The disproportionate impact of cervical cancer in LMICs

- 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

GLOBCAN 2020, Map production: IARC (http://gco.iarc.fr/today)
Cervical cancer elimination through vaccinations, screening and treatment

90% of girls aged 9 - 14 years are vaccinated for HPV

70% of women are screened (once at 35 years and again at 45), with a high performance test.

90% 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

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.
**Objective:** To leverage HPVsimg 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

Age standardized cervical cancer incidence rates as screening probabilities are varied

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

Age standardized cervical cancer incidence rates based on the performance of primary screening technologies
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

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### Coefficients

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<td>Specificity</td>
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### Dependent variable: ASIR in 2040

### Significant independent variables:
- screening probability
- treatment probability
- 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))

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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.
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