Enhanced cervical cancer and HIV interventions reduce the disproportionate burden of cervical cancer cases among women living with HIV: A modeling analysis

Cara J Bayer, Ruanne V Barnabas, Gui Liu, Thesla Palanee-Phillips, **Darcy White Rao**
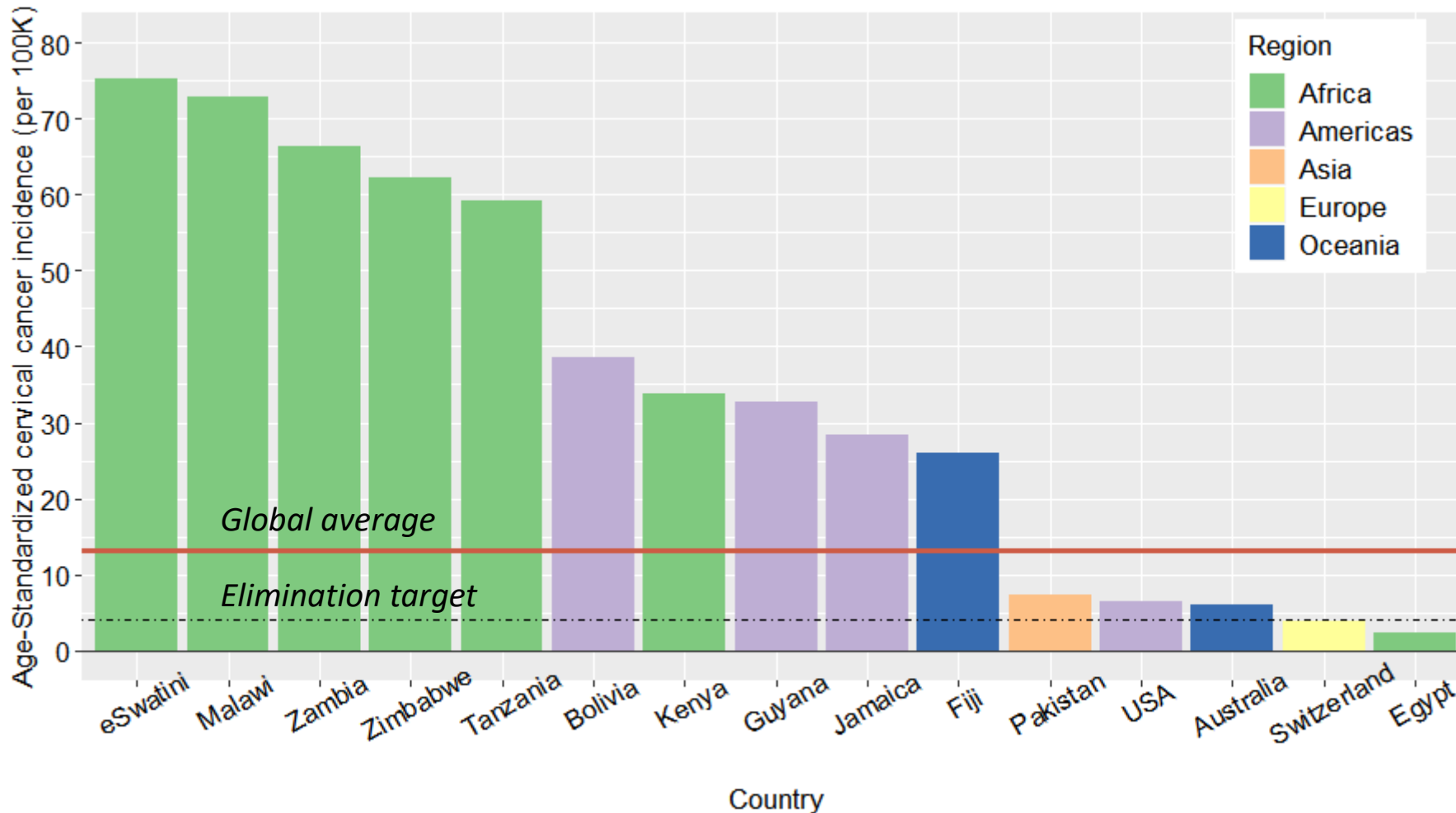
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Geographic disparities in cervical cancer

- Over 80% of cervical cancer cases and nearly 90% of deaths in 2018 were in low- and middle-income countries

- Synergies with HIV contribute to higher cancer incidence in sub-Saharan Africa

- Cervical cancer is preventable

- Scalable prevention strategies will be needed to reach the **elimination threshold** of 4/100,000

Figure created using data from Arbyn 2020, *Lancet Glob Health*

HIV increases cervical cancer risk

- Women living with HIV are at increased risk of HPV infection, persistence, invasion, and treatment failure

- **6-fold** relative risk of cervical cancer
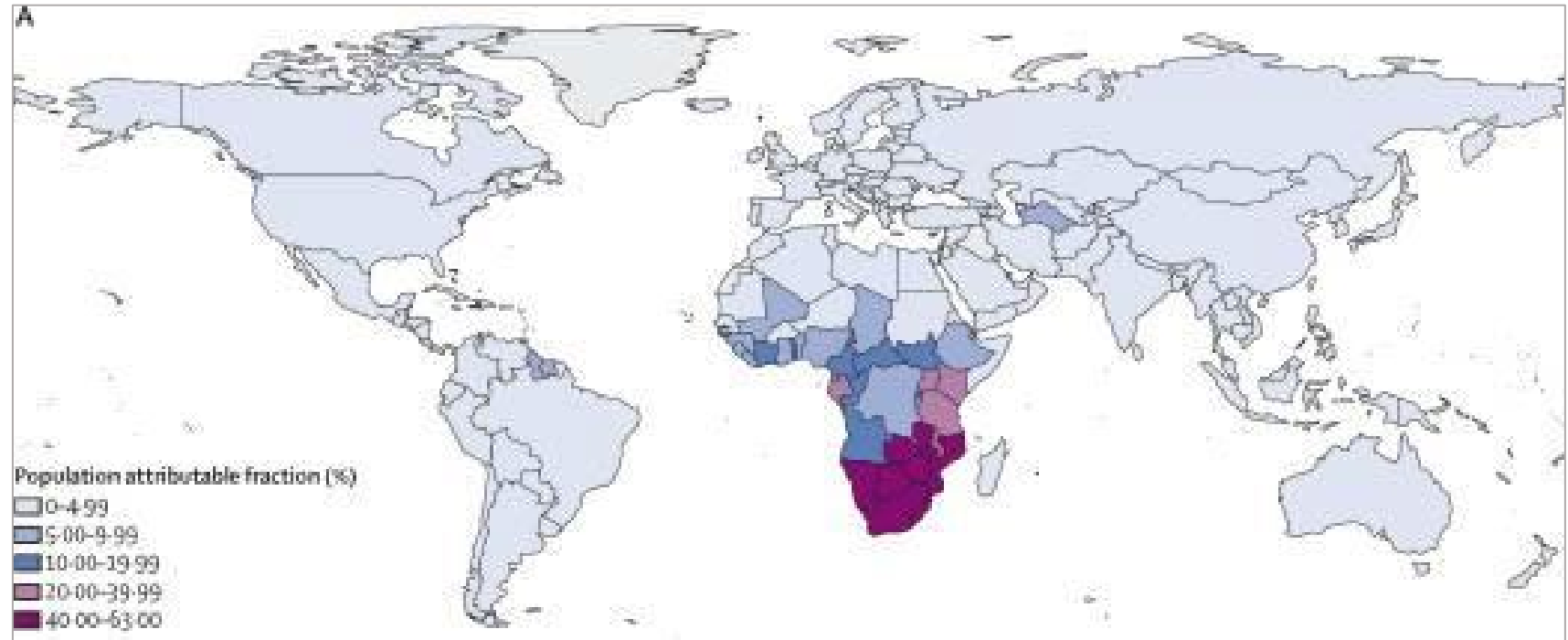
Population attributable fraction of women with cervical cancer living with HIV in 2018
(Fig 4 from Stelzle et al. 2021)

Liu 2018, *AIDS;* Strickler 2005, *JNCI*; Abraham 2013, *JAIDS*; Massad 2009, *Am J Obstet Gynecol.*; Stelzle 2021, *Lancet Glob Health*

Cervical cancer and antiretroviral therapy (ART)

- Decreased cancer risk
  - Lower HPV incidence and progression
  - Increased regression
  - Greater benefits with earlier ART initiation
  - Population-level effects through reduction in HIV transmission

- Increased survival
  - More likely to survive to ages of peak cancer incidence
 - Risk remains higher than HIV-negative women

Kelly 2018, *Lancet HIV*; Rohner 2019, *Int J Cancer*

Objectives

1. Evaluate trends in cervical cancer incidence coinciding with ART scale-up in a setting with high HIV prevalence

2. Describe the proportion of cervical cancer cases among women living with HIV over time

3. Examine the impact of cervical cancer prevention strategies on these trends

HIV-HPV transmission model

- Deterministic compartmental model
- Setting: KwaZulu-Natal, South Africa
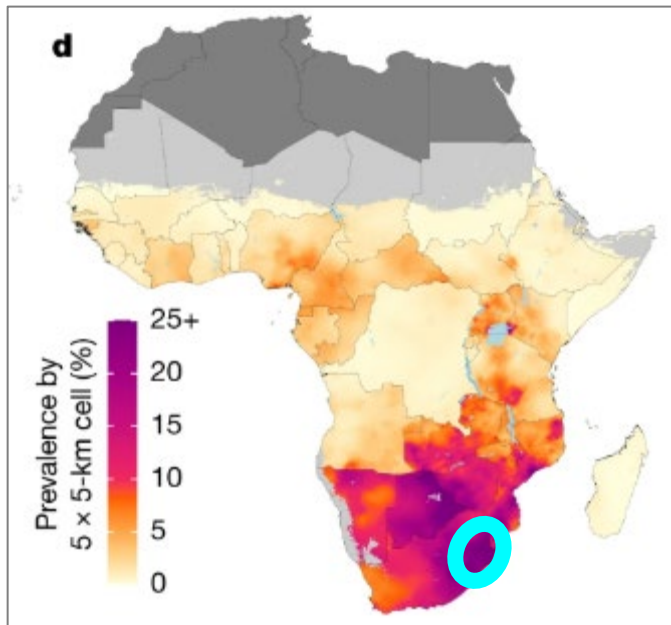

HIV prevalence ~30% (15-49)
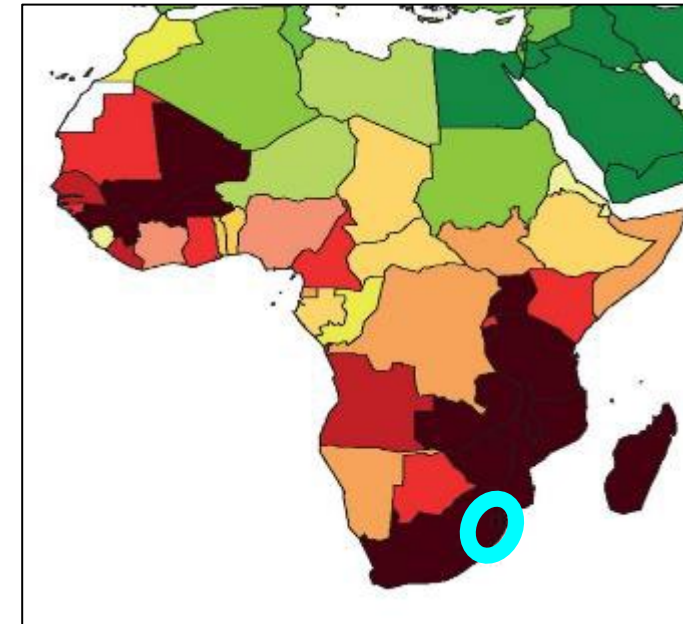
Cervical cancer incidence >43 per 100K

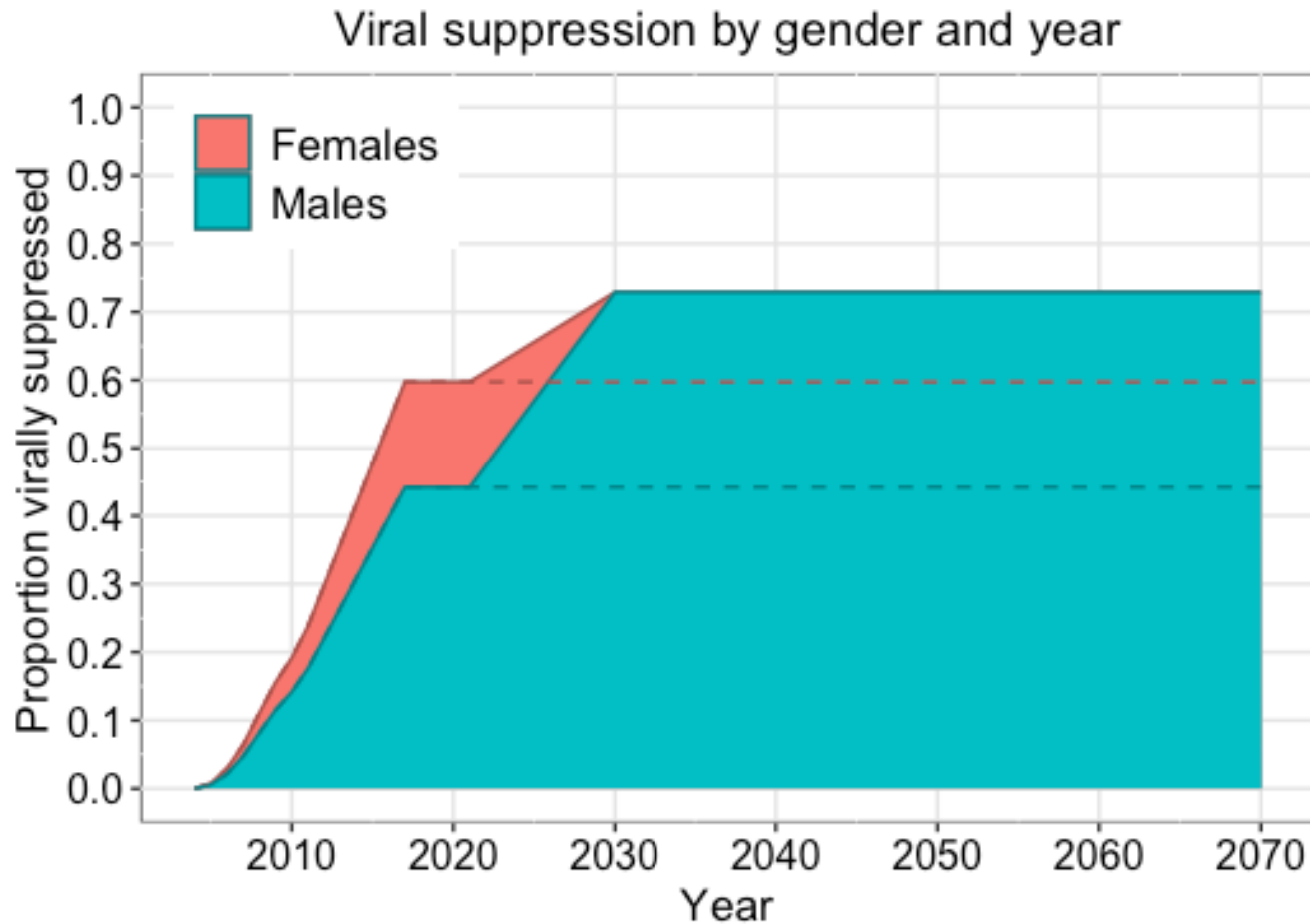South Africa Demographic and Health Survey, 2016: Key Indicators Report. Statistics South Africa; 2017

Bruni et al. Human Papillomavirus and Related Diseases in South Africa. Summary Report 17 June 2019

HIV-HPV transmission model

- Model components
  - Demography
  - Sexual behavior
  - HIV & HPV transmission and natural history
  - Interventions: ART, condoms, circumcision, cervical cancer screening, treatment, HPV vaccination

- Calibration
  - Multidimensional fitting to historic demographic data and epidemiological outcomes

- Analyses
 - Cervical cancer incidence and HIV prevalence 2001-2070

Transitions modified by HIV disease state

Tan et al., *Vaccine* 2018
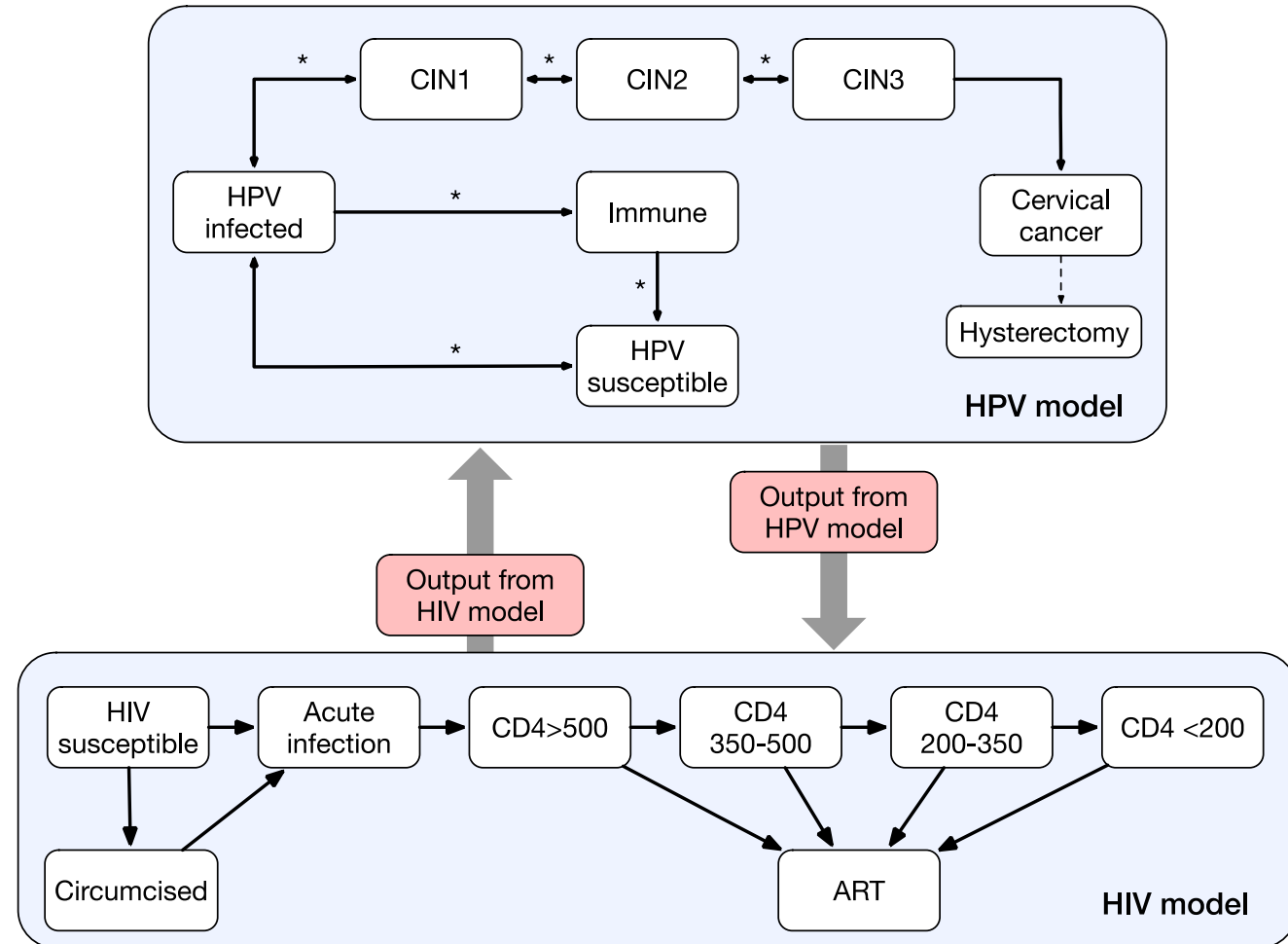
ART inputs and assumptions

Viral suppression by gender and year

- **Baseline scenario**: No ART scale-up from 2017

- **Enhanced scenarios**: ART scaled-up to 90-90-90 targets between 2021-2030

- With viral suppression:
  - No HIV transmission; reduced HIV-associated mortality
  - HPV acquisition similar to women without HIV
  - HPV clearance, progression, regression, and cervical-cancer associated mortality similar to untreated women with high CD4
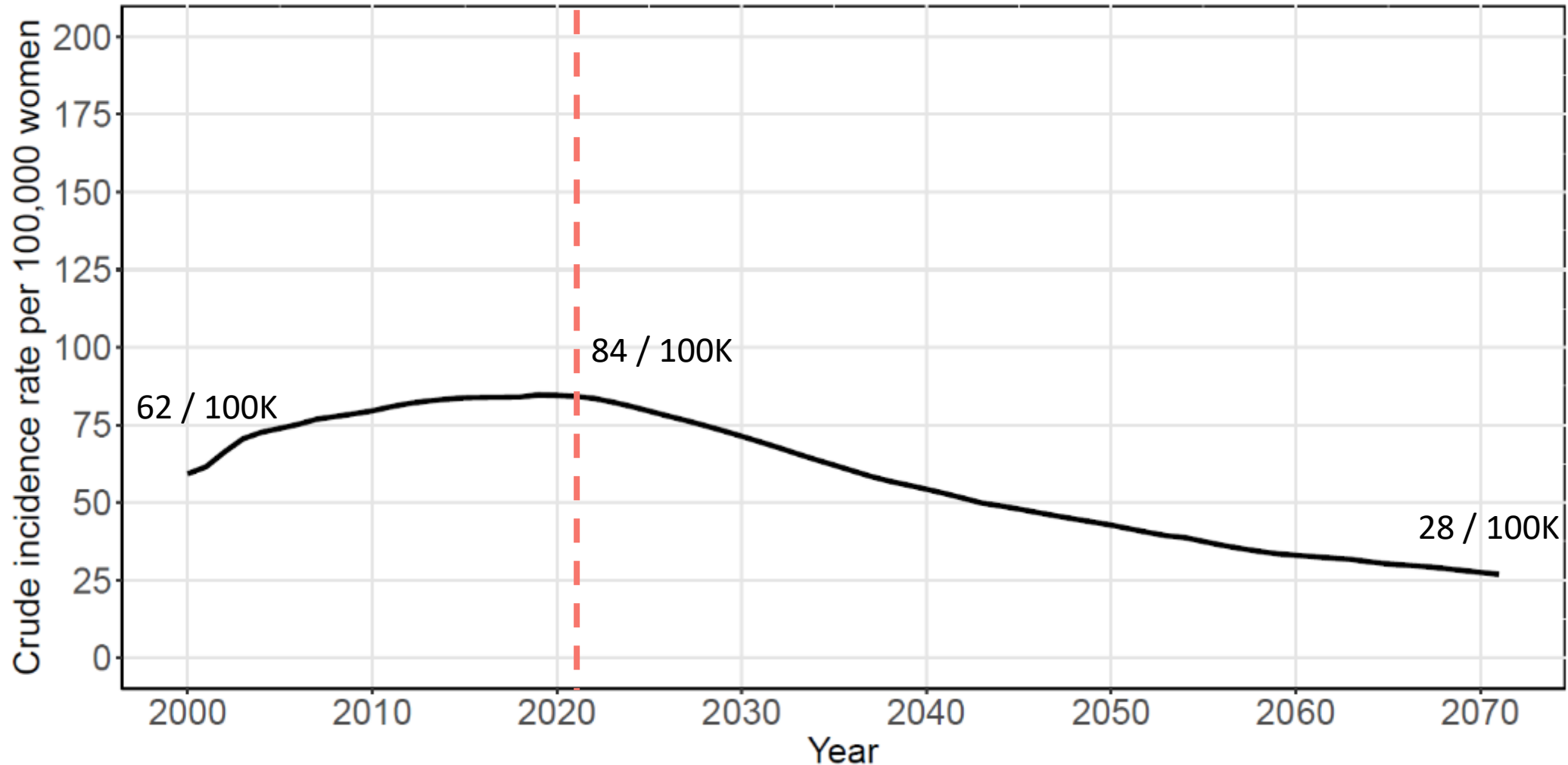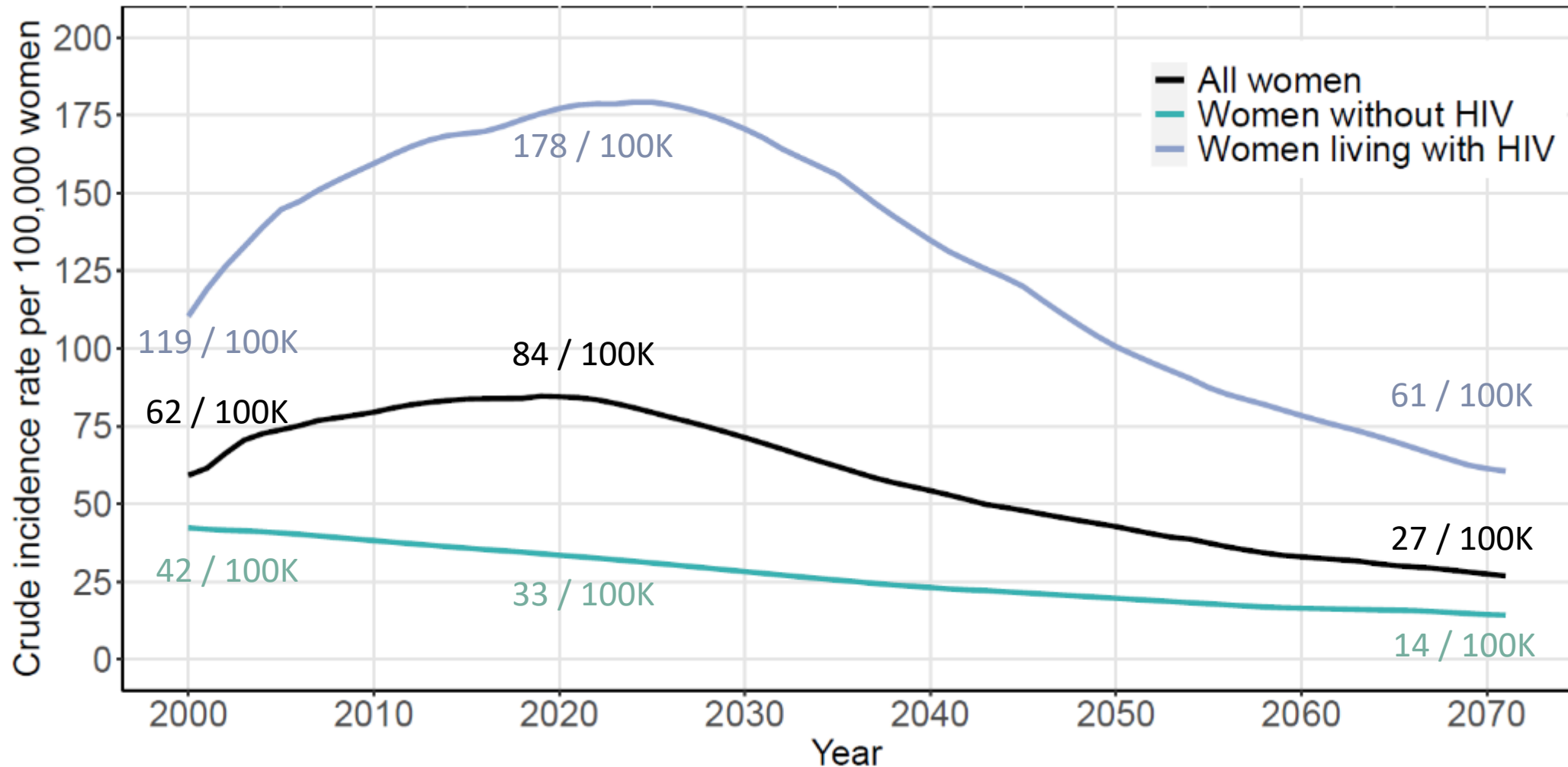
Modeled scenarios (2021-2071)
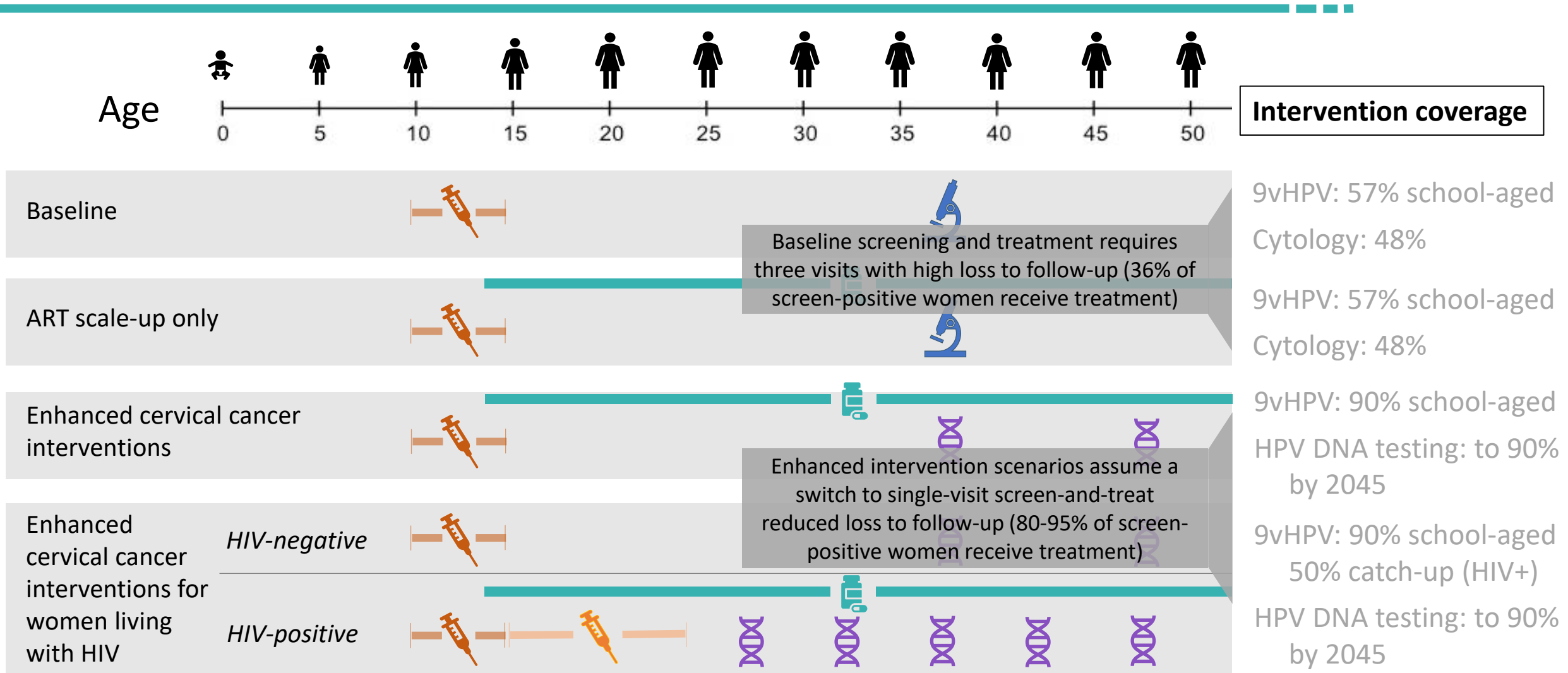
Cancer incidence among women aged 15+
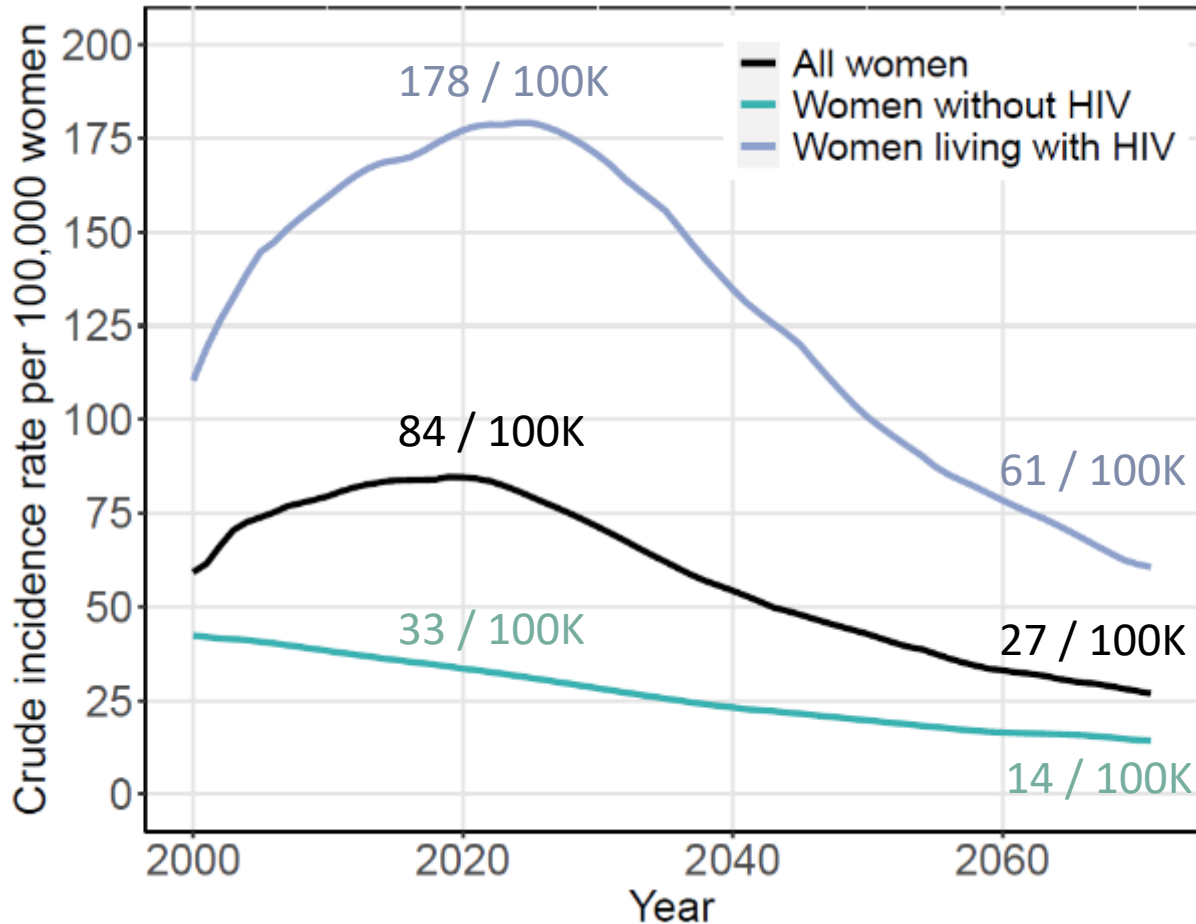## – Baseline scenario without ART scale-up –

Cancer incidence among women aged 15+
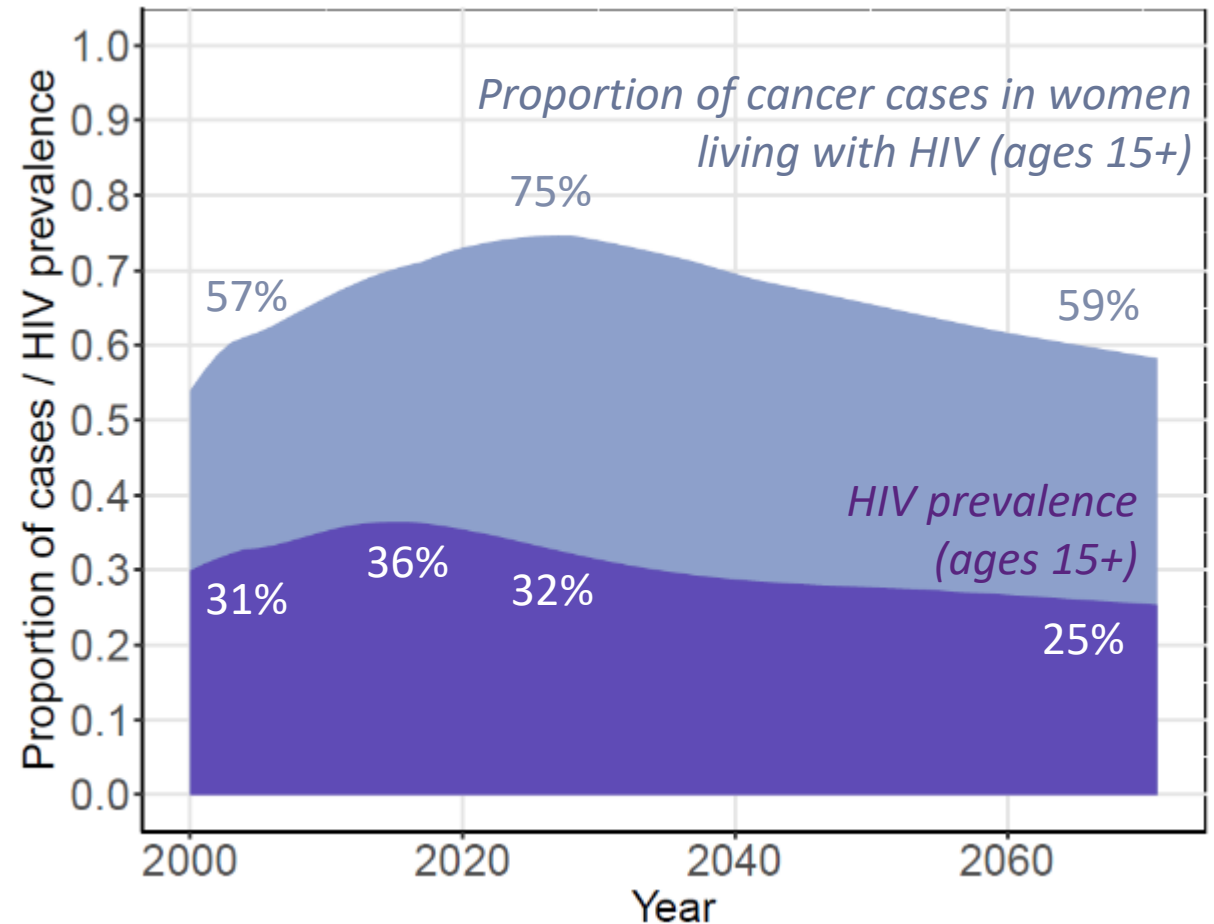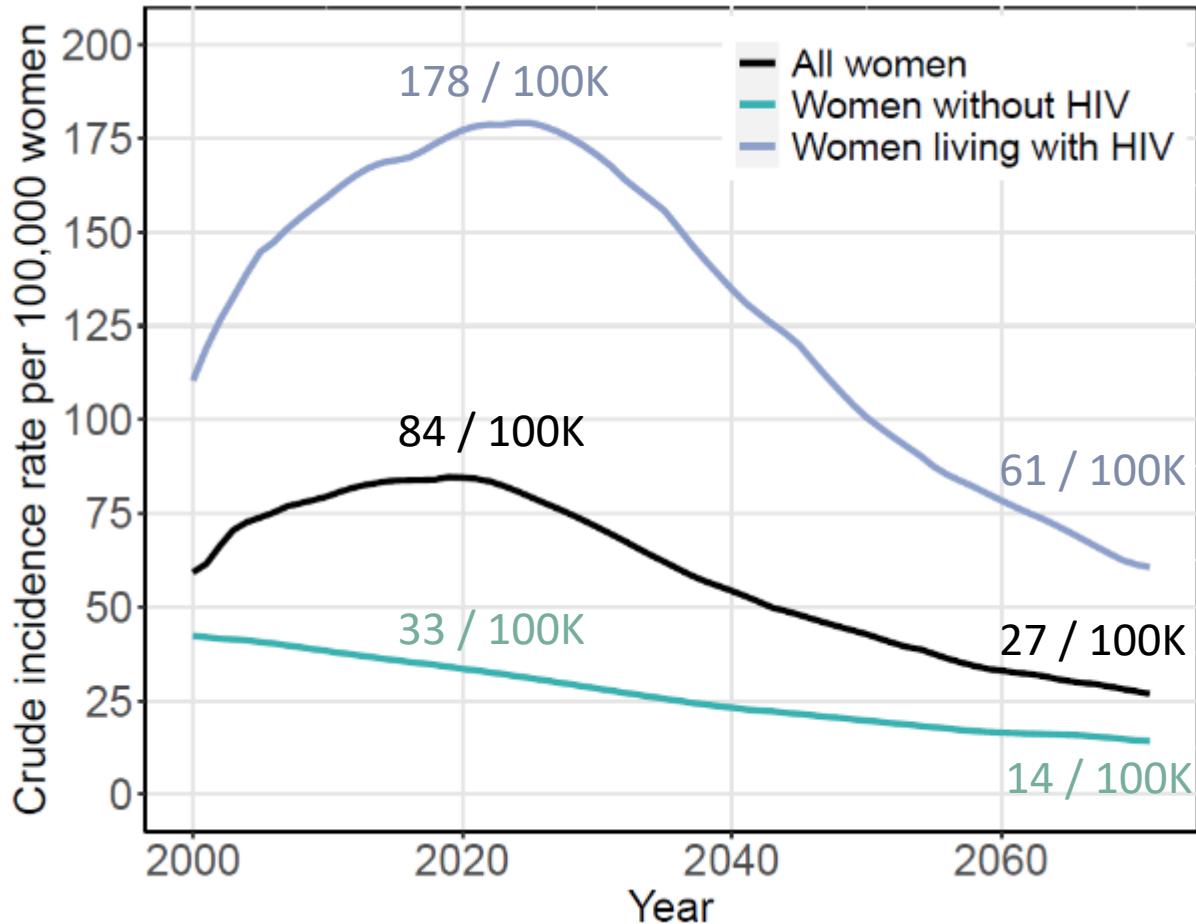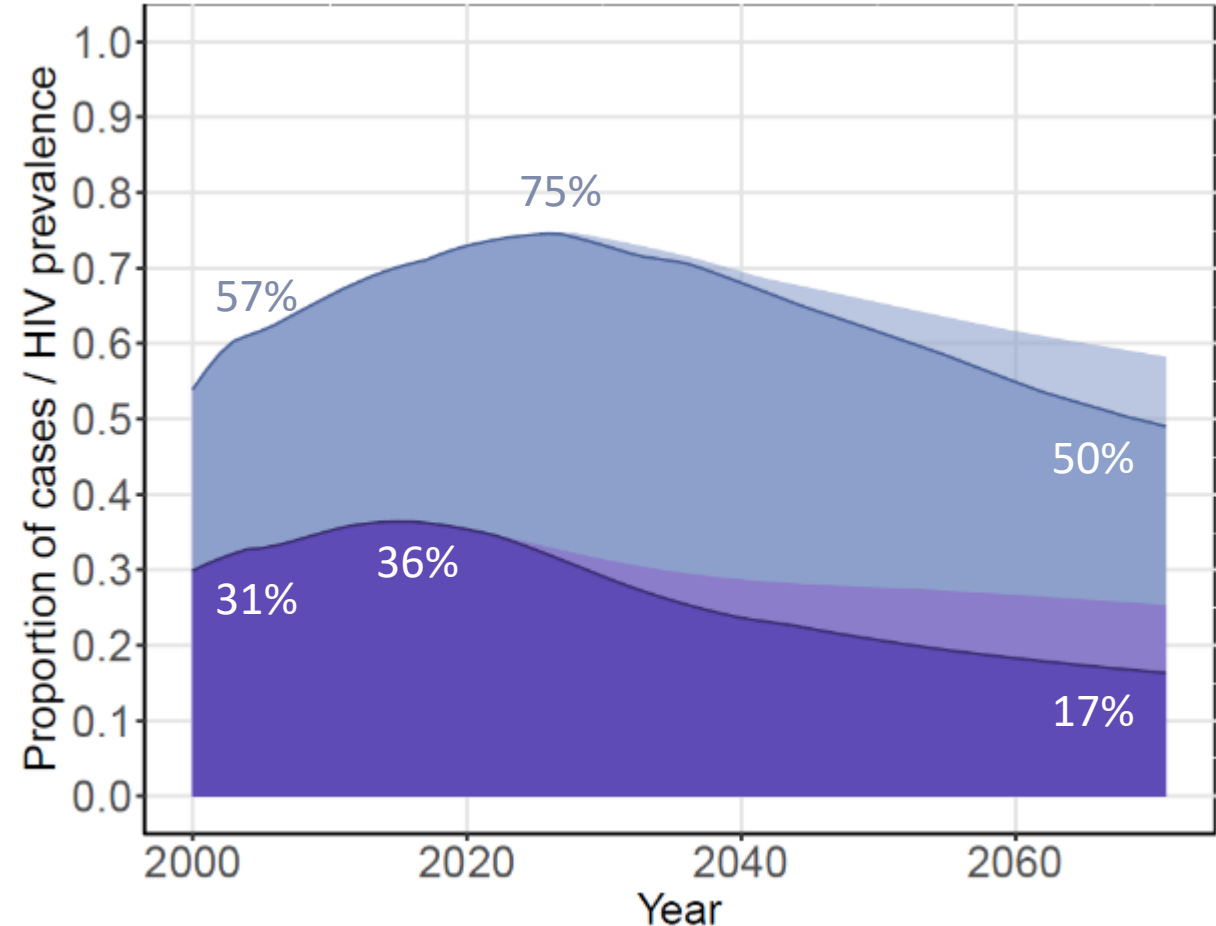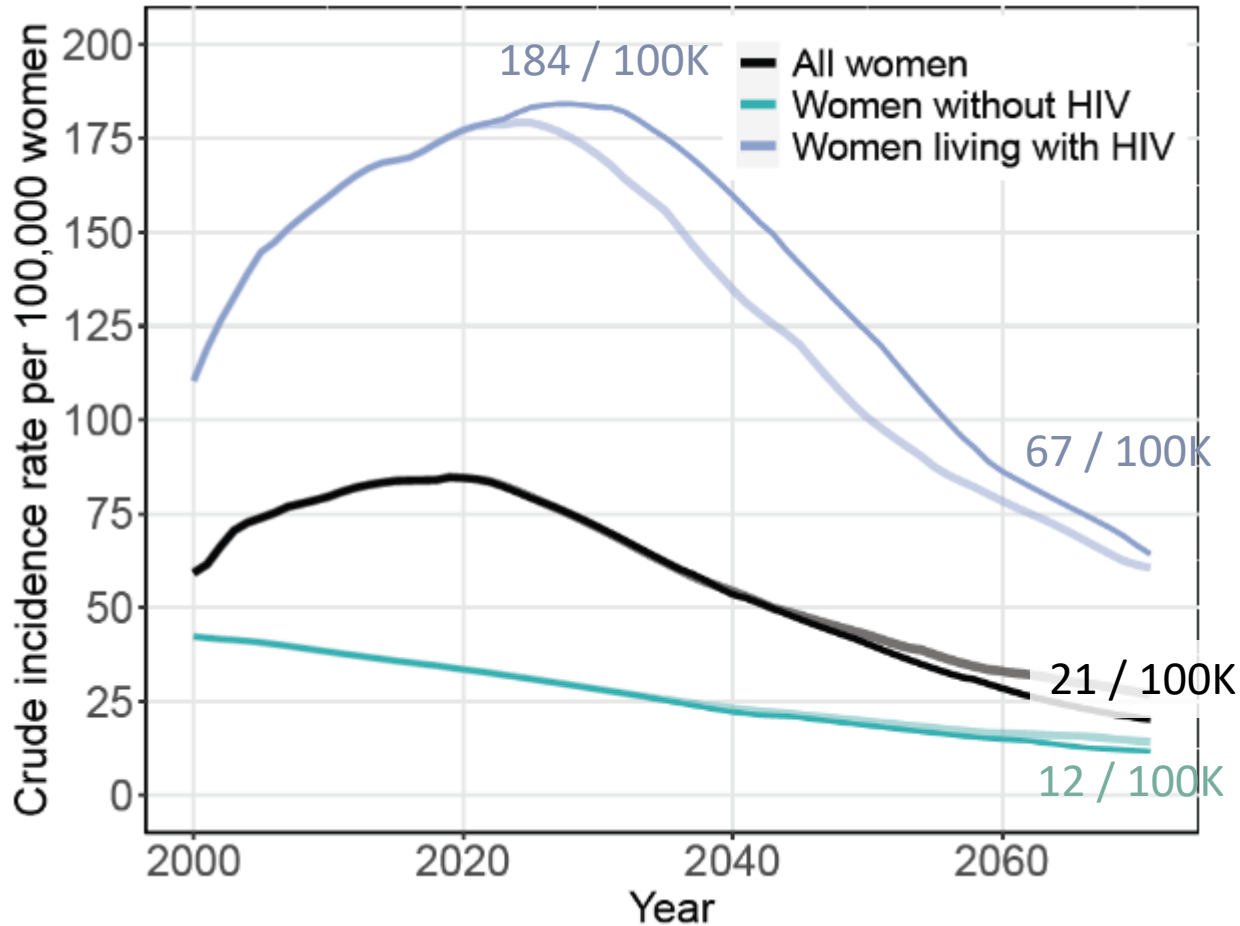## – Baseline scenario without ART scale-up –

Cancer incidence and distribution of cases
– Baseline scenario without ART scale-up –
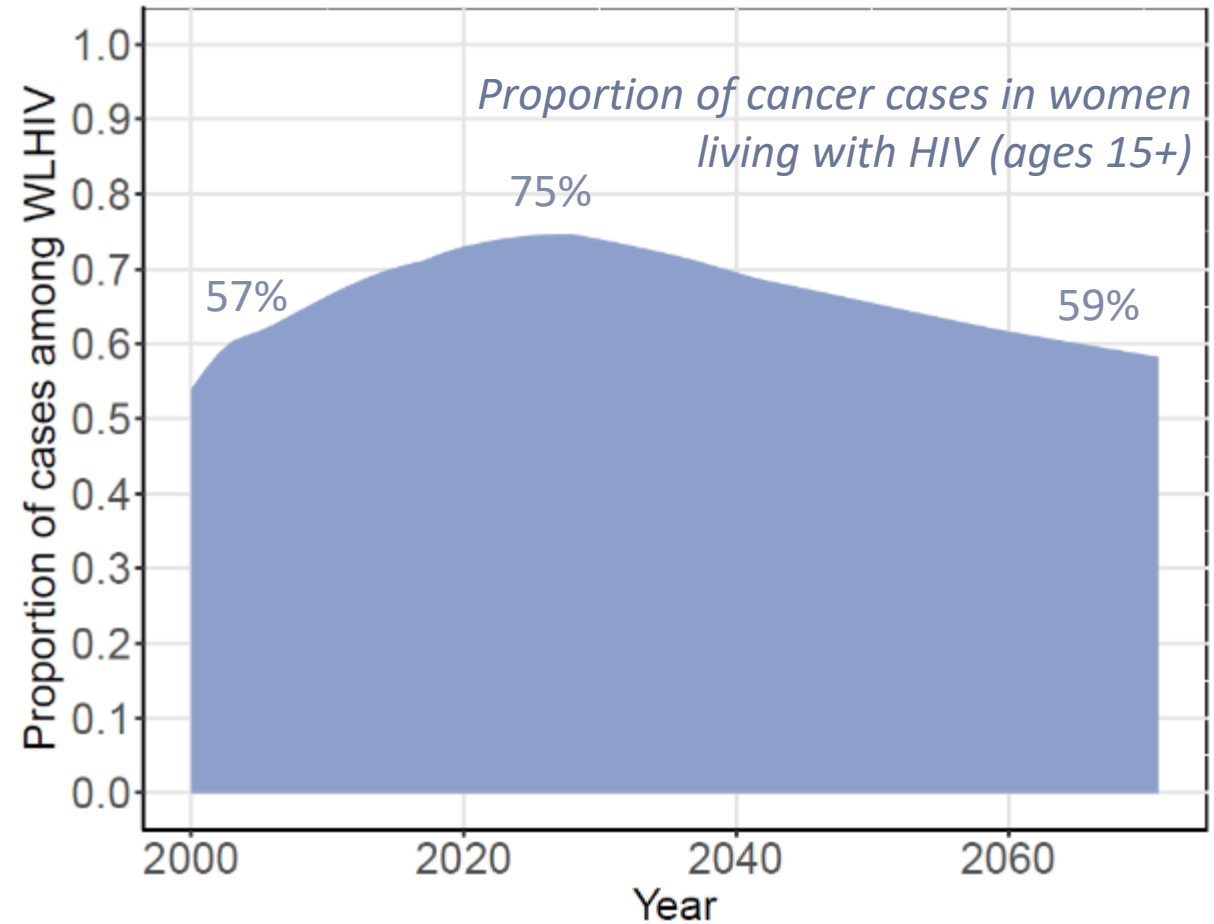
Cancer incidence and distribution of cases
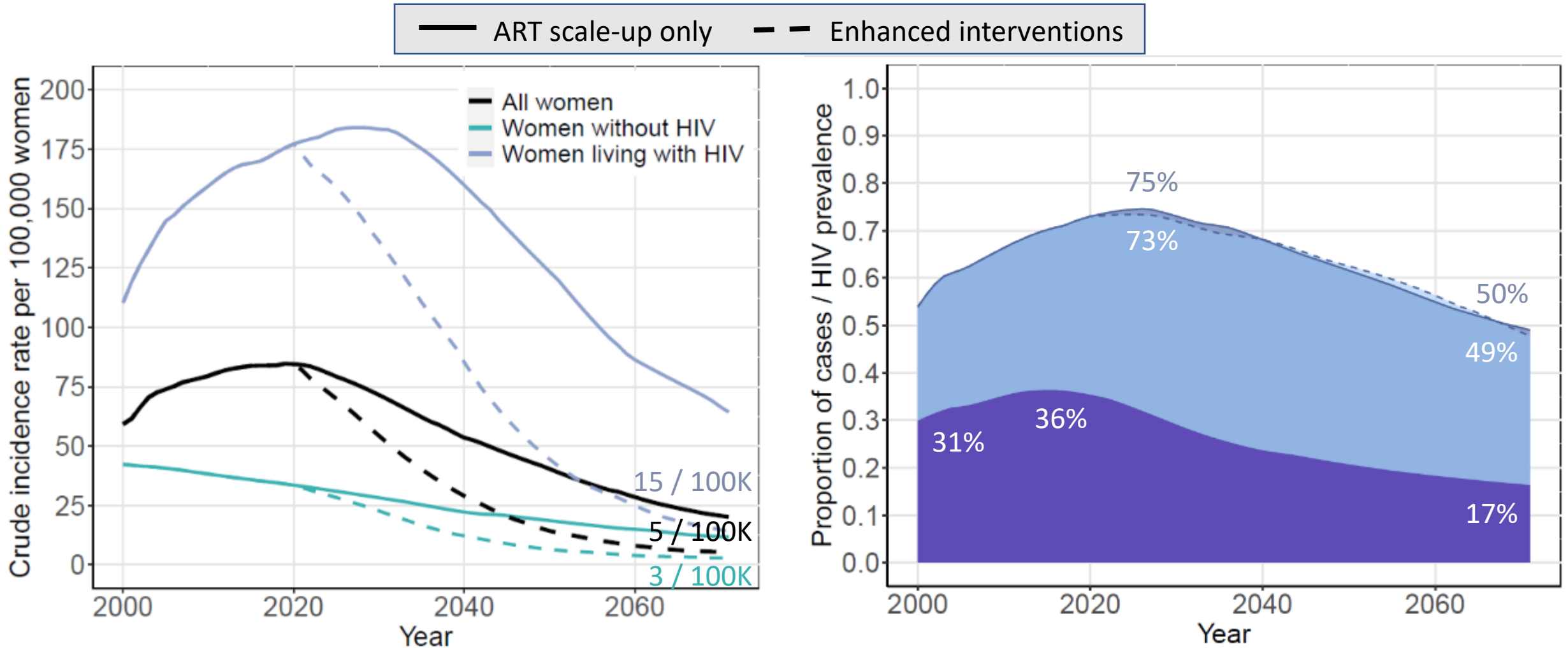## – Baseline scenario without ART scale-up –

Cancer incidence and distribution of cases
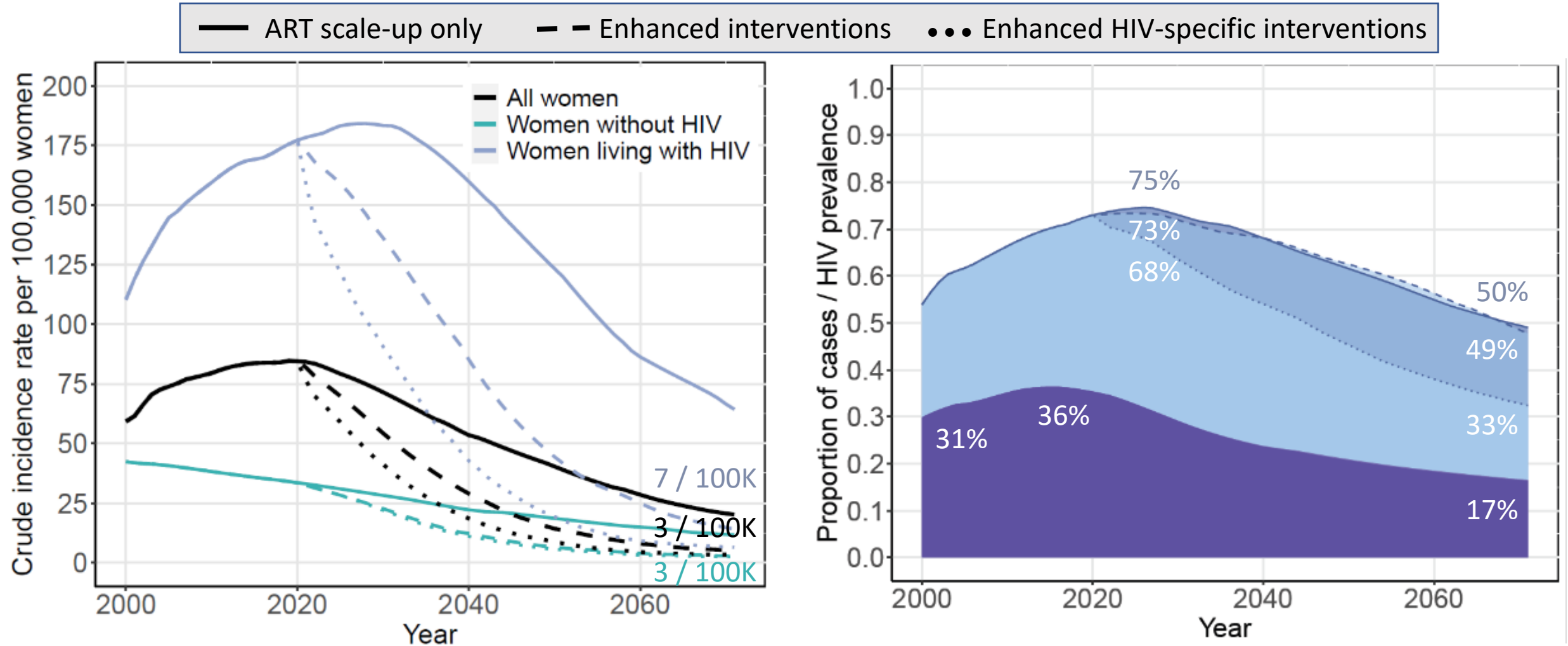## – Baseline scenario **with and** without ART scale-up–

Cancer incidence and distribution of cases
– Baseline and enhanced cervical cancer interventions with ART scale-up
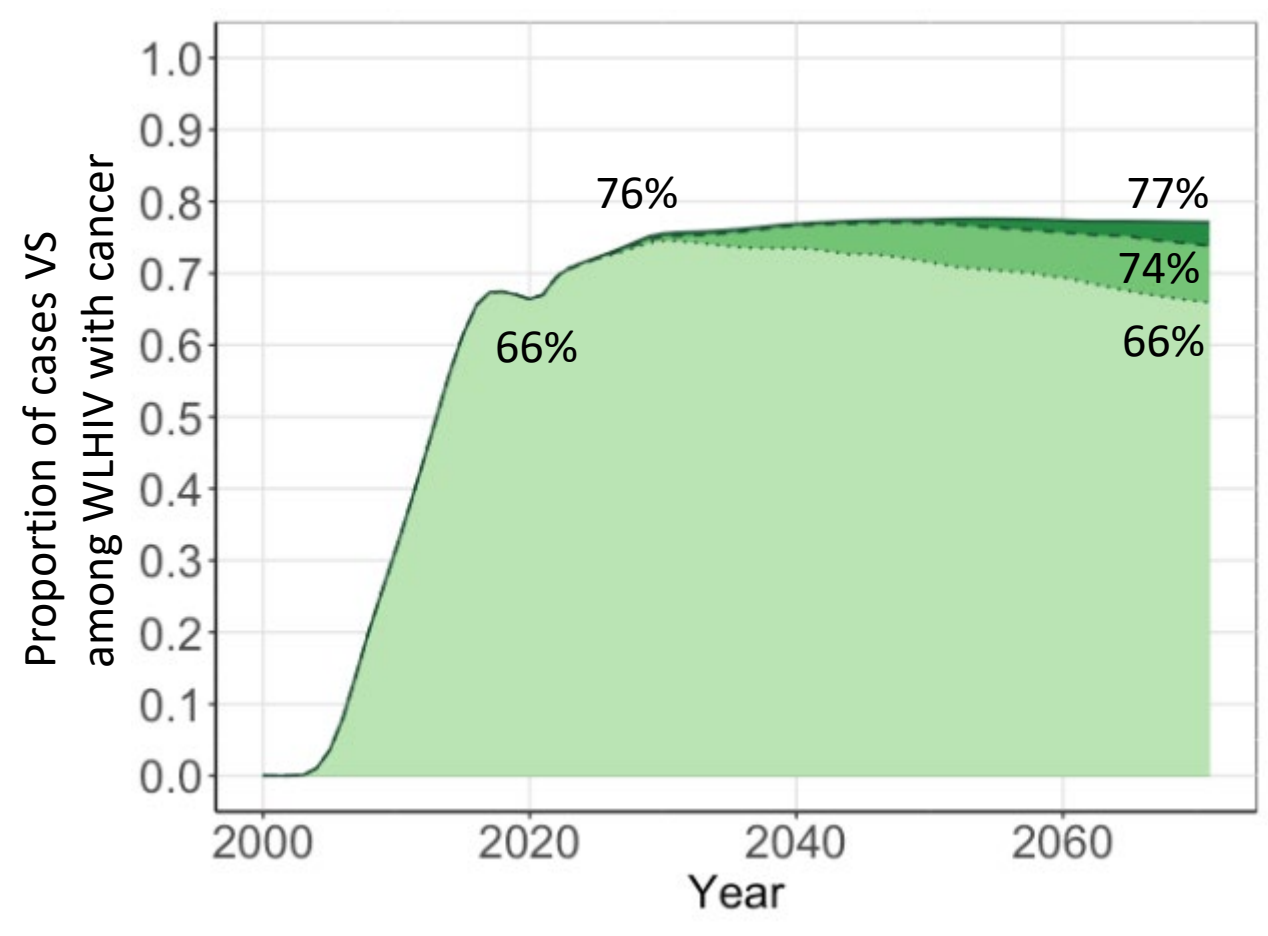
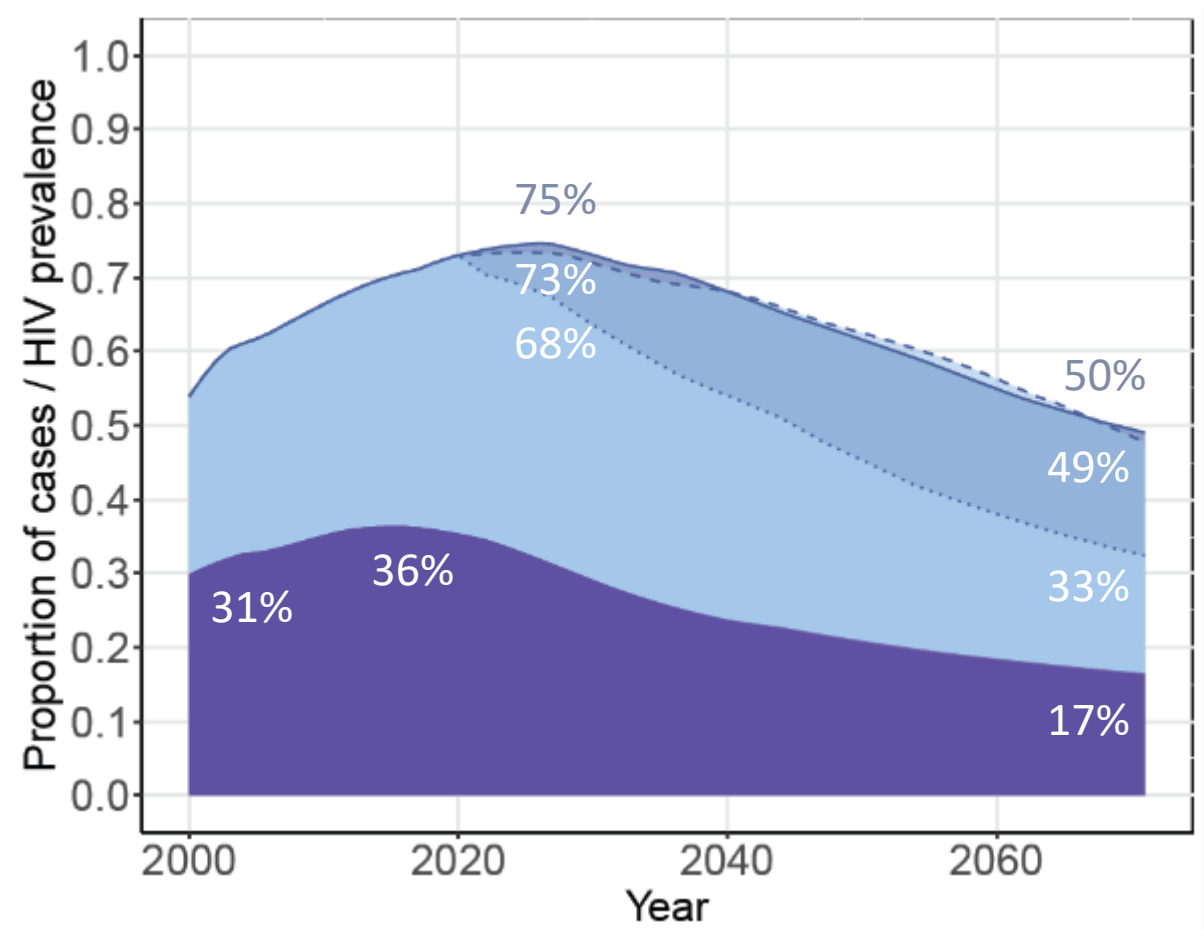# Cancer incidence and distribution of cases
– All intervention scenarios with ART scale-up –

Distribution of cases *among WLHIV*

Key limitations

- We assume no discontinuation of ART

- Our model does not account for future changes in behavior or other interventions (i.e., PrEP)

- There is considerable uncertainty related to model structure, parameterization, and calibration targets

Conclusions

- Scale-up of ART and adoption of single-visit screening and treatment are both expected to contribute to reductions in cervical cancer incidence

- Targeting enhanced cervical cancer prevention for women living with HIV will accelerate reductions in incidence and reduce disparities by HIV status
  - Our findings support integration of HIV and cervical cancer prevention.
  - Complementary efforts to reach women who are out of care will be valuable.

Acknowledgements

University of Washington

  Monisha Sharma

  Nick Tan

CISNET Cervical Cancer Modeling Group

Imperial College London

  Marie-Claude Boily

Harvard University

  Minttu Rönn

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