Age at last screening and remaining lifetime risk of cervical cancer: a modelling study

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Conflicts of Interest

- Talía Malagón, Shalini Kulasingam: None to declare.
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Good reasons why we might want to screen older women

- Screening >65y can prevent cancers.
- Cervical cancer mortality rates increase with age.
- Ageing populations in many countries will lead to more cancers being diagnosed in women ≥65 years old.

However, benefits of screening at older ages are likely overvalued and harms undervalued.

Data from Statistics Canada: CANSIM Table 13-10-0392-01
Why use a decision model?

- Time lag between moment of screening and prevention of cervical cancer ~5-20 years
- Need to extrapolate results from trials/observational data to different ages, screening intervals, & algorithms
- Decision models used to assess benefits, harms, & cost-effectiveness of screening recommendations in USA¹, UK², and Australia³

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2. Kim JAMA 2018;320(7):706-714

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Figure data from: Peto Br J Cancer 2004;91(5); Trent Cancer Registry 2012; Baay Int J Cancer 2004;108
Methods: Model description

- State transition (Markov) model of cervical cancer natural history & screening
- Reproduces Canadian cervical cancer epidemiology, CIN prevalence, HPV prevalence\(^1\text{-}^3\)
- Cohorts of women from ages 10-100
- **Unvaccinated cohorts**

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Methods - Measuring screening outcomes

Measuring screening harms and benefits:

- **Cost-effectiveness (not evaluated)**
  - Incremental cost/life-year gained
  - Incremental cost/QALY
  - Incremental cost/cancer prevented

- **Absolute cancer risk/incidence**
  - Useful for risk-based management & target thresholds
  - E.g. <4/100,000 women-years for elimination target

- **Balance of benefits & harms**
  - Life years gained/colposcopy
  - Cancers prevented/screening test
  - Net benefit (QALY)

Net QALY benefit of screening:

- \((\text{QALY gained from prevented cancers & deaths}) - (\text{QALY lost from screening tests & procedures})\)

QALY = Quality-Adjusted Life Year:

<table>
<thead>
<tr>
<th>Event/health state</th>
<th>Value</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perfect health</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Screening, negative result</td>
<td>0.9967</td>
<td>(1)</td>
</tr>
<tr>
<td>Screening, abnormal cytology result</td>
<td>0.96</td>
<td>(2)</td>
</tr>
<tr>
<td>Screening, HPV positive result</td>
<td>0.94</td>
<td>(3)</td>
</tr>
<tr>
<td>CIN1 diagnosis+management</td>
<td>0.89</td>
<td>(2)</td>
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<tr>
<td>CIN2 diagnosis+management</td>
<td>0.89</td>
<td>(2)</td>
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<tr>
<td>CIN3 diagnosis+management</td>
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<td>(2)</td>
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<tr>
<td>Cervical cancer</td>
<td>0.67</td>
<td>(4)</td>
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<tr>
<td>Cancer remission</td>
<td>0.82</td>
<td>(4)</td>
</tr>
<tr>
<td>Dead</td>
<td>0</td>
<td>-</td>
</tr>
</tbody>
</table>

(1) Simonella 2014; (2) Insinga 2007; (3) Howard 2008; (4) Kuppermann 2010
Methods – Age equitability issues

- If screening benefit is measured in terms of **cancers prevented** or **cancer risk**, then all cancers are considered equal regardless of age.

- If screening benefit is measured in terms of **life years** and **quality-adjusted life years** (QALY), more value is placed on preventing cancer at younger ages.
  - Largest benefit from cancer screening is prevention of early mortality.

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1. Statistics Canada. Life tables, Canada, provinces and territories, catalogue no. 84-537-X.
Age to end screening – absolute risks

Cervical cancer incidence rates (/100,000) predicted if women stop screening at different ages with cytology-based screening:

5-year predicted risks of developing cervical cancer:


Copyrighted image. See: doi: 10.1016/S1470-2045(18)30536-9
Lifetime balance of benefits & harms of cytology screening program 20-69y

Copyrighted image. See: doi: 10.1158/1055-9965.EPI-20-0190
Ages where benefits outweigh harms - HPV testing

- Screening a **35y woman** who never screened before:
  - **843** prevented cancers/100,000 screenings
  - **24** average life years gained/prevented cancer death

- Screening a **65y woman** who never screened before:
  - **286** prevented cancers/100,000 screenings
  - **7** average life years gained/prevented cancer death

- Screening a **70y woman** who never screened before:
  - **86** prevented cancers/100,000 screenings
  - **1** quality-adjusted life year gained/prevented cancer (mostly prevented morbidity, not mortality)

Copyrighted image. See: doi: 10.1158/1055-9965.EPI-20-0190
Comparison with other modeling studies – age to end screening

- **Kim et al. JAMA 2018**
  - USA
  - Benefits/harms analysis (colposcopies/life year gained)
  - Focus: age to stop screening

- Increasing screening end age from 65 to 75 yielded few additional life years from prevented deaths (~3-4 per 1000 women screened with cytology)

- Adopting HPV-based screening led to substantially more life years gained than increasing age to end screening.
Summary

- Predictions are generally not very different between models
  - Benefits of screening are low below <25y and decline after >65y
  - Screening efficiency highest between 30-60y

- Differences are in the value judgements & interpretation of model results by decision-makers
  - Below what threshold is cervical cancer risk sufficiently low not to screen?
  - How many colposcopies/screening tests are worth one prevented cancer or life year?
  - How should we value harm outcomes vs benefit outcomes? Few women who screen will benefit, while many more will incur harms.
  - What is our cost-effectiveness threshold?