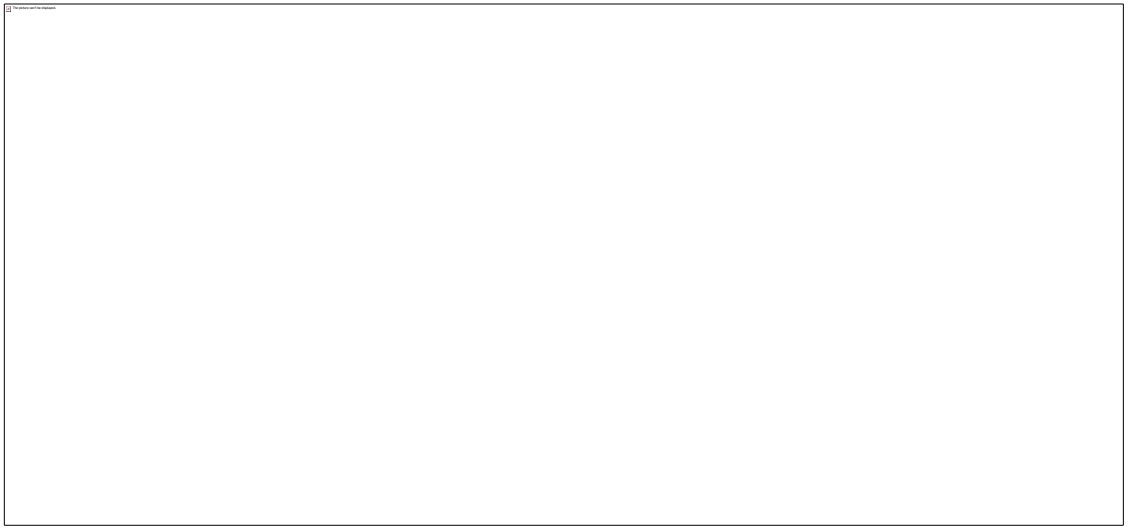
The disproportionate impact of cervical cancer in LMICs



GLOBOCAN 2020, Map production: IARC (http://gco.iarc.fr/today)

- The burden of disease is concentrated in LMICs, with over 90% of cervical cancer deaths occurring in these countries.
- In 2020, ~600,000 new cervical cancer cases and 342,000 deaths[1]

1. WHO fact sheet, https://www.who.int/news-room/fact-sheets/detail/cervical-cancer

Cervical cancer elimination through vaccinations, screening and treatment

of girls aged 9 - 14 years are **vaccinated for HPV**

Of women are **screened (once at 35 years and again at 45),** with a high performance test.

of positively screened cases are **treated / cancer managed**

World Health Organization, “Global Strategy to Accelerate the Elimination of Cervical Cancer as a Public Health Problem.”

Visual Inspection with acetic acid - VIA

Image source: IARC*Atlas of visual inspection of the cervix with acetic acid for screening, triage, and assessment for treatment* https://screening.iarc.fr/atlasviadetail.php?Index=26&e=

AI based cervical cancer screening using Automated Visual Evaluation (AVE)

- **Smartphone based app** that applies machine learning to detect precancerous lesions
- **Preferable relative to existing screening** methods such as pap smears (which require lab infrastructure), or VIA which has varying ranges of accuracy, when interpretation is performed by a healthcare provider.
- GHLabs has developed an AVE app, currently being tested across 6 countries.

Source: Hu, Liming, et al https://pubmed.ncbi.nlm.nih.gov/30629194/

Objective: To leverage HPVsim to understand the impact of AI based screening interventions such as AVE

By evaluating the impact of:

- Sensitivity & Specificity of AVE,
- Screening probability and
- Treatment probability

On health outcomes (Age standardized cervical cancer incidence (ASIR))

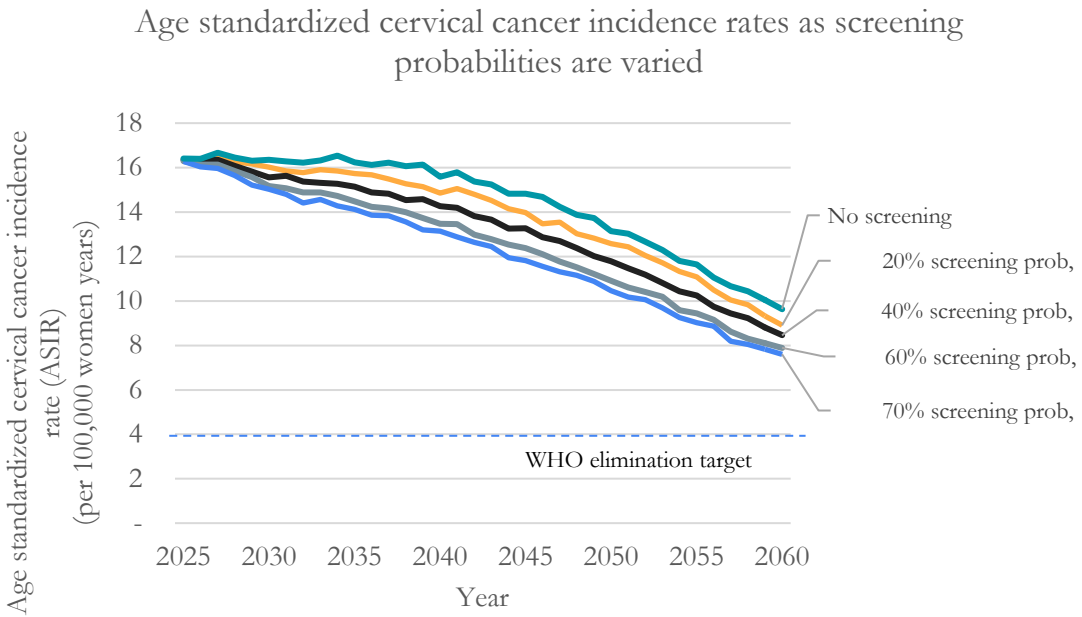
Methodology (part A)

Sensitivity analysis on key variables

a) Screening probability – 0%, 20%, 40%, 60%, **70%**
b) Treatment probability – 20%, 40%, 60%, 80%, **90%**
c) AVE sensitivity / specificity: 62%/86%, 82%/86%, 90%/83%

Note:
- Default vaccination campaign (90% coverage assumed) throughout analysis
- All results are based on HPVsim version: Mar'23, which modeled Nigeria

Sensitivity analysis results – Screening probability



Assumptions:

- 90% of 9 – 14-year-old girls vaccinated

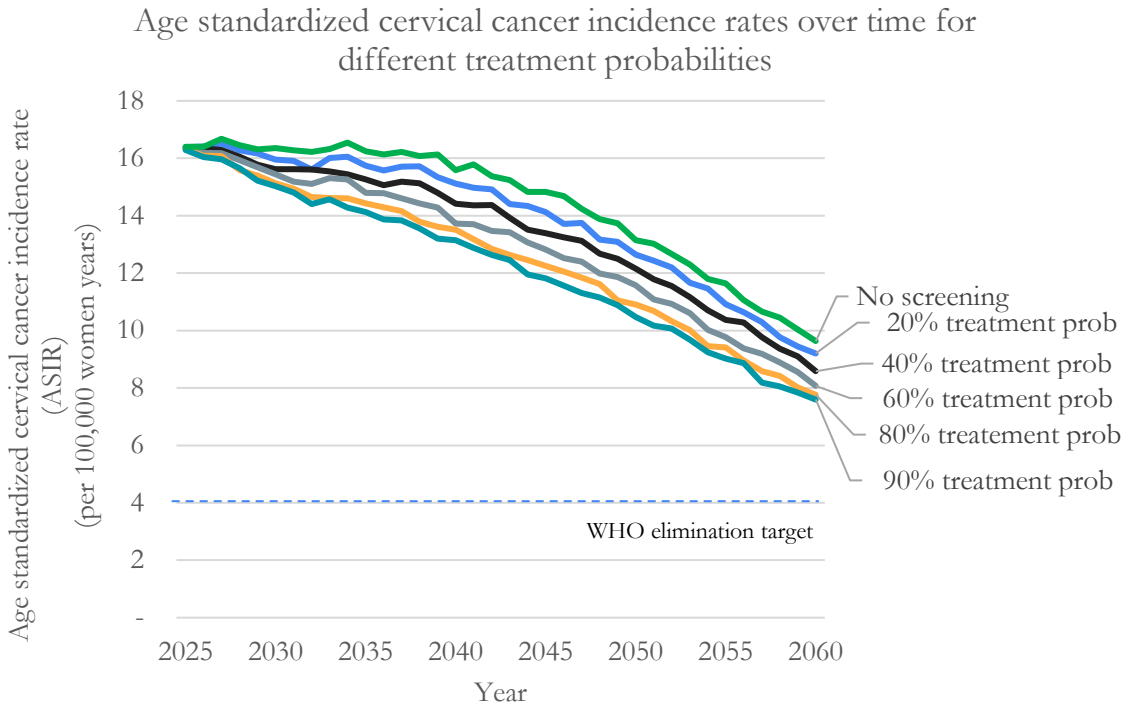
90% of positively screened cases are treated

AVE sensitivity / specificity :82%/86%

Key insights:

- Increasing the proportion of vaccinated women, decreases ASIR.
- In 2060,the difference between screening 70% of women vs not screening any women is found to reduce ASIR by 12%.
- In the short term, screening can play a key role in reducing ASIR while vaccination effects take time to be realized.

Sensitivity analysis results – Treatment probability



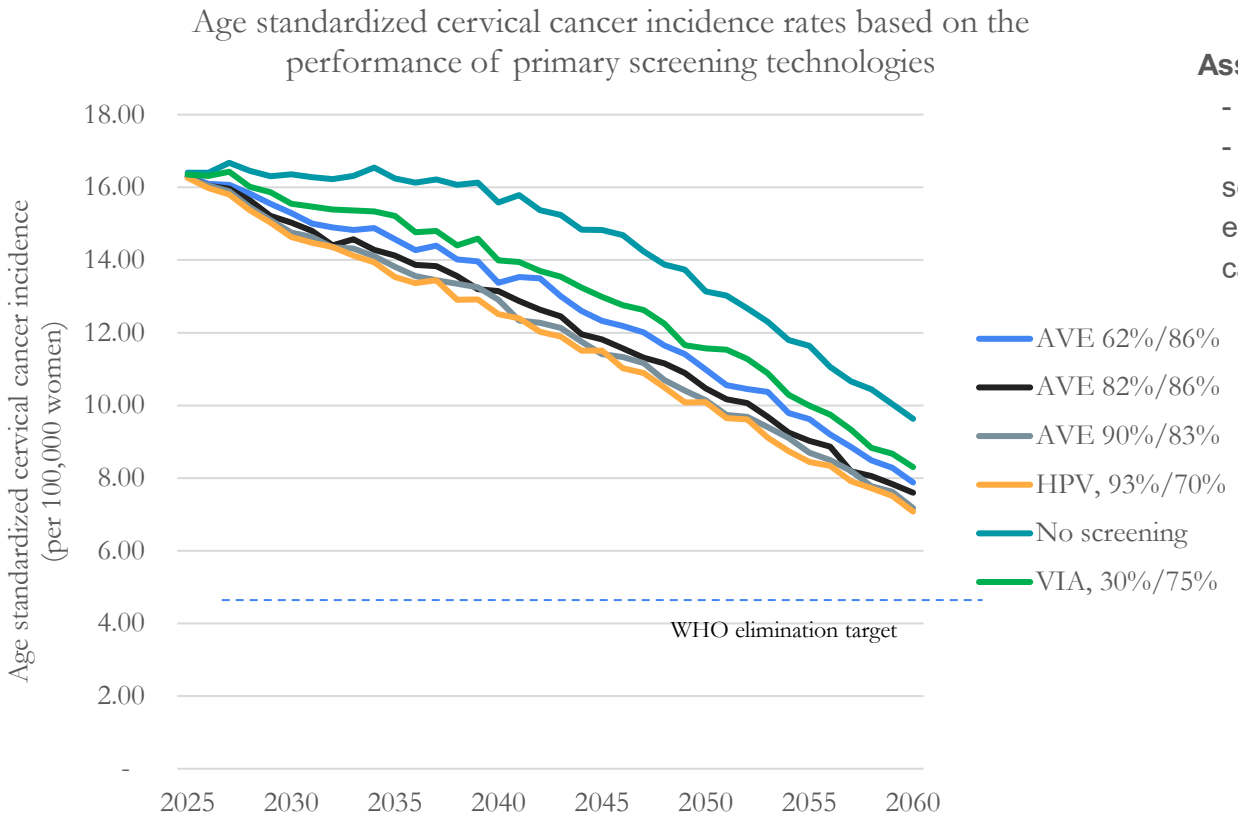
Assumptions:

- 90% of 9 – 14-year-old girls vaccinated
- 70%. Of women between the ages of 35 – 45 screened, using AVE (VIA + AVE) approx. every 5 years
- AVE sensitivity / specificity :82%/86%

Key insights:

- Screening and treatment go hand in hand, without treatment, the effects of screening are negated
- As treatment probability increases, ASIR decreases
- In the short term, while vaccinations have not taken full effect, the impact of screening and treatment are greater than the impact of vaccinations.

Sensitivity analysis results – AVE sensitivity and specificity



Assumptions:

- 90% of 9 – 14-year-old girls vaccinated
- 70%. of women between the ages of 35 – 45 screened, using AVE (VIA + AVE) approx. every 5 years and 90% of positively screened cases are treated

Key insights:

- AVE at high levels of sensitivity and specificity can have similar impacts to HPV DNA tests

Methodology (part B)

Data-set creation

HPVsim used to generate incidence rate predictions based on unique combinations of:

a) Screening probability
b) Treatment probability
c) AVE sensitivity
d) AVE specificity

-125 data points generated for a Nigeria like country

Regression & results interpretation

Exclusion of certain fields, formatting variable outputs

Dependent variable: Age Standardized cervical cancer incidence rates in 2040 and 2060

Independent variables: screening probability, treatment probability, sensitivity and specificity of AVE

Note: Default vaccination campaign (90% coverage assumed) throughout analysis

Results (Short term outlook (2040))

Regression Statistics	
R Square	0.83
Adjusted R Square	0.82
Standard Error	0.32
Observations	125

	Coefficients	*Standard Error*	*P-value*
Intercept	16.26	2.14	0.00
Screen prob	-1.66	0.14	0.00
Treatment prob	-1.71	0.09	0.00
Sensitivity	-0.86	0.31	0.00
Specificity	0.87	2.37	0.71

Dependent variable: ASIR in 2040

Significant independent variables: screening probability, treatment probability and sensitivity

Assuming a vaccination campaign with 90% coverage for girls 9-14

1% increase in screening probability → 0.017 reduction in ASIR

1% increase in treatment probability → 0.017 reduction in ASIR

1% increase in sensitivity → 0.009 reduction in ASIR

Results (Long term outlook (2060))

Regression Statistics	
R Square	0.84
Adjusted R Square	0.83
Standard Error	0.26
Observations	125

	Coefficients	*Standard Error*	*P-value*
Intercept	9.83	1.73	0.00
screen prob	-1.32	0.11	0.00
treatment prob	-1.45	0.07	0.00
sensitivity	-0.73	0.25	0.00
specificity	1.09	1.92	0.57

Key takeaways:

- Screening probability, treatment probability and sensitivity are significant, specificity is not
- Greater influence of screening variables in the short term vs in the long term, as a result of vaccine effects being realized over longer periods.

Limitations / Considerations

1. Our results assume a vaccination campaign with 90% coverage. If screening was modeled as the sole strategy we expect greater effects / coefficients than shown in the results
2. We assume that the only screening mechanism was AVE (as the primary method).
3. Relative influence of each variable (screening probability, treatment probability, and AVE sensitivity or specificity) must be interpreted with an understanding of the costs. Effectively how much does it cost to improve screening probability by 1% vs AVE sensitivity by 1%?
4. Preliminary analysis – expectations of continuous refinement and understanding of the model and model outputs

Discussion

HPVsim was used as a **decision making tool to support analysis** on public health intervention strategies for cervical cancer :

1. Providing the ability to determine the significance and impact of **screening probability, treatment probability and sensitivity and specificity of AVE** in influencing ASIR
2. Highlighted the importance and urgency for **screening in the short term**, which has implications for strategy with respect to the tradeoff between device accuracy and speed of the device release.
3. The value in **“screen and treat” approaches**: Loss to follow up in low resource settings can be high, negating the effect of screening. Screening probability and treatment probability have the greatest influence on ASIR and cancer deaths in the short term - therefore efforts should be made to maximize both.

Acknowledgements

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