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

2023 IDM symposium
May 24, 2023
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
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)
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

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 & HPV transmission and natural history
- Demography
- Sexual behavior
- HIV interventions: ART, condoms, circumcision
- HPV/CC interventions: condoms, circumcision, screening, treatment, HPV vaccination

- Calibration
  Multidimensional fitting to historic demographic data and epidemiological outcomes related to HIV and HPV

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

- **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)

### Baseline
- **9vHPV: 57% school-aged**
- **Cytology: 48%**
- Baseline screening and treatment requires three visits with high loss to follow-up (36% of screen-positive women receive treatment)

### ART scale-up only
- **9vHPV: 57% school-aged**
- **Cytology: 48%**

### Enhanced cervical cancer interventions
- **9vHPV: 90% school-aged**
- **HPV DNA testing: to 90% by 2045**

### Enhanced cervical cancer interventions for women living with HIV
- **HIV-negative**
- **HIV-positive**
- Enhanced intervention scenarios assume a switch to single-visit screen-and-treat, reduced loss to follow-up (80-95% of screen-positive women receive treatment)
- **9vHPV: 90% school-aged**
- **50% catch-up (HIV+)**
- **HPV DNA testing: to 90% by 2045**
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 –

Proportion of cancer cases in women living with HIV (ages 15+)

HIV prevalence (ages 15+)

31% 36% 32% 25%
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

**Graph 1:**
- **Crude incidence rate per 100,000 women**
  - **ART scale-up only**
  - **Enhanced interventions**

**Graph 2:**
- **Proportion of cases / HIV prevalence**
  - **Year:** 2000 to 2060
  - **Values:**
    - 73%
    - 50%
    - 49%
    - 36%
    - 17%
    - 31%
Cancer incidence and distribution of cases
– All intervention scenarios with ART scale-up –

- ART scale-up only
- Enhanced interventions
- Enhanced HIV-specific interventions

Graphs showing the incidence rate and proportion of cases per 100,000 women over time.
Distribution of cases among WLHIV

Proportion of cases VS among WLHIV with cancer

- ART scale-up only
- Enhanced interventions
- Enhanced HIV-specific interventions

Proportion of cases / HIV prevalence

Proportion of cases VS among WLHIV with cancer

Year
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

Funding
NCI U01 CA199334

Partial support for this research came from a Eunice Kennedy Shriver National Institute of Child Health and Human Development research infrastructure grant, P2C HD042828, to the Center for Studies in Demography & Ecology at the University of Washington.