Impact of catch-up human papillomavirus vaccination on cervical cancer incidence in Kenya: A mathematical modelling evaluation of HPV vaccination strategies in the context of moderate HIV prevalence

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Outline

- Background
- Methods
- Results

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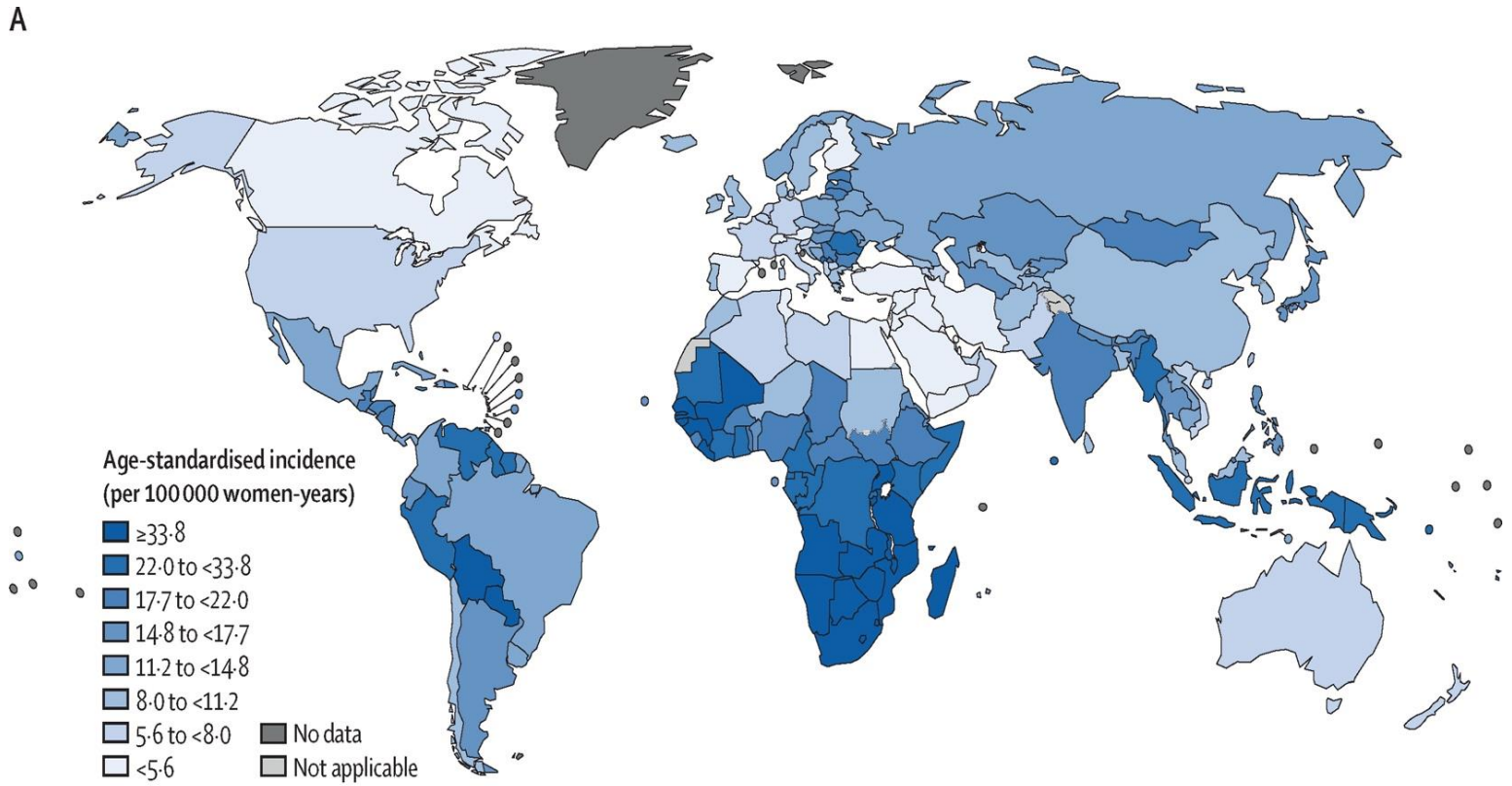
Although elimination is possible, cervical cancer remains disproportionally a leading cause of cancer globally, with high mortality.



In 2020, there were ~600 K cases and ~340 K deaths globally with disparities in distribution. Countries with effective programs are expected to eliminate cervical cancer.

Singh, et. al. Lancet Global Health, 2020

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In licensure trials, HPV vaccines are highly efficacious at preventing persistent HPV infection, a surrogate marker for cervical cancer.

- Multi-dose vaccine efficacy (VE) in clinical trials
  - Bivalent VE = 94%
  - Quadrivalent VE = 96%
  - Nonavalent VE = 96%

Harper, HPV Vaccine Review, Gynecologic Oncology, 2017

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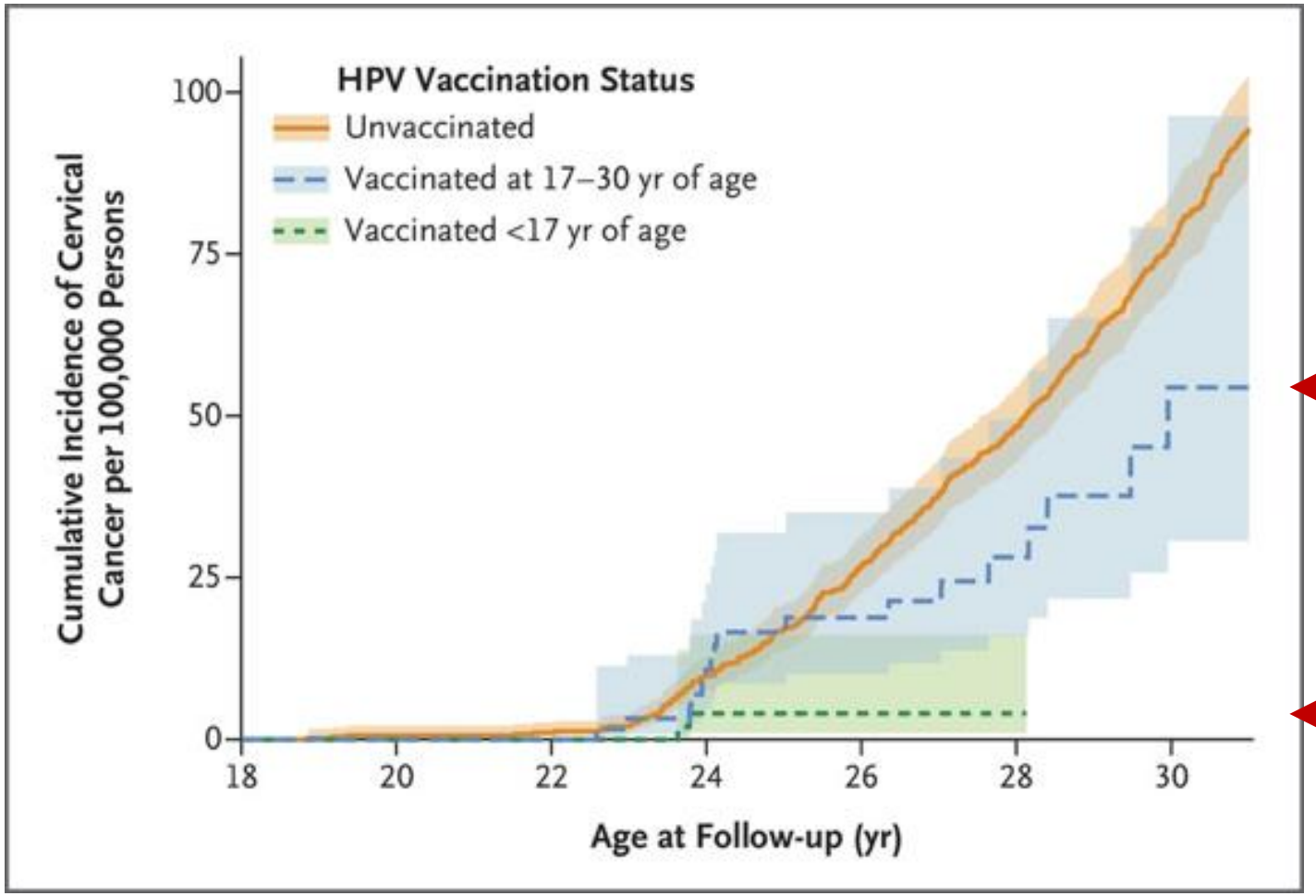
HPV vaccines are highly effective at preventing cervical cancer.



53% lower than unvaccinated

Cervical cancer incidence rate is 0.10 (0.02–0.39)/100 000 person-years among persons vaccinated at <17 years of age (88% lower than unvaccinated)

Lei J, et. al. HPV Vaccination and the Risk of Invasive Cervical Cancer. New England Journal of Medicine. 2020

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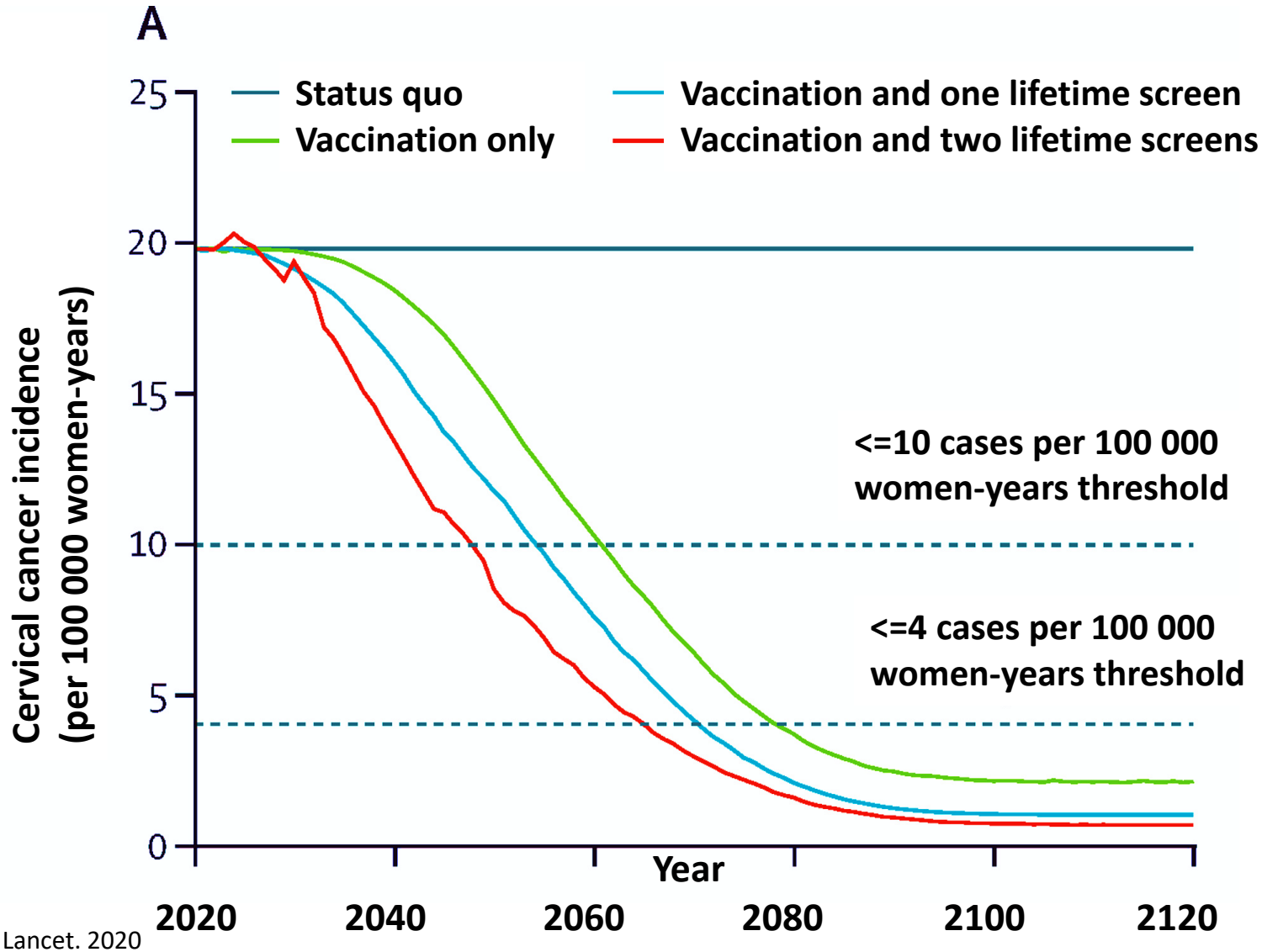
Reaching the global target for HPV vaccination would decrease cervical cancer cases by 89%; averting 60 million cases in the next century.



Brisson, Kim, Canfell et al. Lancet. 2020

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Background

- HIV increases the risk of HPV acquisition and persistence
  - 2-5x higher risk of cervical cancer
- Catch-up vaccination could accelerate cervical cancer prevention
  - In settings with high dual burden of HPV and HIV
- Population-level effectiveness of catch up vaccination in different HIV prevalence is unknown

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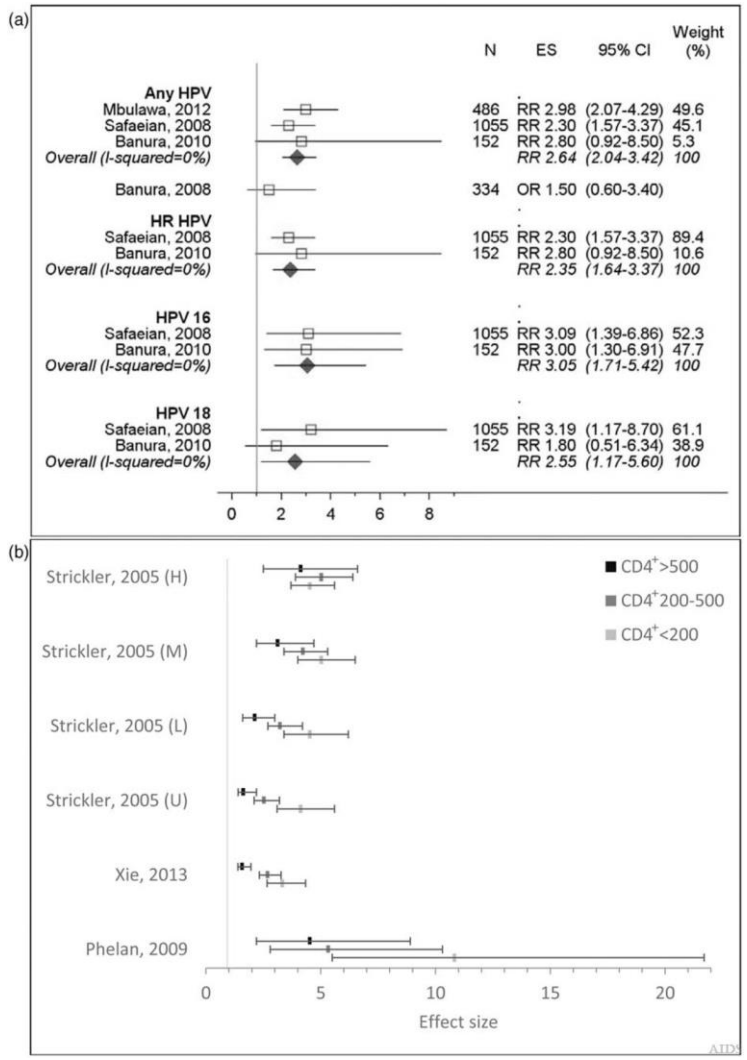
HIV-positive women have higher risk of human papilloma virus infection, precancerous lesions, and cervical cancer



Liu, Gui; Sharma, Monisha; Tan, Nicholas; Barnabas, Ruanne V.

AIDS32(6):795-808, March 27, 2018.

doi: 10.1097/QAD.0000000000001765

HPV incidence among HIV-positive women compared with HIV-negative women.N, sample size; ES, effect size. (a) Incidence of HPV infection by HPV type. Banura et al.[21] was not included in calculating the overall effect because it reported odds ratio; other studies reported relative risk. (b) Relative incidence of any HPV infection, by CD4+ cell count. The effect estimates from Strickler et al.[5] were stratified HIV RNA load; U = undetectable (<4000 copies/ml), L, low (4000–20 000 copies/ml), M, moderate (20 001–100 000 copies/ml), and H, high (>100 000 copies/ml). Effect size was measured in odds ratios in Phelan et al.[28] and hazard ratios in Xie et al., 2013 and Strickler et al.[5]. Effect estimates from Mbulawa et al.[26], Denny et al.[23], and Mane et al.[25] were not included in the figure. Mbulawa et al.[26] used a different CD4+ cell count cutoff (>350 vs. <350) and Denny et al.[23] and Mane et al.[25] evaluated CD4+ cell count as a continuous variable.

Acquisition of HPV and HIV among women

Characteristic	HPV	HIV
Moderate HIV prevalence setting (Kenya)		
- Prevalence	29% (normal cytology)*	5%
- Incidence	9% for persistent HPV	<2%@
- Age at acquisition	50% by age 20 years*	27 years#
High HIV prevalence setting (KZN, South Africa)		
- Prevalence	50% (normal cytology)*	25%
- Incidence	~9% for persistent HPV	2%-5%@
- Age at acquisition	70% by age 18 years^	25 years#

- HPV associated with 2-3 fold increase in HIV acquisition

*Ogembo RK, et. al., PLOS One, 2015; ^Ebrahim, S, et. al. PLOS One, 2016; #Risher, K. A, Lancet HIV, 2021, @Birdthistle, PLOS Med, 2021 (DREAMS), UNAIDS, KEN SHE

Objectives

Estimate and compare the impact of catch-up vaccination on cervical cancer incidence

1. In moderate HIV burden setting, accounting for HIV-HPV interactions
2. Evaluate increasing the coverage of vaccination

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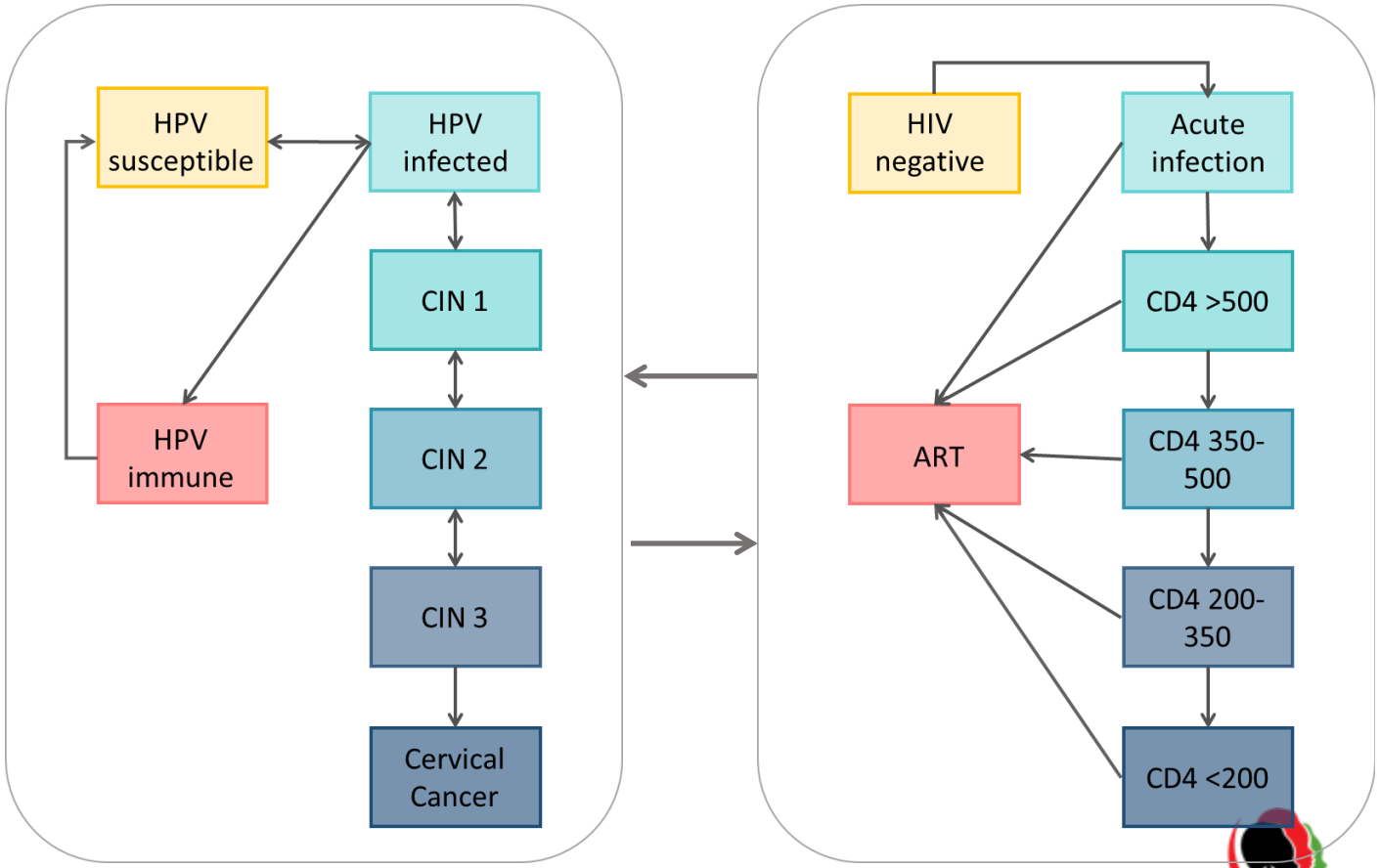
Model description

- Settings
  - Kenya (~5% HIV prevalence)
  - Western Kenya (~15% HIV prevalence)
- Model characteristics
  - HPV and HIV coinfection
  - Heterosexual mixing
  - Sexual activity risk levels
- Calibration targets
  - Demographics
  - HIV prevalence
  - HPV and CIN prevalence
  - Cervical cancer incidence



Tan et al, 2018. Vaccine, 36(32 Pt A), 4830–4836.

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Interventions and scenarios

1. No vaccination. This is the baseline for evaluating the impact of vaccination strategies.
2. Single-age-cohort vaccination. 90% of girls vaccinated by age 10. This scenario reflects Kenya's vaccination strategy in 2019.
3. Multi-age-cohort (MAC) vaccination. Girls aged 10-14 are vaccinated at 90% coverage. This scenario represents the vaccination strategy proposed by the WHO to eliminate cervical cancer.11
4. MAC plus moderate-coverage catch-up vaccination. Vaccinating girls aged 10-14 at 90% coverage, with one year of catch-up vaccination for women aged 15-24 years at 50% coverage.
5. MAC plus high-coverage catch-up vaccination. Vaccinating girls aged 10-14 at 90% coverage, with one year of catch-up vaccination for women aged 15-24 years at 80% coverage. Scenarios 4 and 5 reflect the strategies adopted by several high-income countries.
6. HPV-FASTER. Vaccinating girls aged 10-14 at 90% coverage, with one year of vaccination for women aged 15-44 at 80% coverage. This scenario is similar to the strategy proposed by Bosch et al based on clinical trial data showing high vaccine efficacy among mid-adult women up to aged 45. Although Bosch et al proposed HPV-based screening for women older than 30 years in addition to vaccination, we are modeling only the vaccination component of the strategy.

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Impact of catch-up human papillomavirus vaccination on cervical cancer incidence in Kenya: A mathematical modeling evaluation of HPV vaccination strategies in the context of moderate HIV prevalence

Gui Liu,[a,*] Nelly R Mugo,[a,b] Cara Bayer,[a] Darcy White Rao,[c] Maricianah Onono,[b] Nyaradzo M Mgodi,[d] Zvavahera M Chirenje,[e] Betty W Njoroge,[b] Nicholas Tan,[f] Elizabeth A Bukusi,[a,b,g] and Ruanne V Barnabas [a,c,g,h]

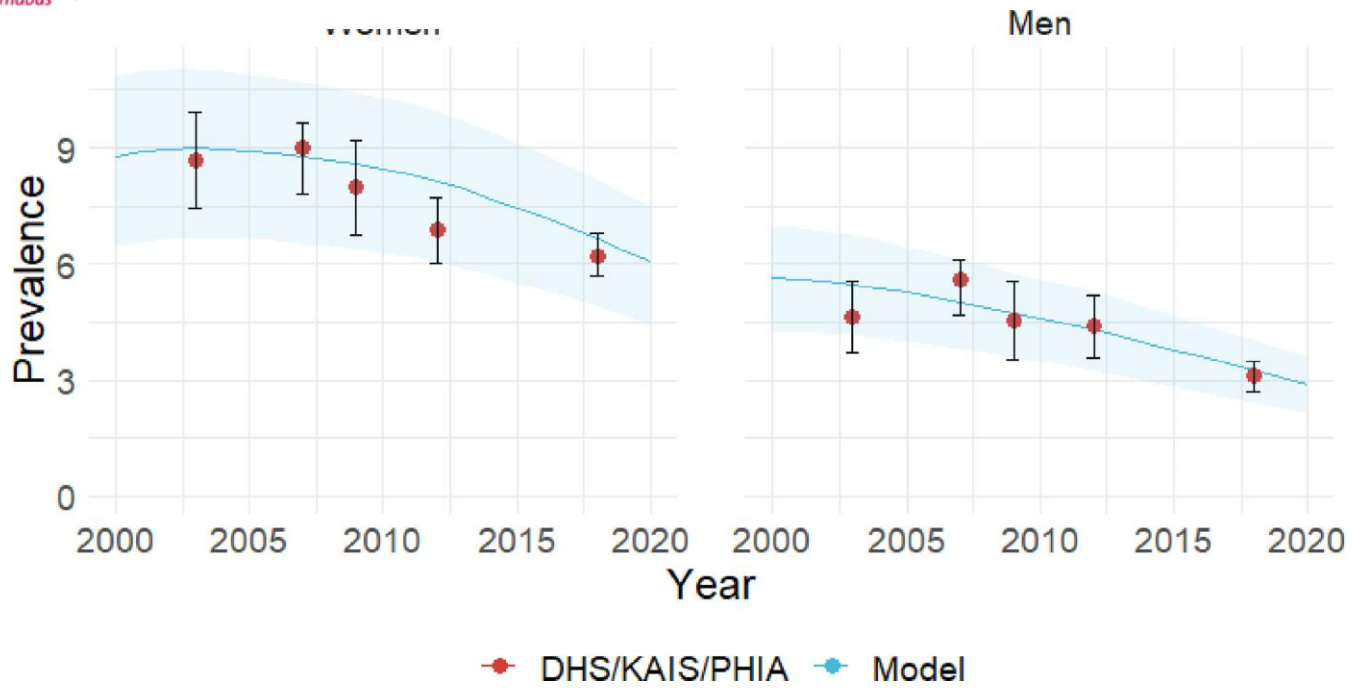

Figure 1 Model estimated HIV-prevalence among men and women between 2000-2020 (blue line) compared to data (red dots) from 2003 and 2008-2009 Demographic and Health Surveys (DHS), 2007 and 2012 Kenya AIDS Indicator Surveys (KAIS), and 2018 Population-based HIV Impact Assessment (PHIA). Shaded areas represent interquartile ranges of the model estimates.

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eClinicalMedicine 2022;45DOI: (10.1016/j.eclinm.2022.101308)

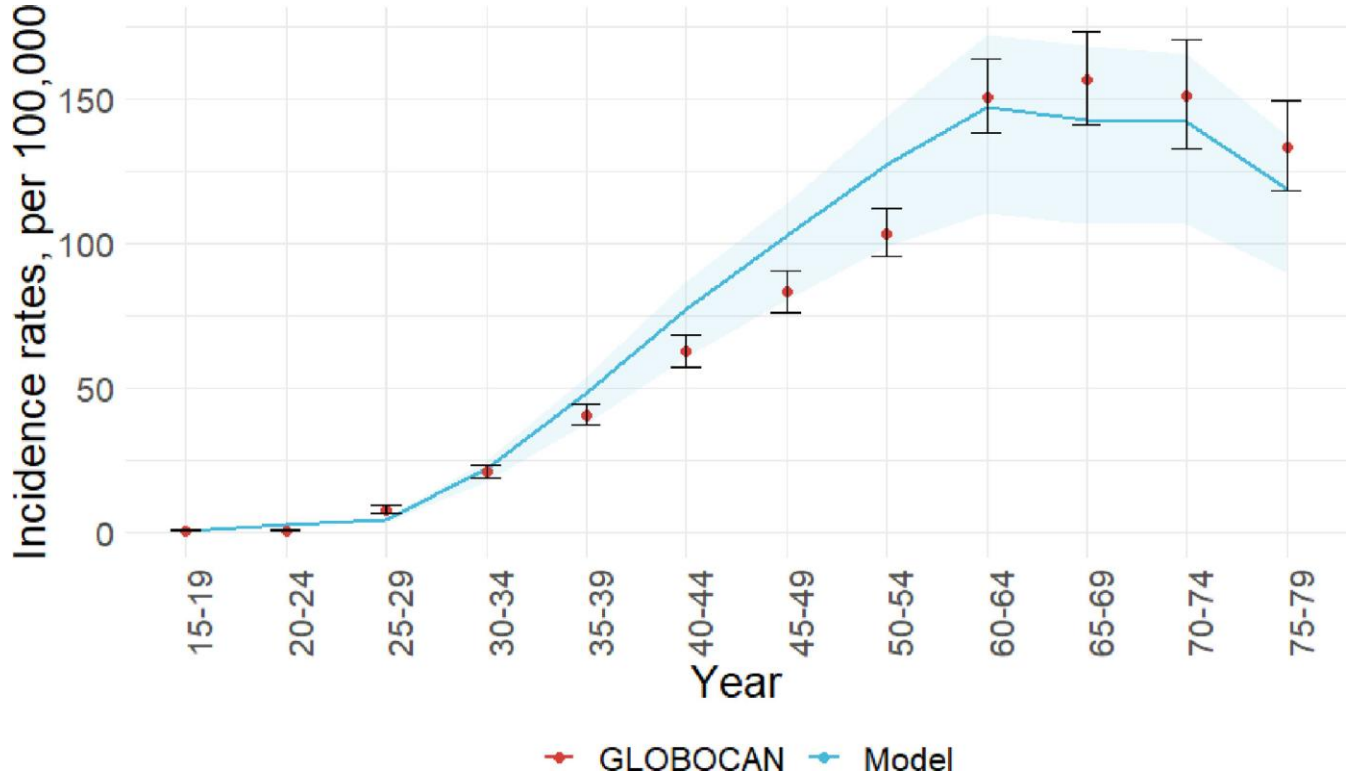

Figure 2 Model estimated age-specific cervical cancer incidence rates (blue line) compared to GLOBOCAN 2012 estimates (red dots). Shaded areas represent interquartile ranges of the model estimates.

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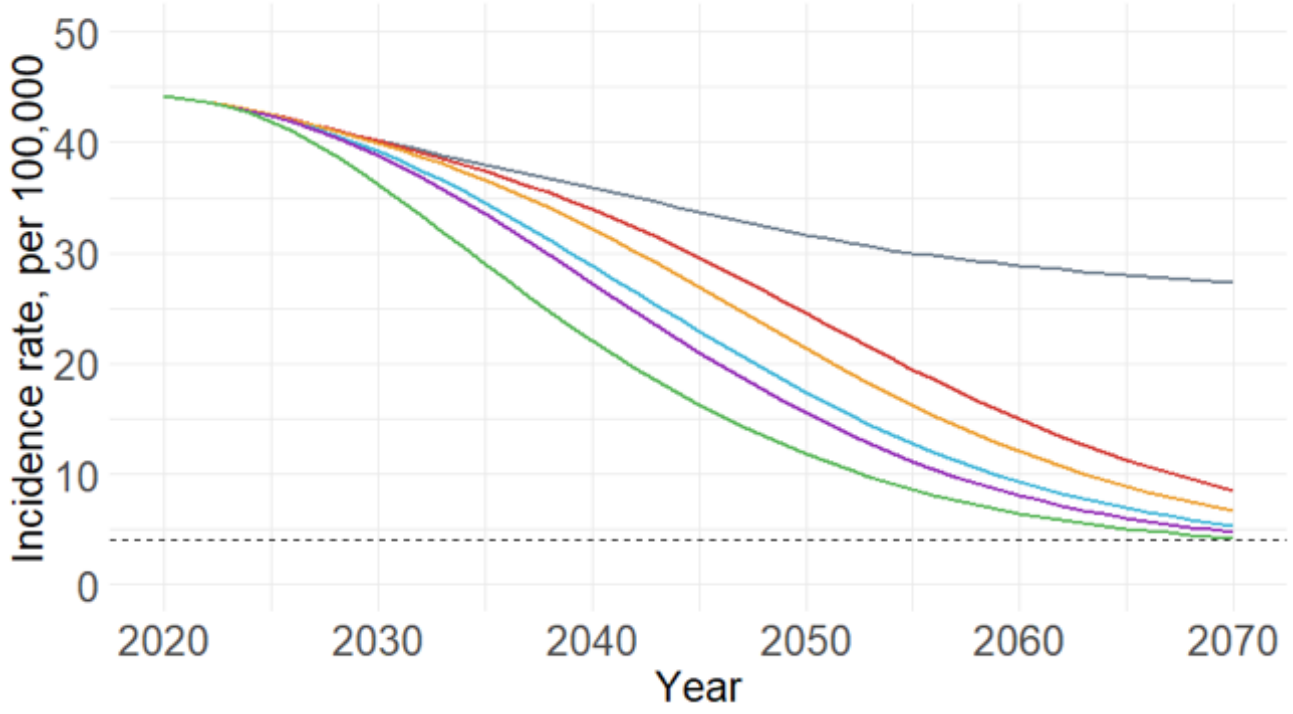
Accounting for HPV-HIV synergies, scaling up HPV vaccination including multi-age cohort (MAC) and catch-up vaccination accelerates cancer elimination

Modeling the impact of single-dose HPV vaccine scale-up in a moderate HIV prevalence setting (Kenya) on Cervical cancer incidence



	IR	RR
No vaccination	27 (20-33)	Ref
Single age	9 (6-10)	0.32
MAC	7 (5-8)	0.25
Moderate catch-up	5 (4-7)	0.20
High-coverage catch-up	5 (4-6)	0.18
HPV-FASTER	4 (3-5)	0.16

Liu, G, et al. Impact of catch-up vaccination in a moderate HIV prevalence setting. eClinicalMed, 2022

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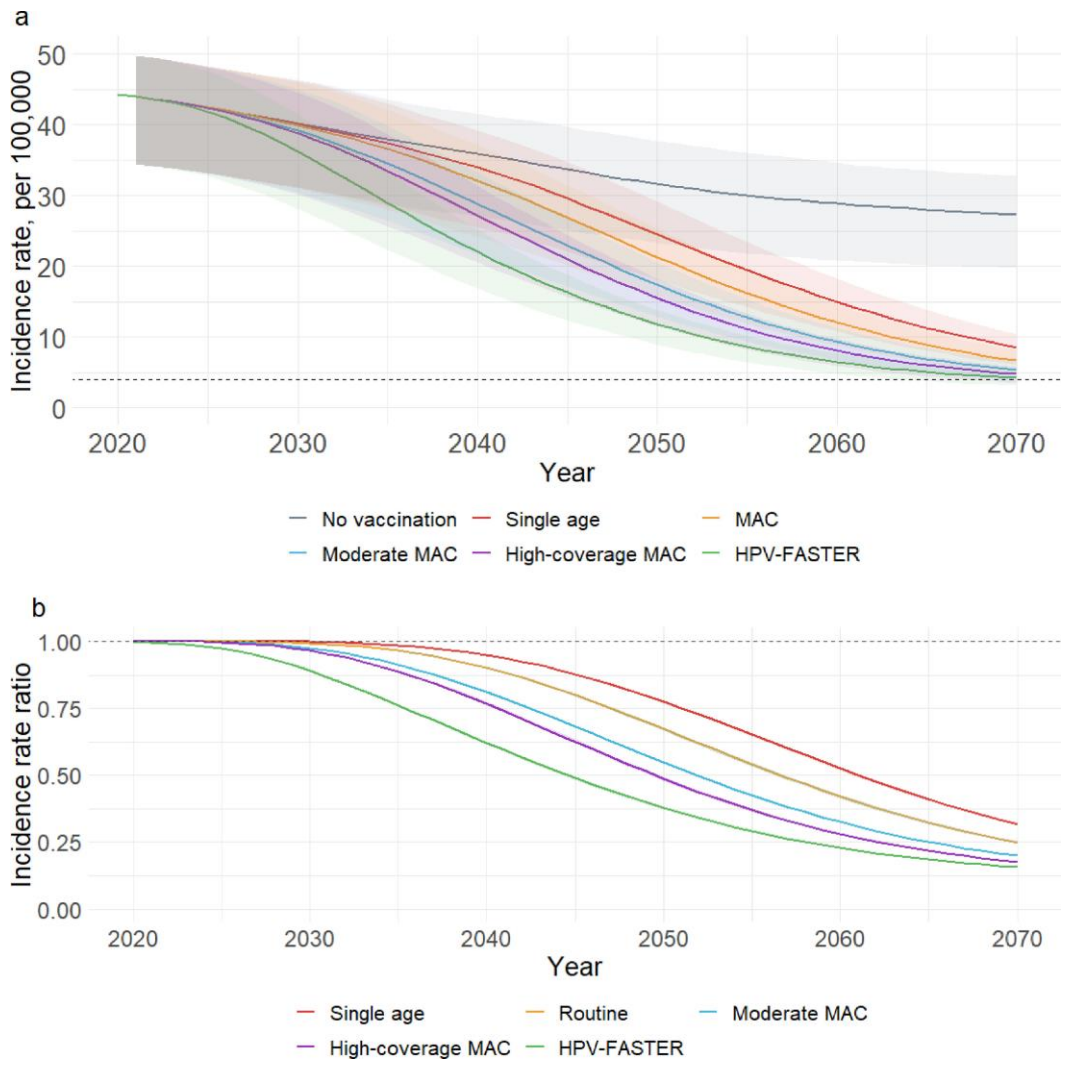

Figure 3 HPV vaccination impact on cervical cancer outcomes. a). Yearly age-standardized cervical cancer incidence rates from 2020-2070 by model scenario. The dashed line indicates the cervical cancer elimination threshold of 4 cases per 100,000 women. b). Yearly incidence rate ratios compared to no vaccination, with dashed horizontal line indicating no change relative to the scenario without vaccination. Shaded areas represent interquartile ranges of the model estimates. The HPV-FASTER scenario is similar to the strategy proposed by Bosch et al,[18] except that only the vaccination component is modelled in this scenario.

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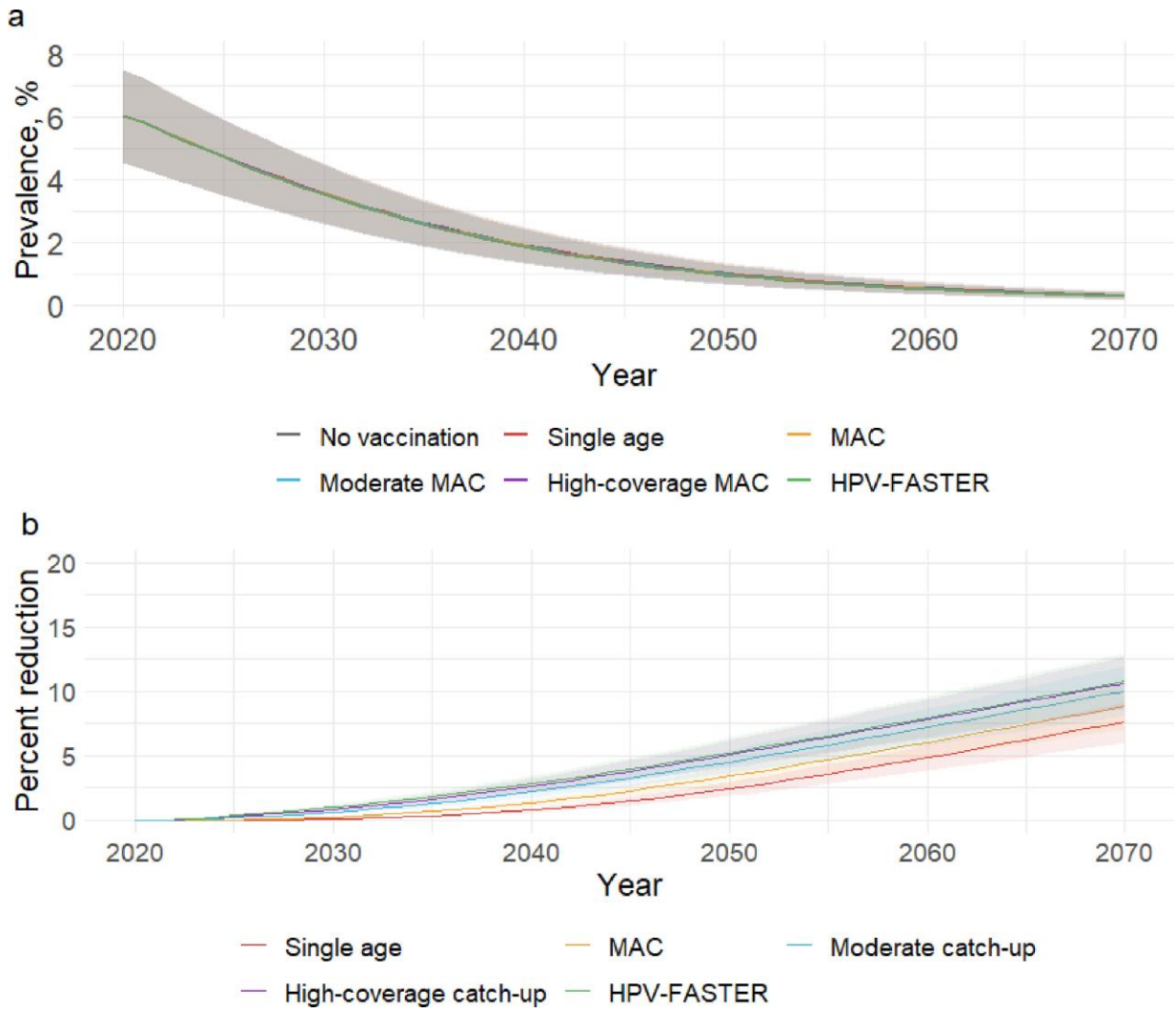

Figure 4 HPV vaccination impact on HIV burden in women. a) HIV prevalence among women over time by scenario. Because HIV prevalence was similar in all scenarios, the estimates and interquartile ranges for all scenarios overlap almost completely. b) Percent reduction in HIV prevalence relative to no vaccination. Shaded areas represent interquartile ranges of the model estimates. The HPV-FASTER scenario is similar to the strategy proposed by Bosch et al, except that only the vaccination component is modelled in this scenario.

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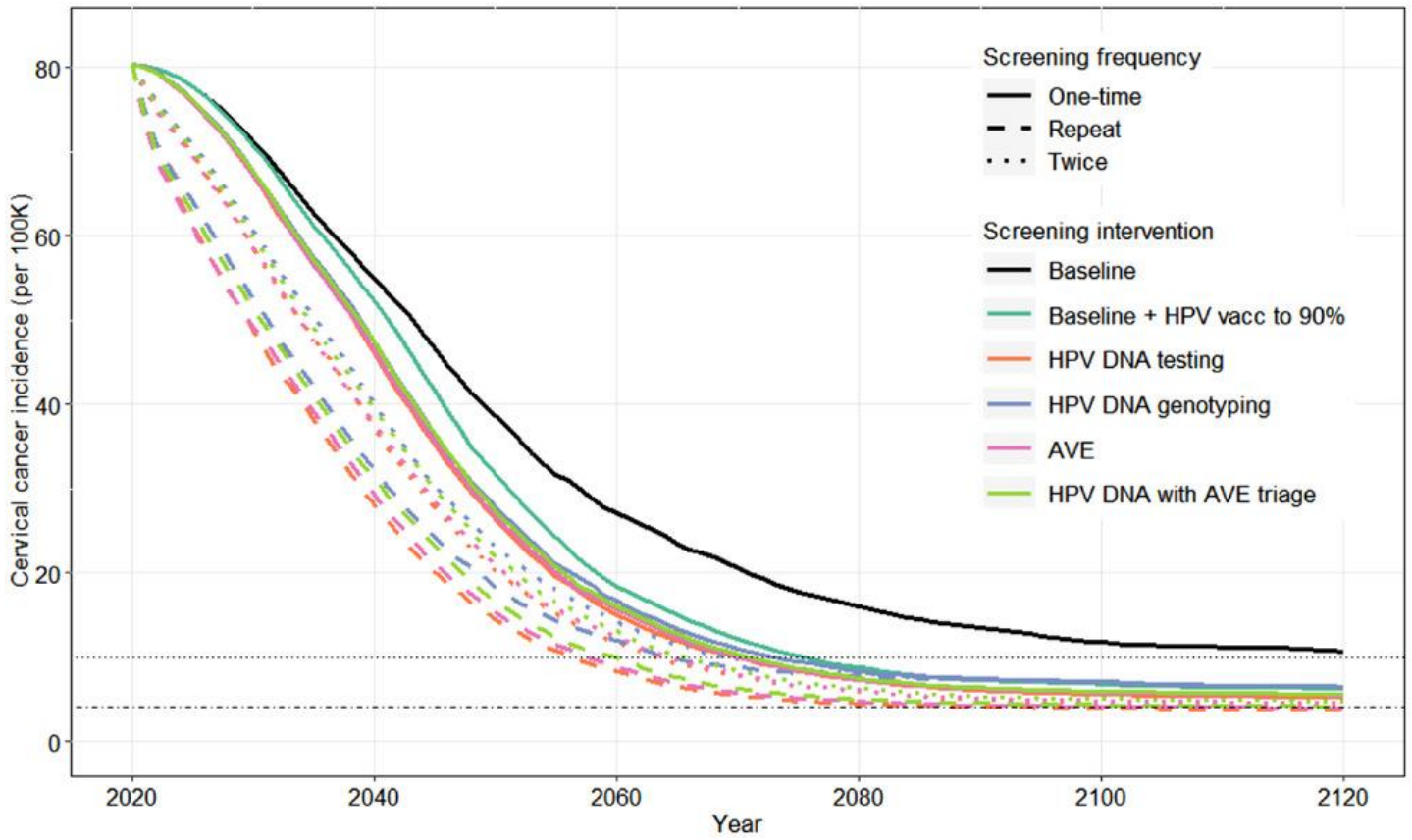
Modelling cervical cancer elimination using single-visit screening and treatment strategies in the context of high HIV prevalence: estimates for KwaZulu-Natal, South Africa

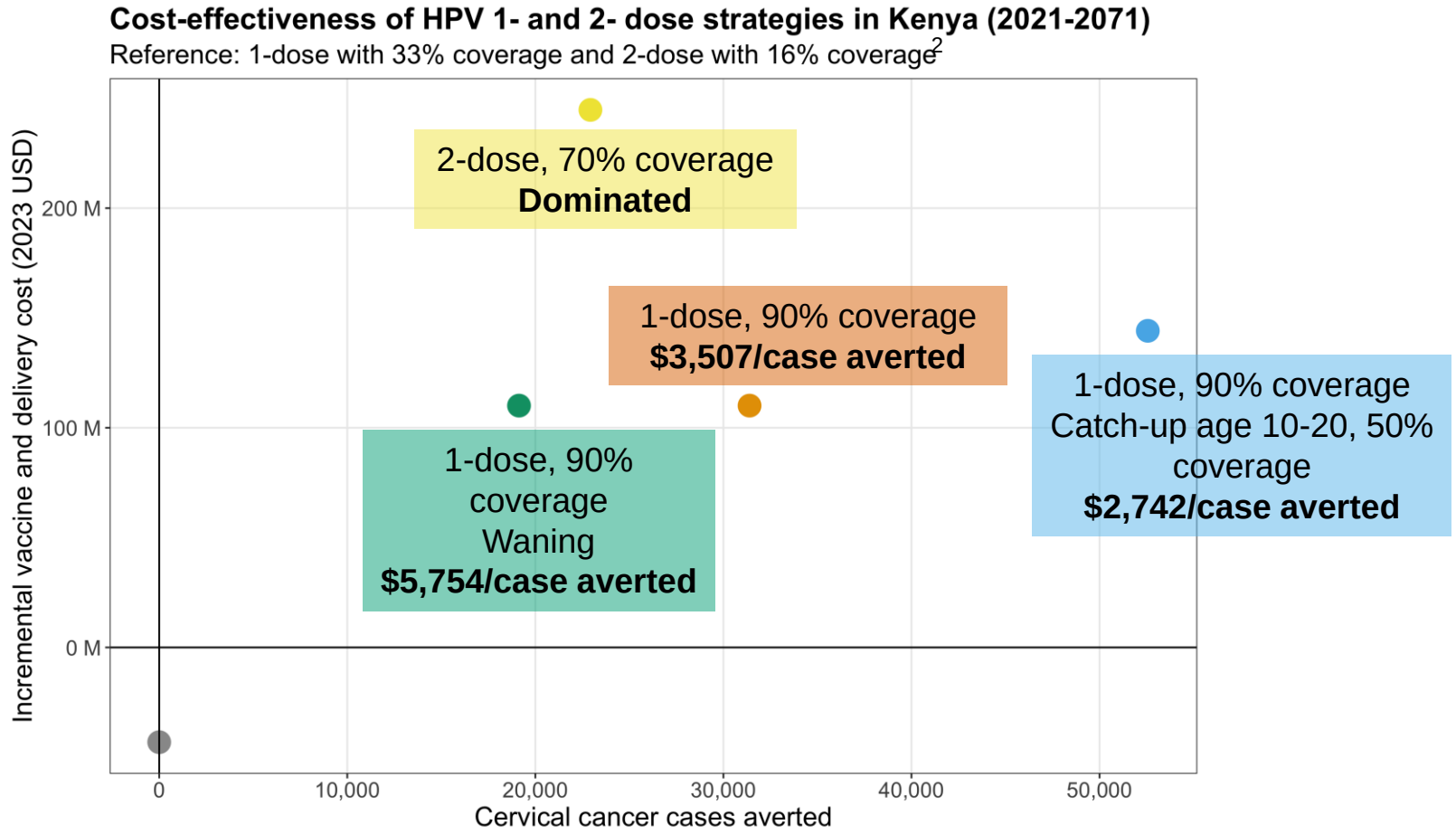
Darcy White Rao, Cara J. Bayer, Gui Liu, Admire Chikandiwa, Monisha Sharma, Christine L. Hathaway, Nicholas Tan, Nelly Mugo, Ruanne V. Barnabas



Rao and colleagues, JIAS, 2022, Projected cervical cancer incidence under scenarios that differ in HPV vaccination coverage and cervical cancer screening and treatment frequency, method, and loss to follow-up.

Cervical cancer screening and treatment is necessary to accelerate cervical cancer elimination

A single-dose HPV vaccine strategy is more cost-effective for cervical cancer prevention than a multi-dose approach, with MAC + catch-up most cost-effective.



Umutesi G., Hathaway, C., Heitner, J. et al. (personal communication)
Vaccine cost is $4.50/dose[3] and vaccine delivery cost is $6.18/dose (adjusted by health expenditure per capita)[4]. Costs discounted by 3% per year.

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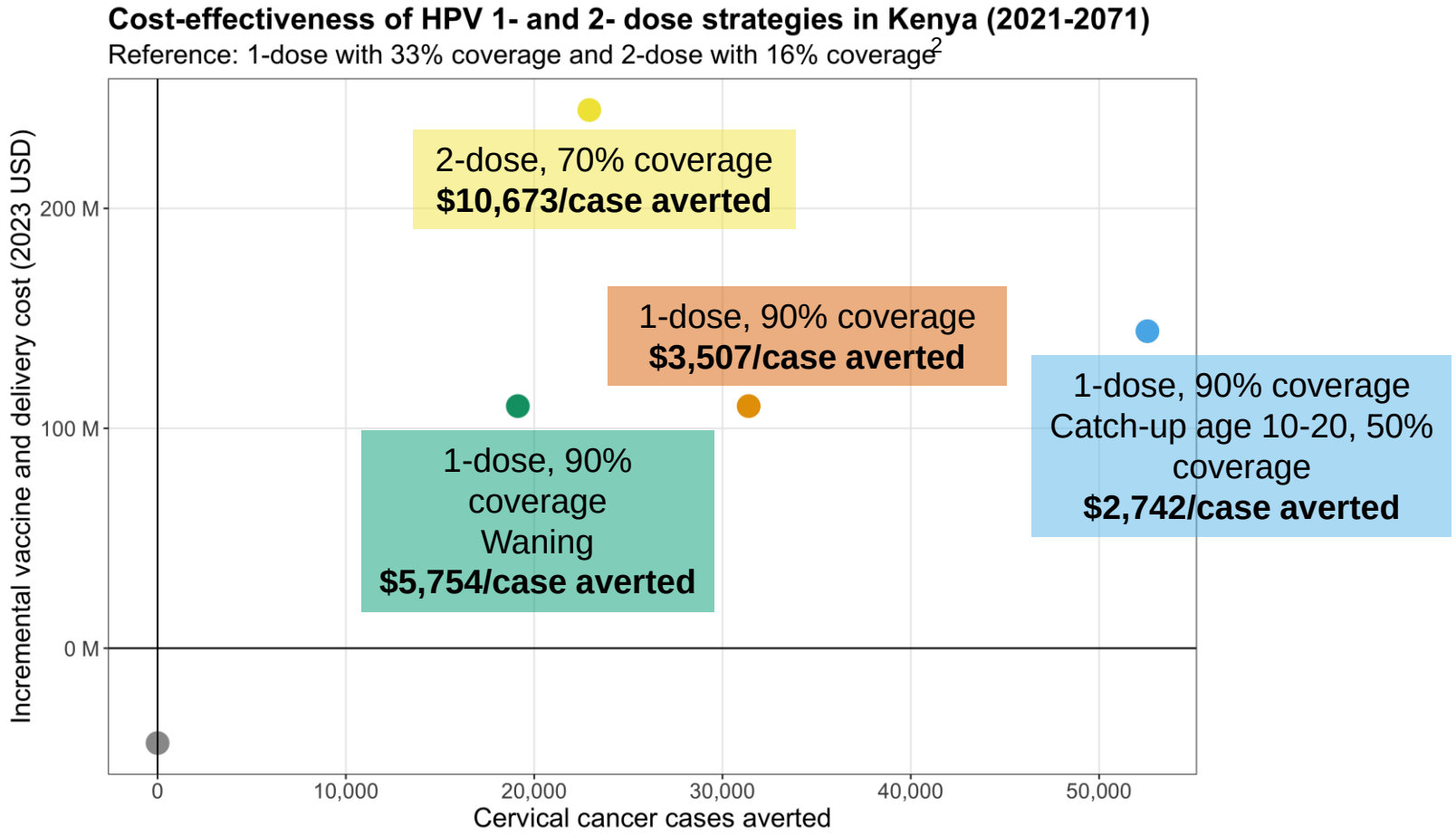
A single-dose strategy would save over 100 Million USD; the projected cost of rotavirus vaccination[1] in Kenya



Vaccine cost is $4.50/dose[3] and vaccine delivery cost is $6.18/dose (adjusted by health expenditure per capita)[4]. Costs discounted by 3% per year.

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Conclusions

- Catch-up vaccination reduce cancer incidence regardless of HIV prevalence
  - Reduction was greater in Western Kenya
  - And among HIV-positive population
- High coverage of catch-up vaccination accelerated incidence reduction
  - No difference by HIV status or HIV prevalence
- Expanding HPV vaccine eligibility to include adolescents and young adults can considerably alleviate cervical cancer burden

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