional to percentage of days symptomatic (so higher vaccination rate if HIV positive or if have frequent symptomatic shedding)
- Vaccine reduces shedding (both asymptomatic and symptomatic) with 50%, 80% or 100% efficacy
- Vaccine provides lifelong protection
- Model vaccination rates to give 20/40/60% coverage after 40 years among those with symptomatic infection.

Results – Main Scenarios



- A therapeutic vaccine is projected to have a smaller but still substantial impact on HSV-2 and HIV incidence, and could considerably reduce the number of days with GUD
- **50% efficacy, 40% coverage**: reduces GUD days by 33% after 40 years
- **80% efficacy, 60% coverage**: reduces GUD days by 68% after 40 years
- Modest to moderate impact on population-wide HSV-2 and HIV incidence
- **E.g. 50% efficacy, 40% coverage** reduces HSV-2 incidence by 19% and HIV incidence by 17% over 40 years

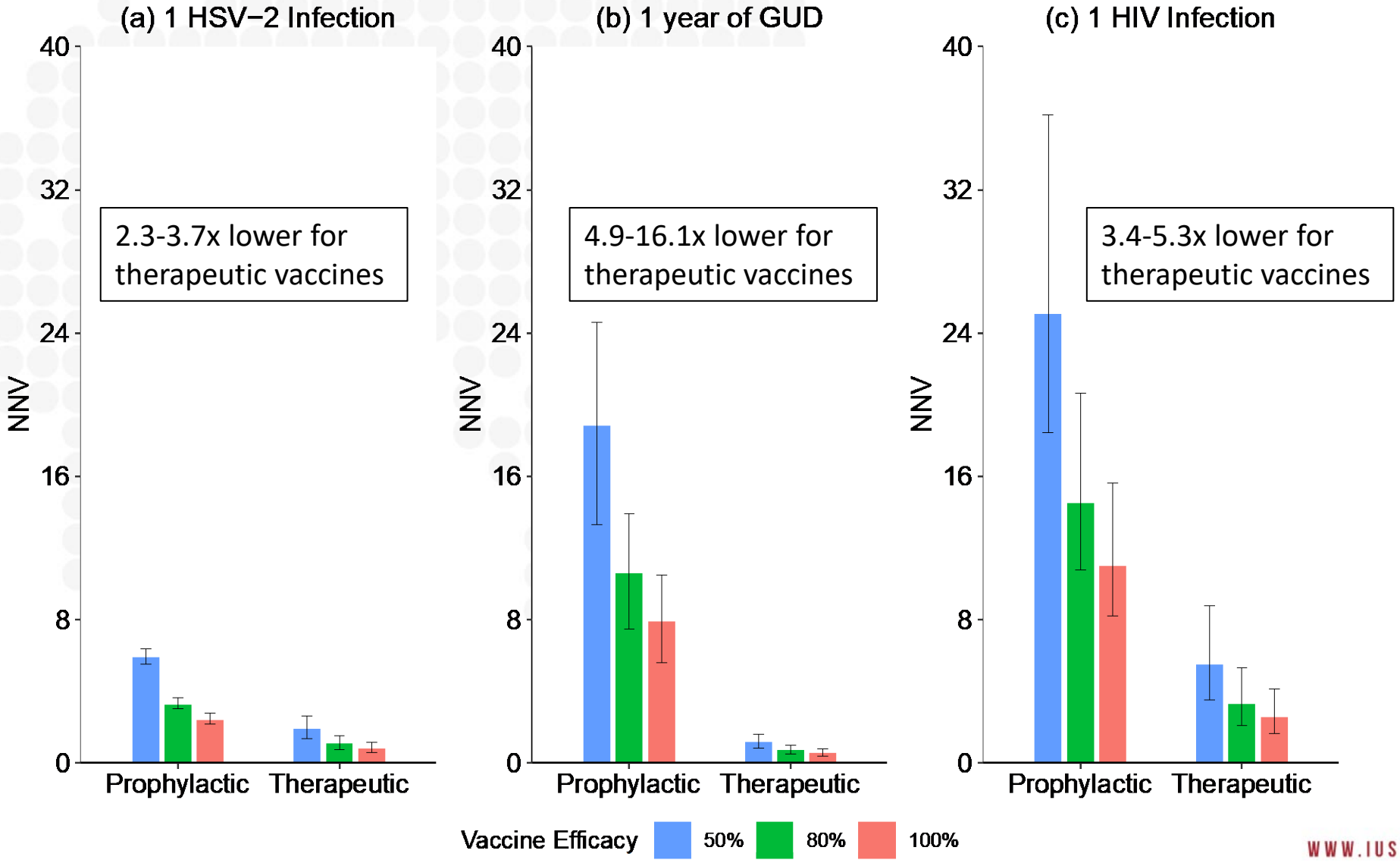
Results – Sensitivity Analyses



Impact highly sensitive to the duration of protection and proportion regularly receiving boosters (to extend duration of protection):

- 50-87% less impact if 0% receive boosters.
- 28-43% less impact if 50% regularly receive boosters.

NNV with Baseline Vaccines



CONCLUSIONS

Conclusions

- Prophylactic and therapeutic vaccines offer two complementary approaches for reducing large burden of HSV-2 infection and disease both in South Africa and globally.
  - Even low efficacy vaccines could have important impacts.
- Our results suggest that in high HIV prevalence populations such as South Africa, both types of vaccines could be an important additional tool for controlling HIV
- Therapeutic versus prophylactic vaccines:
  - Much greater impact per vaccination for therapeutic vaccines with similar efficacy, BUT
  - Less overall impact from therapeutic vaccination than prophylactic vaccination due to large proportion with asymptomatic HSV-2 infection.
- Duration of protection will limit impact, particularly of therapeutic vaccines
  - Use of boosters could be important

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