

Modelled impact of delays in elimination scale-up on cervical cancer deaths averted for 78-LMICs

K. Simms, A. Keane, K. Canfell

Introduction - elimination targets

- oIn August 2020, the World Health Assembly committed to a Strategy to eliminate cervical cancer as a public health problem by implementing "90-70-90" targets by 2030:
 - o 90% of girls fully vaccinated with the HPV vaccine by age 15.
 - o70% of women screened with a high-performance test by age 35, and again by 45 years.
 - o90% of women identified with precancer or cervical cancer receive adequate treatment and care.

If this Strategy is adopted, **62 million women's lives could be saved over the next** century.^{1,2}

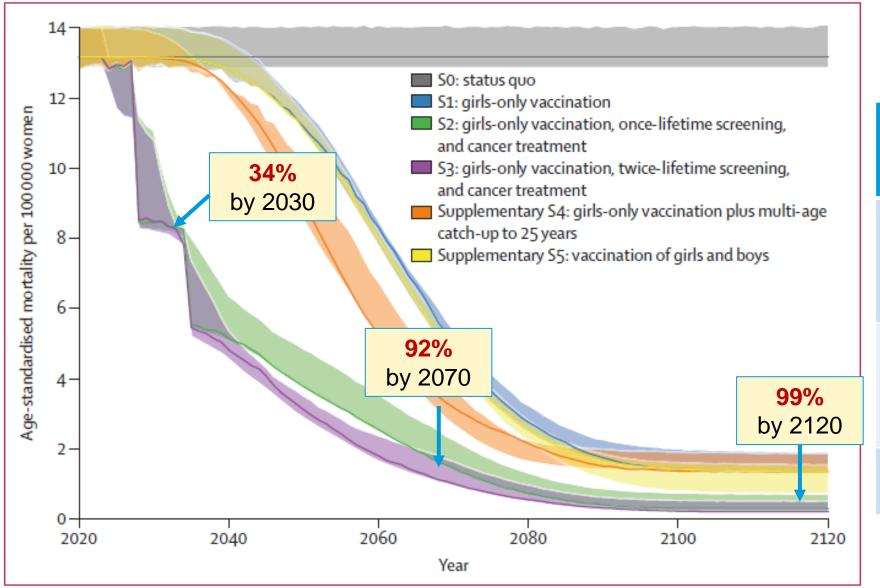
^{1.} Canfell/Kim/Brisson, Lancet 2020

^{2.} Brisson/Kim/Canfell, Lancet 2020

^{3.} Bruni, Lancet GH, 2016.

^{4.} Simms, Lancet Onc, 2019.

Impact of elimination strategies on cervical cancer mortality



Intervention	Timeframe when intervention takes effect
Vaccination	30-40 years later, Steady-state impacts take many decades.
Screening	Impacts seen within a few years; most effects observed 10+ years.
Cancer treatment	Impacts seen within 10 years.

Introduction - elimination targets

- oIn LMICs, coverage is low
 - Vaccination coverage in LMICs
 substantially lower than HICs
 - <10% of women in less-developed regions are screened,² and many with lower sensitivity tests such as VIA.
 - •Cancer treatment access is also minimal in LMIC, estimated <30% of women in LMIC have access to adequate treatment and care.³

Countries with HPV vaccine in the national immunization programme (Nov. 2019)

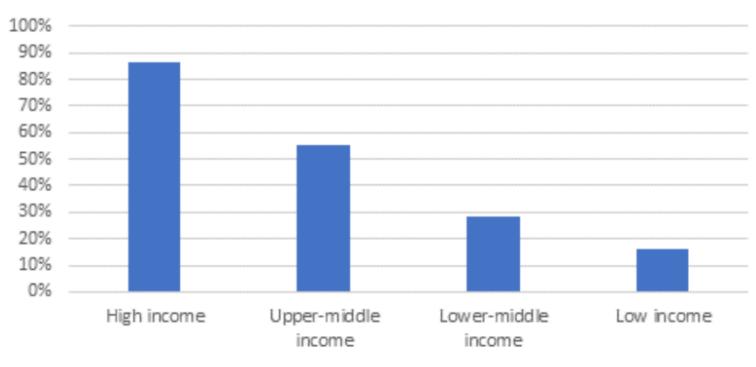


Figure taken from Draft Strategy for cervical cancer elimination https://www.who.int/docs/default-source/cerv-cancer-elimn-strategy-16dec-12pm.pdf?sfvrsn=3cd24074_8

^{1.} WHO, Draft strategy for Cervical Cancer Elimination 2019

^{2.} Simms, Lancet Onc, 2019.

^{3.} Canfell, Kim, Brisson et.al Lancet 2020

Introduction - impact of COVID-19

COVID has already disrupted existing services, due to staff redistribution to COVID-related programmes, patient safety concerns, lockdowns preventing movement and access

HPV vaccination - vaccine shipments disrupted due to impact on airplane industry, school-based delivery systems impacted by school closures, and some LMICs have delayed introduction;¹

HPV vaccine supply shortages also remain until 2025.

- Screening programs universally affected, with reductions in staffing and patient presentation.²
- Cancer treatment services affected, with postponed or cancelled surgeries and other treatments for all conditions including gynaecological cancers.

Cancer diagnosis delayed to do delayed presentation with potential stage-shifting.

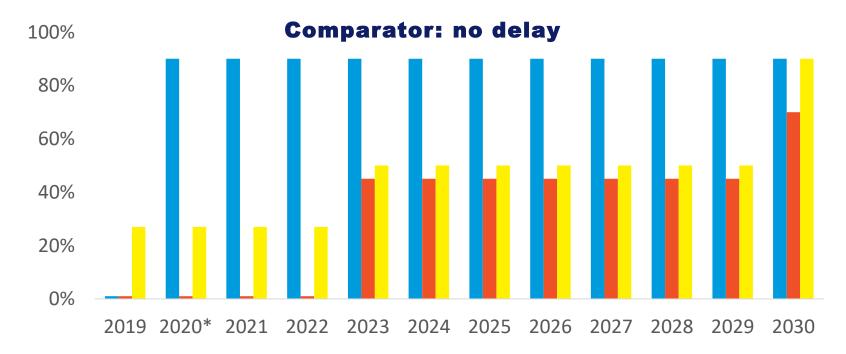
^{1.} UNICEF HPV Supple and demand Update, October 2020

^{2.} DeSanjose, HPVWorld 2020.

Aims

We aimed to evaluate the additional deaths that would occur due to the combined effect of

- 1. Delayed HPV vaccination scale-up by 1-year (2020 -> 2021)
- 2. Delayed cervical cancer screening + precancer treatment scale-up by 1-year (2023 -> 2024)
- 3. Delayed cancer treatment scale-up by 1-year (2023 -> 2024)

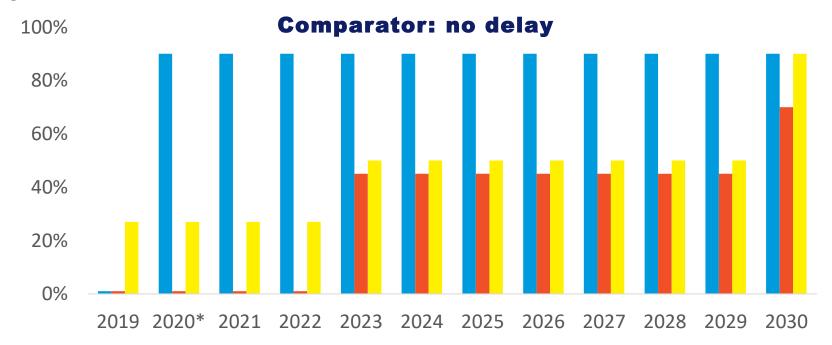


^{*} Females aged up to 15 years are vaccinated in the first scale-up year

Aims

We aimed to evaluate the additional deaths that would occur due to the combined effect of

- Delayed HPV vaccination scale-up by 1-year
 - By counting deaths over the lifetime of females who turn 16 in 2021 (i.e no longer eligible).
- 2. Delayed cervical cancer screening + precancer treatment scale-up by 1-year
 - By counting deaths over the lifetime of women who turn 46 in 2024 (i.e no longer eligible).
- Delayed cancer treatment scale-up by 1-year
 - By counting deaths of women with cervical cancer in 2023 without survival benefit of scale-up.



^{*} Females aged up to 15 years are vaccinated in the first scale-up year

Aims (part 2)

- Exploratory analysis of 'worse than status-quo'
 - Impacts of COVID on the status-quo delayed symptomatic presentation of cervical cancer in 2020 (1 year delay) as well as a 2 year delay.

Policy1-Cervix model platform

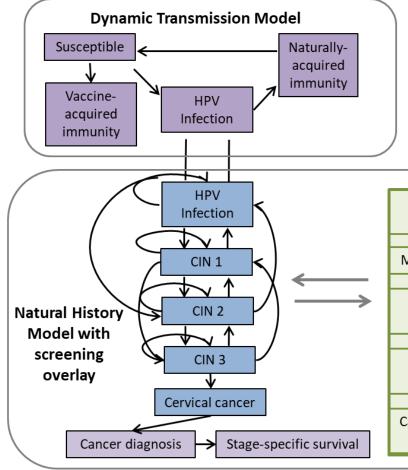
Policy1-Cervix is a dynamic model of sexual behaviour, HPV transmission, cervical screening and vaccination.

It models HPV transmission, typespecific natural history, cervical screening, diagnosis and treatment

Platform extensively validated against data from a range of countries¹⁻²⁴

- 1. Canfell/ Kim/ Brisson et.al. Lancet 2020
- 2. Brisson/Kim/Canfell et.al Lancet 2020
- 3. Burger/Smith et.al. Lancet PH 2020
- 4. Simms/Hanley/Smith et.al. Lancet PH 2020
 - Hall et.al. PlosOne 2020
- 6 uill et.al. JID 2020
 - mith et al, MJA 2016

Smith et al, BMC HSR 2016



Test probability matrix to define screening and diagnostic outcomes based on underlying health state

Management according to screening history and test outcome.

Colposcopy, biopsy and treatment module incorporating diagnostic test accuracy and treatment efficacy

Post-treatment natural history module (incorporating systematic review on probability of recurrence)

Cancer diagnosis through symptomatic presentation or screendetection, stage- and country-specific survival

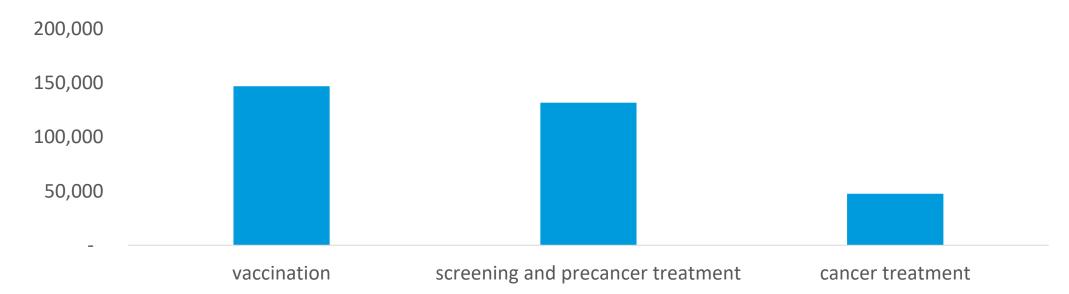
- 9. Smith et al, BMC HSR 2016
- 10. Simms et al Lancet Onc 2019
- 11. Lew et al, PLoS One 2016
- 12. Simms et al, Int J Cancer 2016
- 13. Simms et al, Lancet PH 2016
- 14. Simms et al, PLoS One 2017
- 15. Lew/Simms et al, Lancet PH 2017
- 16. Velentzis et al, Int J Cancer 2017

- 17. Hall et al, PLoS One 2018
- 18. Hall et al, Lancet PH 2018
- 19. Smith and Canfell, BMC RN 2014
- 20. Kitchener et al, HTA UK 2014
- 21. Smith and Canfell, PLoS One 2014
- 22. Walker et al, Stat Med 2012
- 23. Legood et al, BMJ, 2012
- 24. Lew et al, BMC HSR, 2012



Results: Longer-term impacts of delays in elimination targets

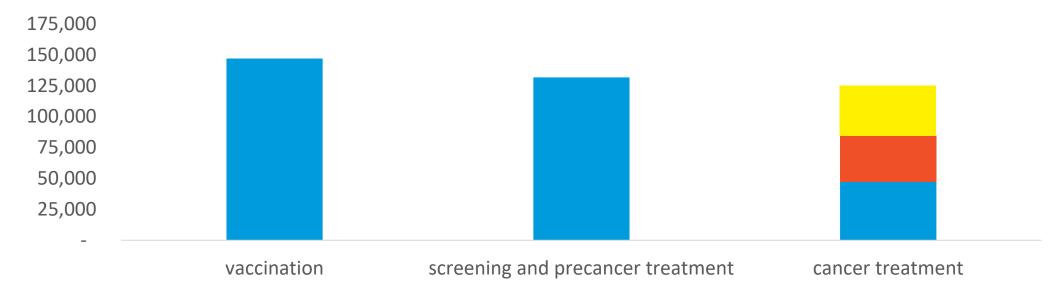
Intervention	Additional deaths occurring in 78 LMIC over the long term for each year scale-up is delayed	
Vaccination*	146,800	
Screening and		
precancer treatment	131,600	
Cancer treatment	47,600	
Total	326,000	



^{*}Assuming that these cohorts receive cervical screening twice a lifetime at 70% coverage and that 90% of women diagnosed with cervical cancer would receive adequate treatment and care

Results: Longer-term impacts of delays in elimination targets

Intervention	Additional deaths occurring in 78 LMIC over the long term for each year scale-up is delayed	Supplementary: Additional deaths if symptomatic presentation delayed 1 year*	Additional deaths if symptomatic presentation delayed 2 years*
Vaccination*	146,800		
Screening and			
precancer treatment	131,600		
Cancer treatment	47,600	+30,900	+30,900 +46,500 (+77,400)
Total	326,000	356,000	403,000



^{*}Assuming that these cohorts receive cervical screening twice a lifetime at 70% coverage and that 90% of women diagnosed with cervical cancer would receive adequate treatment and care

Conclusion

•For each year there are delays in scaling-up the three elimination intervention targets is predicted to result in *326,000 additional deaths* over the lifetime of affected cohorts, (assuming no catch-up for missed cohorts)

This represents one-quarter of total global deaths directly due to COVID-19 for 2020 (1.29 million)

- o146,800 additional from HPV vaccination
- 131,600 additional from screening and precancer treatment
- o47,600 additional from Cancer treatment

If the current status-quo worsens, and women delay presentation with symptoms, then we could observe

- An additional 30,900 deaths with 1 year delay
- An additional 77,400 deaths across a 2-year delay



Conclusion

- Vaccination programs could offer catch-up to older females to ensure that all girls who would have been 9-15 years old in 2020 will eventually receive vaccination
 We anticipate much of the damage would be offset by catch-up.
- Cervical cancer screening programs could similarly offer catch-up to older women
 We anticipate much of the damage would be offset by catch-up.
- Cancer treatment service delays are likely to have irreversible impacts
 - The survival benefit from cervical cancer treatment services comes from immediate action for newly diagnosed cases, and are unlikely to be mitigated.

Extending recommended ages for screening and vaccination could mitigate damage from delays in these interventions;

Ensuring women with symptoms can be safely investigated, and prioritizing access to cancer treatment services to prevent thousands of additional deaths