# 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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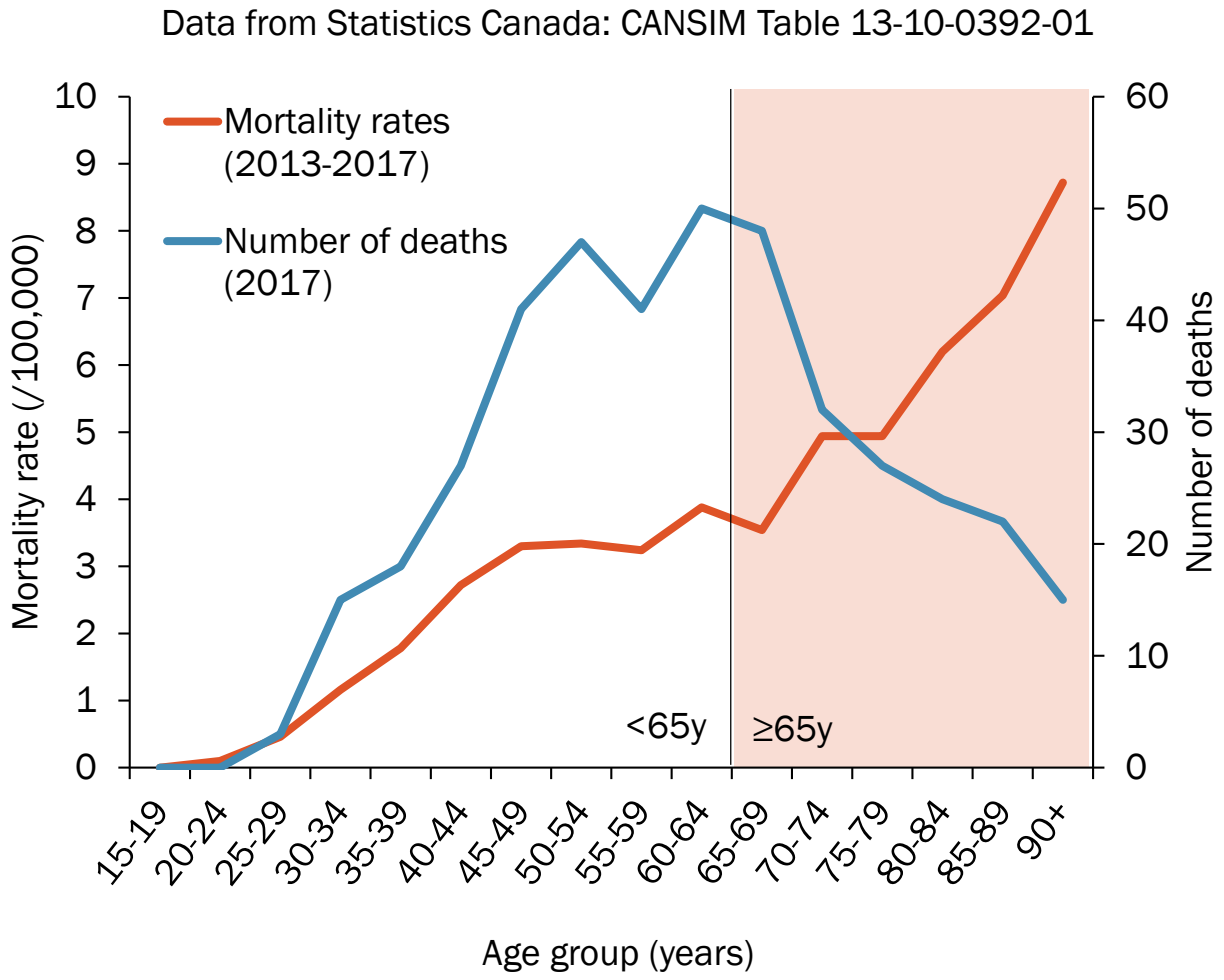
# Good reasons why we might want to screen older women

- 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.**



# 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 USA[1], UK[2], and Australia[3]

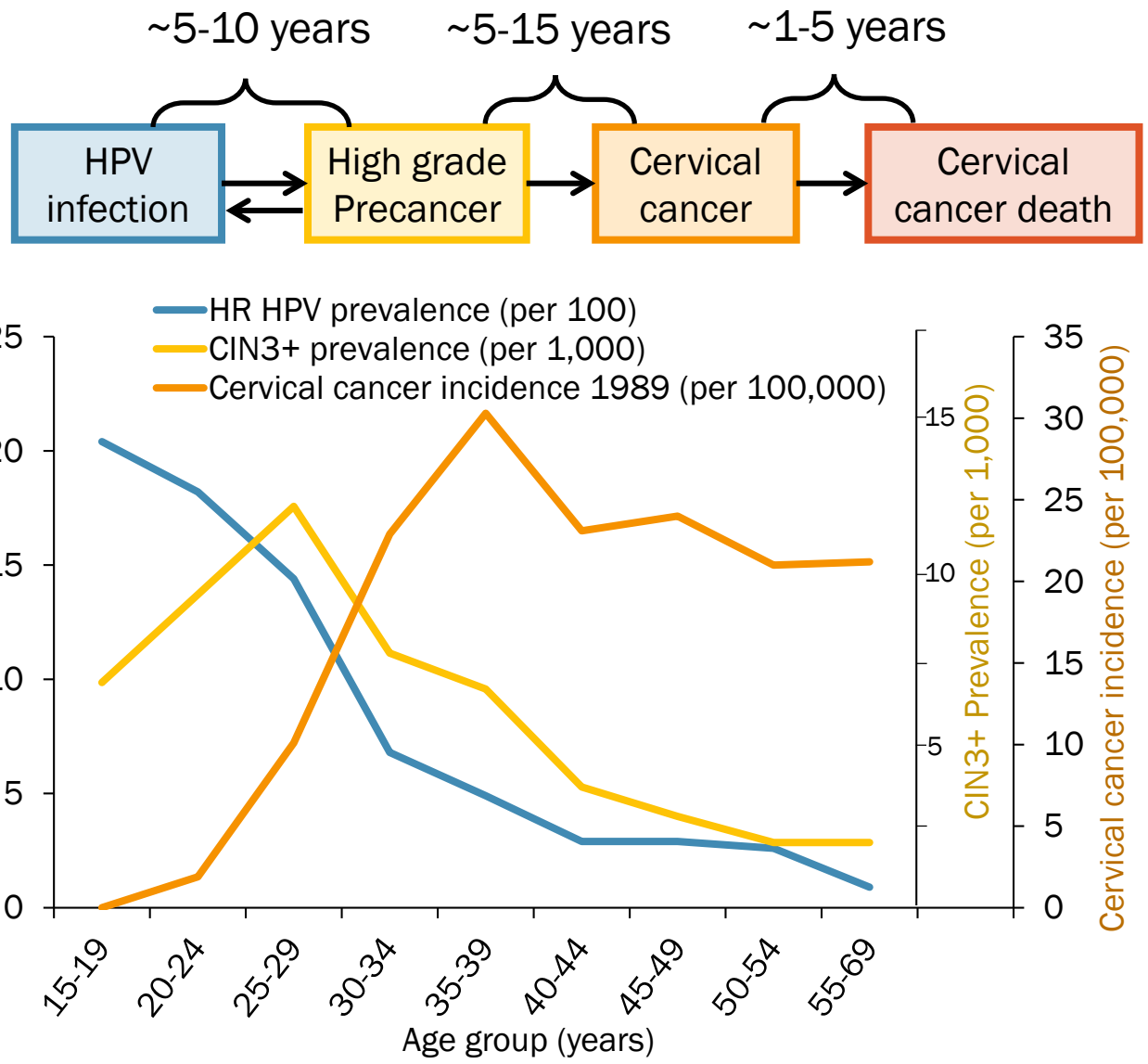



Figure data from: Peto Br J Cancer 2004;91(5); Trent Cancer Registry 2012; Baay Int J Cancer 2004;108


1. Owens *Ann Intern Med.* 2016;165:501-508
2. Kim *JAMA* 2018;320(7):706-714
3. Kitchener *Health Technol Assess* 2014;18:1-196
4. Lew *Lancet Public Health* 2017;2: e96–107

# Methods: Model description

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



1. Ogilvie et al. *Vaccine* 2013; 2. CANSIM Table 103-0550;
3. BC Cancer Agency Annual Report 2014

# 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:

- (QALY gained from prevented cancers & deaths) – (QALY lost from screening tests & procedures)

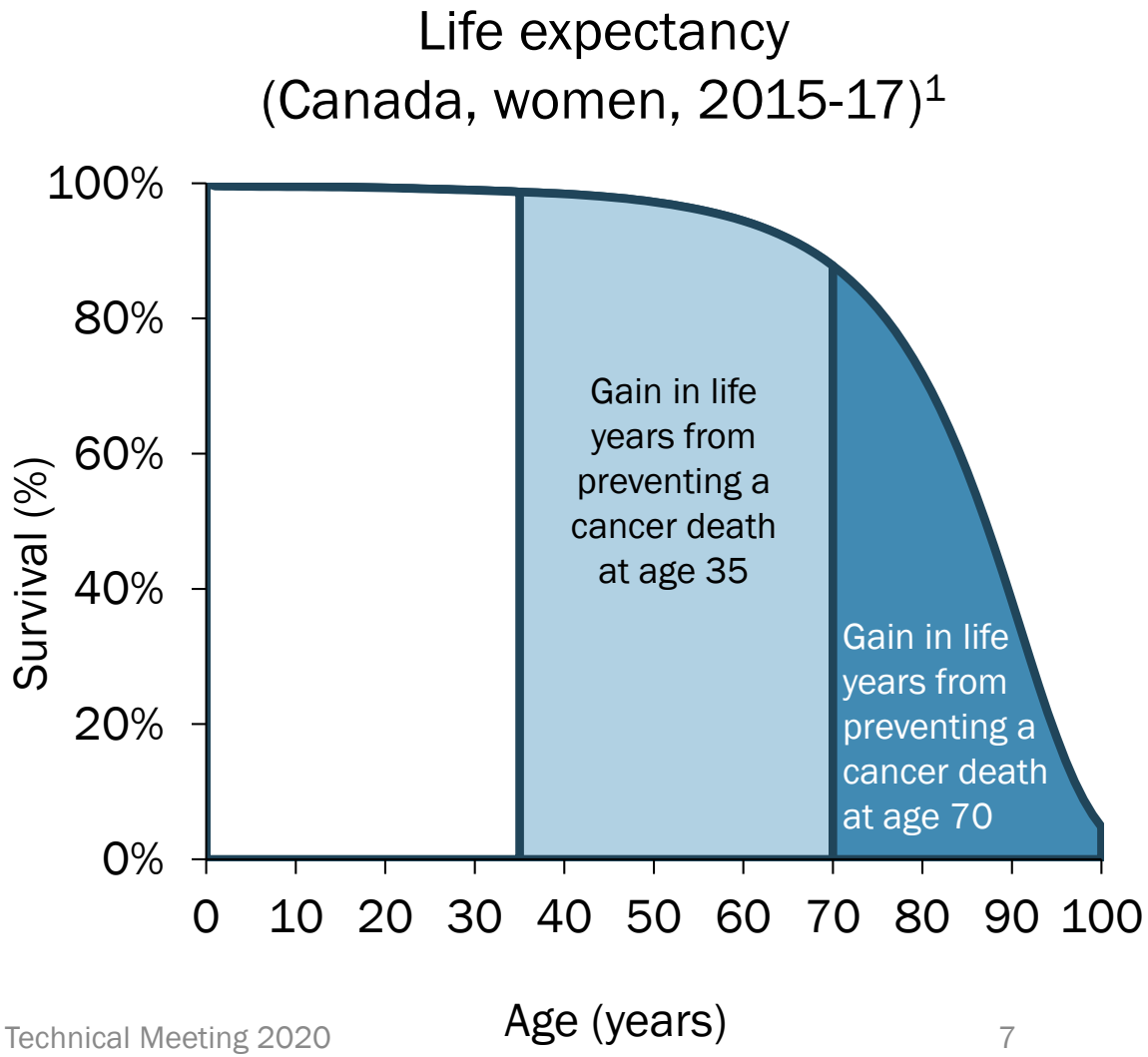
QALY = Quality-Adjusted Life Year:

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

(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.




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:



1. Malagón Lancet Oncol 2018; 19(12):1569-1578

# Lifetime balance of benefits & harms of cytology screening program 20-69y


doi: *10.1158/1055-9965.EPI-20-0190*

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# 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)



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# 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.



Kim *et al.* JAMA 2018; 320(7)

# 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?