Model-based evaluation of an infant HPV prophylactic vaccination program in Nigeria

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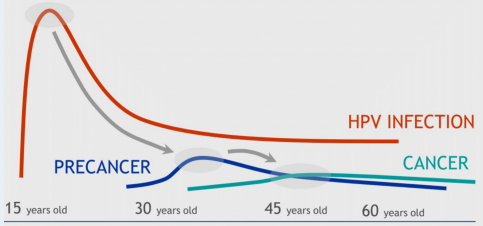
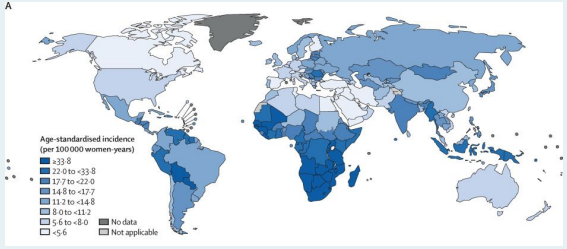
Cervical cancer is a major public health problem, but we have the tools to fix it

The epidemiology of cervical cancer (CxCa)

- 660K cases/year, 350K deaths[1]
- 99% of cases attributable to human papillomavirus (HPV), a very common STI

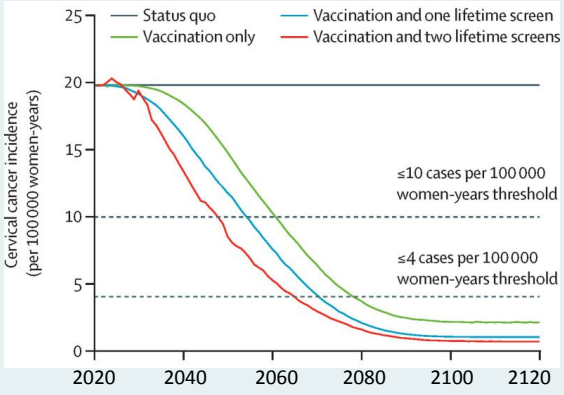


- Unequal global burden[1]



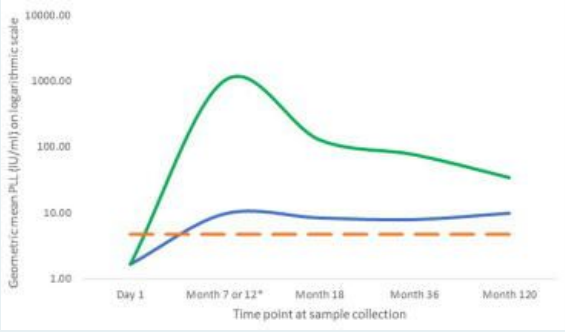
We have proven, effective tools to prevent cervical cancer…

- We have very, very effective vaccines (~100%)
- Secondary prevention: screening and treating precancerous lesions
- Modeling has predicted that 90% vx coverage could avert 61M cancers over the next century[2]



… and vaccination is proving even better than first thought[3]

- Trials have shown **high and durable immune response** in single-dose recipients of HPV vaccine at **10-years** post vaccination



How can we increase coverage of these very effective vaccines?

Current global coverage: **27%**
WHO target: **90%**

1. WHO estimates, 2022 | 2. Brisson et al 2020, *Lancet* | 3. Joshi et al 2023, *Vaccines*
Abbreviations: CxCa: cervical cancer; HPV: human papillomavirus; STI: sexually transmitted infection; WHO: World Health Organisation

Supply constraints are lessening, but other barriers to increased HPV vaccine coverage remain

Global vaccine supply has been constrained[1,2]

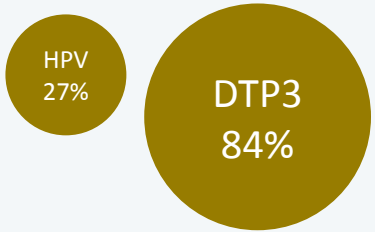
- Many countries introduced HPV vaccination over 2010s → newly elevated demand
- Introduction of gender-neutral vaccination in higher-income countries
- 3-dose schedule
- Limited number of manufacturers

… but supply constraints are lifting[3]

1. Single dose strategy
2. Increased capacity from manufacturers
3. Sluggish demand during the pandemic

… nevertheless, delivering a vaccine to 9-14yo girls remains a challenge

Global coverage is much lower than for childhood vaccination[4]



- HPV vaccines are targeted at pre-adolescent girls, an age group that has not been traditionally reached with routine health care services
- School-based programs miss out-of-school youth
- Targeting girls just prior to sexual debut with a vaccine that prevents acquisition of an STI has fueled vaccine hesitancy that also limits uptake

Aims of this work

1. **Objective:** to determine what an infant HPV vaccine would need to be impactful	– Inform data collection prioritization – Help motivate field studies
2. **Study design**: simulation study using an agent-based model of HPV & cervical cancer	– In silico evidence needed before trials – Low cost study using existing HPV model
3. **Setting**: Nigeria	– High burden of cervical cancer – HPV vaccination introduced in 2023

1. Prem et al 2024, *eClinicalMedicine* | 2. Malvolti et al 2024, *Vaccines* | 3. IPVC statement, 2023 | 4. WHO estimates, 2024

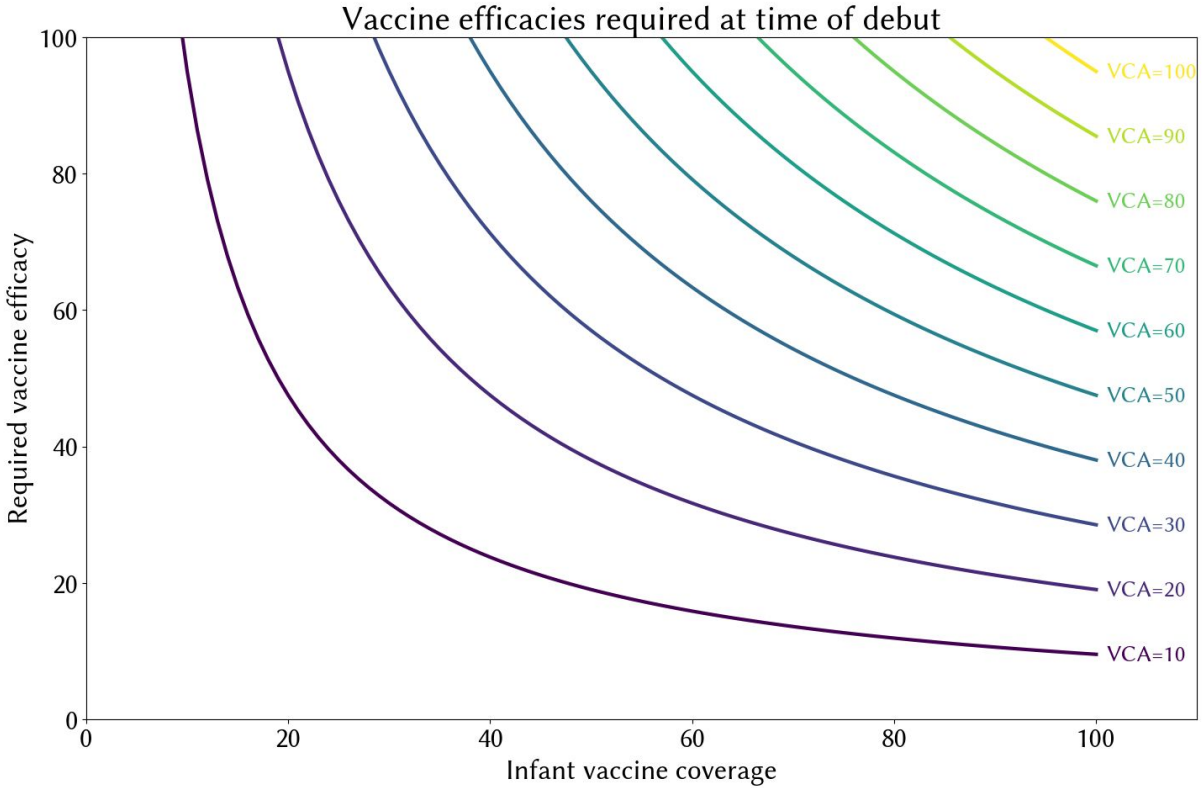
Abbreviations: HPV: human papillomavirus; DTP3: three doses of the vaccine against diphtheria, tetanus, and pertussis

Effective coverage isocurves

Effective coverage

$$VE_i \times VC_i \geq VE_a \times VC_a$$

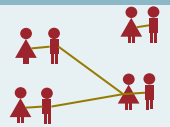
VE_i : vaccine efficacy at age of debut if delivered to infants
VC_i : infant vaccine coverage
VE_a : vaccine efficacy when delivered to pre-adolescents (95%)
VC_a : pre-adolescent vaccine coverage

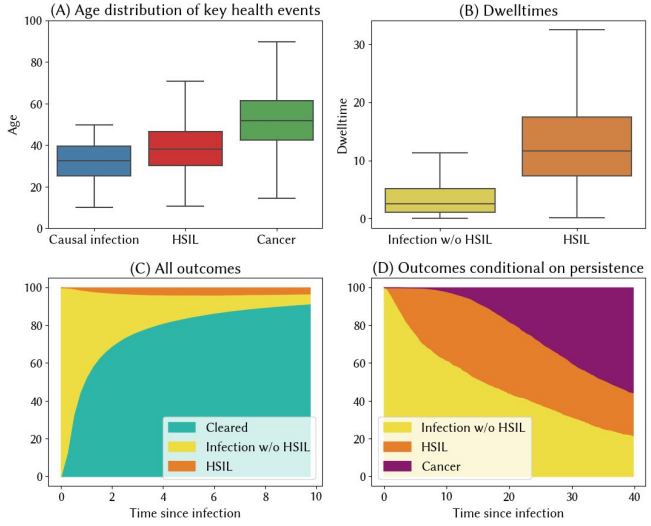


Transmission model approach and overview

Model structure

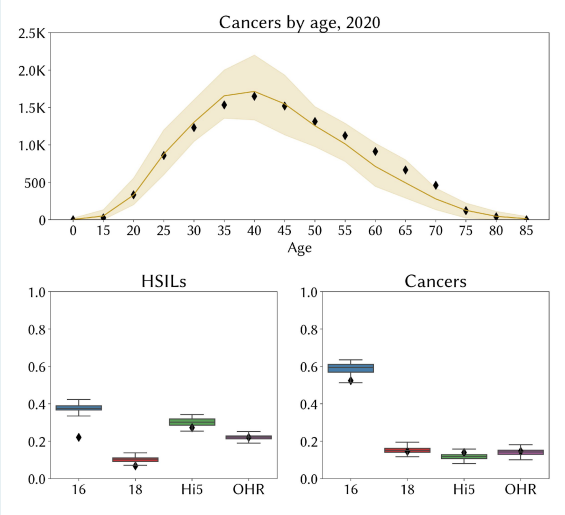
- **Agent-based model** (HPVsim) with a risk- and age-stratified sexual network[1]





Model implementation & calibration

- Implemented in the HPVsim software[1]
- Calibrate HPV transmission and sexual behavior parameters to fit cervical cancers by age



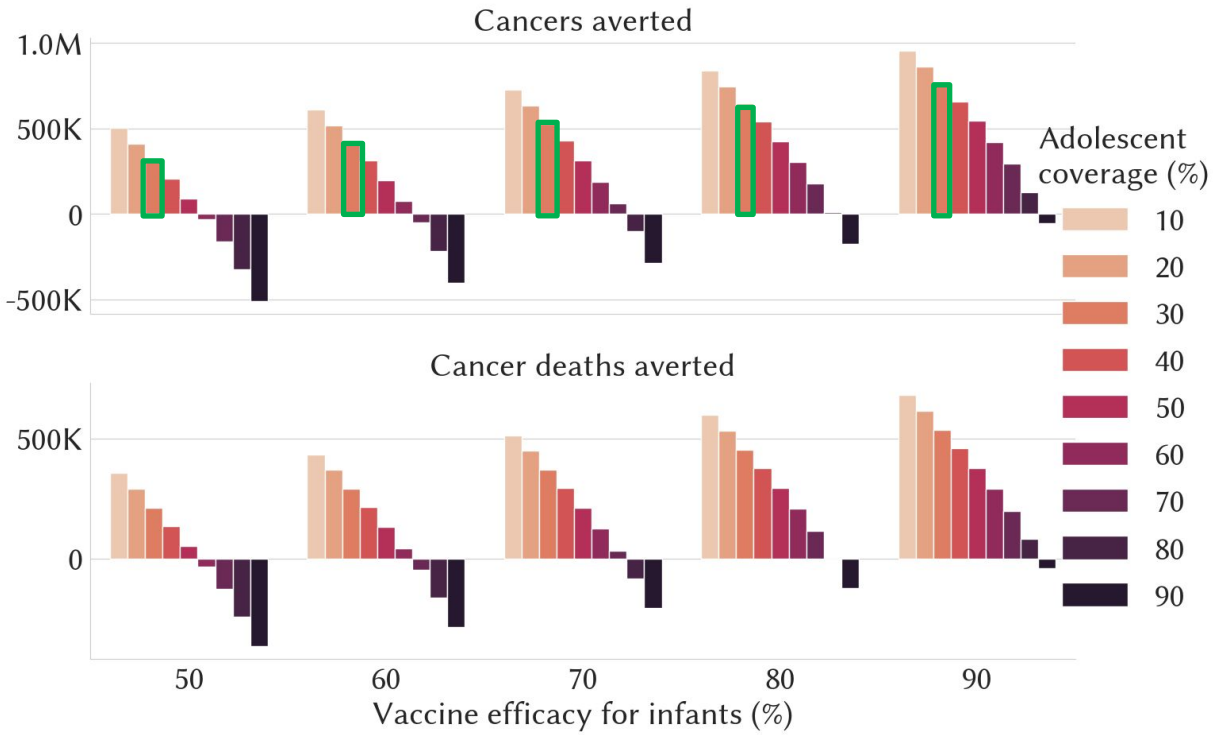
Analysis

1. Run simulations with varying levels of coverage for 9-14 year old girls (10-90%), as well as the efficacy of the infant vaccine at the point of sexual debut (50-90%)
2. Assume that the infant vaccine program would be able to attain coverage levels of 90%
3. Model the delivery of a bivalent vaccine offering 95% protection against HPV types 16 and 18
4. Compute cervical cancer cases & deaths over 2025–2100

1. Stuart et al, 2024

Abbreviations: HSIL: high-grade squamous epithelial lesion (precursor to cervical cancer); HPV: human papillomavirus; DTP3: three doses of the vaccine against diphtheria, tetanus, and pertussis

An effective infant vaccine would likely be a competitive vaccination strategy



- If the efficacy of the infant vaccine is high enough (90%), then the health impact of the infant vaccination strategy would be at least as high as the adolescent vaccination strategy
- However, at lower levels of efficacy, the strategy would be inferior unless adolescent coverage levels were lower than 50%.
- An adolescent vaccination program with **30% coverage** would result in **306,000–536,000** more cancer cases over 2025-2100 compared to an infant vaccination strategy with 90% coverage and 50-90% efficacy.

Conclusions & thanks

Conclusions

- Although trials have demonstrated that the HPV vaccine is safe and effective in 9yos, data are not yet available for younger age groups.
- We aimed to provide some motivation for the collection of data on the safety, efficacy, and durability of administering the HPV vaccine to neonates or toddlers.
- We have demonstrated that such a strategy would likely be impactful if it were feasible and safe

Although there is potential value in infant delivery, it is yet to be demonstrated; vaccinating 9-14 year olds remains a proven, effective, and extremely safe way to prevent cervical cancers.

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References

1. WHO Global Health Observatory, 2022
2. Brisson et al 2020, *Lancet*
3. Joshi et al 2023, *Vaccines*
4. Prem et al 2024, *eClinicalMedicine*
5. Malvolti et al 2024, *Vaccines*
6. IPVC statement, 2023
7. Stuart et al 2024, *Plos CB*

For further consideration

- Unclear what dosing schedule would be required for infant administration, which would impact on cost / delivery
- Switching the target age group for the delivery of the HPV vaccine would require a phased approach

Thank you!