Cost and cost-effectiveness of breast cancer screening

Harry J. de Koning, MD PhD

Professor of Public Health & Screening Evaluation
Chair national evaluation breast cancer screening NL
PI EU-TOPIA (towards improved cancer screening in EU)
PI CISNET breast modeling
Assessment before implementation

1. to quantify any positive effects of screening on public health

2. to quantify the disadvantages

3. to assess cost-effectiveness of a range of scenarios, and recommend the more cost-effective ones
Effectiveness - cost analysis
### Evaluation of breast mammography

<table>
<thead>
<tr>
<th>Age range (years)</th>
<th>Reduction in breast cancer mortality</th>
<th>Efficacy</th>
<th>Effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>40–44</td>
<td>Inadequate</td>
<td>Limited</td>
<td></td>
</tr>
<tr>
<td>45–49</td>
<td>Limited</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50–69</td>
<td>Sufficient</td>
<td>Sufficient</td>
<td></td>
</tr>
<tr>
<td>70–74</td>
<td>Inadequate</td>
<td>Sufficient</td>
<td></td>
</tr>
<tr>
<td>Optimal Screening Interval</td>
<td>Inadequate</td>
<td>No data</td>
<td></td>
</tr>
</tbody>
</table>

Women 50 to 69 years of age who were invited to attend mammographic screening had, on average, a 23% reduction in the risk of death from breast cancer;

Women who attended mammographic screening had a higher reduction in risk, estimated at about 40%.
### Possible adverse effects

Mammography screening detects breast cancers that would not have been diagnosed if the women had not been screened (overdiagnosis).

The risk of radiation-induced cancer from mammography in women aged ≥ 50 years is substantially outweighed by the reduction in breast cancer mortality from mammography screening.

Having a false-positive mammogram has short-term negative psychological consequences.

There is a net benefit from inviting women aged 50-69 years to service mammography screening.

Mammography screening for women aged 50-69 years can be cost-effective in countries with high breast cancer incidence.

Breast cancer screening can be cost-effective in low- and middle-income countries.
Breast screening age group 50-69 at 2-yearly intervals (NL)

35% Breast cancer mortality reduction

15 Life-years saved per death prevented

900,000 screens per year

48 million euros per year

30% of the cost of screening is counterparted by savings!

Cost per life-year gained: 2,200 euro
Cost-effectiveness

- Tool for priority setting: maximizing health at minimum cost

- Comparing alternatives:
  - A versus null situation (average CE) or
  - B versus A (incremental CE)

- Efficient frontier: programme has more health effects at same or lower cost, or programme has higher costs, but at lower incremental costs per effectiveness unit

- Direct medical cost/indirect medical cost (travel/time)
Cervical cancer screening

Source: van den Akker-van Marle, 2002
Cervical cancer screening

Source: van den Akker-van Marle, 2002
League table and cut-off point

- Absence of systematic comparisons may be worse
- Problems:
  - incomparability of studies
    (comparison programme, costs included, time period effects, discount rates)
  - external validity (local circumstances, centralised)
  - risk of outdating
  - uncertainty in point estimates missing
- 20,000 euro per life-year gained (Europe); 35,000 (NICE)

Commission on macroeconomics and health:
- Less than 3 times Gross Domestic Product/capita
- Less than the per capita GDP: very cost-effective
India, the largest developing country, has a steadily rising incidence of breast cancer. Estimates and comparisons of the cost-effectiveness of feasible breast cancer screening policies in developing countries and identification of the determinants of cost and efficacy are needed.

The estimated cost-effectiveness of CBE screening for breast cancer in India compares favorably with that of mammography in developed countries.

However, in view of competing priorities and economic conditions, the introduction of screening in India represents a greater challenge than it has been in more developed countries.
Epidemiological factors affecting the cost-effectiveness

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Clinical Breast Examination</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dutch value replaced with Indian value</td>
</tr>
<tr>
<td></td>
<td>None</td>
</tr>
<tr>
<td>Life expectancy (years)</td>
<td>79.7</td>
</tr>
<tr>
<td>Incidence 40-60 (x10^5 women-years)</td>
<td>186</td>
</tr>
<tr>
<td>Stage distribution (% N+)</td>
<td>46</td>
</tr>
<tr>
<td><strong>Effectiveness</strong></td>
<td></td>
</tr>
<tr>
<td>Number of breast cancer deaths averted</td>
<td>601</td>
</tr>
<tr>
<td>Number of life years gained</td>
<td>9,784</td>
</tr>
<tr>
<td>Mortality reduction (steady state) (%) †</td>
<td>9.3%</td>
</tr>
<tr>
<td><strong>Total net costs (million Int$) ±</strong></td>
<td>4.3</td>
</tr>
<tr>
<td><strong>Cost-effectiveness</strong></td>
<td></td>
</tr>
<tr>
<td>Cost per death prevented (Int $)</td>
<td>7,229</td>
</tr>
<tr>
<td>Cost per life year gained (Int $)</td>
<td>444</td>
</tr>
</tbody>
</table>
Study design
Life histories of breast cancer patients were modeled as a Markov process using the Dutch MISCAN (MIcrosimulation SCreening ANalysis) model. A lower cumulative incidence and delayed diagnosis based on Indian data was incorporated into the model. Estimates of costs for diagnosis and treatment relied on Dutch data for resource usage and World Health Organization estimates of unit costs for South Asia.
## Estimated costs and effects of varying screening programs

<table>
<thead>
<tr>
<th>Parameter</th>
<th></th>
</tr>
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<tbody>
<tr>
<td>Number of screen tests performed</td>
<td></td>
</tr>
<tr>
<td>Number of cancers detected by screening</td>
<td></td>
</tr>
<tr>
<td>Number of deaths averted</td>
<td></td>
</tr>
<tr>
<td>Number of life years gained</td>
<td></td>
</tr>
<tr>
<td>Steady state mortality reduction (%)</td>
<td></td>
</tr>
<tr>
<td>Number of screen tests per death averted</td>
<td></td>
</tr>
<tr>
<td>Number of screen tests per life year gained</td>
<td></td>
</tr>
<tr>
<td>Net costs of screening</td>
<td></td>
</tr>
<tr>
<td>(Million Int.$)</td>
<td></td>
</tr>
<tr>
<td>Cost Effectiveness</td>
<td></td>
</tr>
<tr>
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<td></td>
</tr>
<tr>
<td>Cost per life year gained (Int.$)</td>
<td></td>
</tr>
<tr>
<td>Incremental cost per life year gained ($) compared to program (x)</td>
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</tr>
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</table>
### One life-time CBE at age 50

(1 million women all ages)

<table>
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<th>Parameter</th>
<th>1 One lifetime CBE age 50</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of screen tests performed</td>
<td>212,008</td>
</tr>
<tr>
<td>Number of cancers detected by screening</td>
<td>217</td>
</tr>
<tr>
<td>Number of deaths averted</td>
<td>45</td>
</tr>
<tr>
<td>Number of life years gained</td>
<td>625</td>
</tr>
<tr>
<td>Steady state mortality reduction (%)</td>
<td>2.0</td>
</tr>
<tr>
<td>Number of screen tests per death averted</td>
<td>4,734</td>
</tr>
<tr>
<td>Number of screen tests per life year gained</td>
<td>339</td>
</tr>
<tr>
<td>Net costs of screening (Million Int.$)</td>
<td>0.5</td>
</tr>
<tr>
<td>Cost Effectiveness</td>
<td></td>
</tr>
<tr>
<td>Cost per death prevented (Int.$)</td>
<td>11,054</td>
</tr>
<tr>
<td>Cost per life year gained (Int.$)</td>
<td>793</td>
</tr>
</tbody>
</table>

Incremental cost per life year gained ($) compared to program (x)
### One lifetime CBE at age 40 compared to at age 50

<table>
<thead>
<tr>
<th>Parameter</th>
<th>1 One lifetime CBE age 50</th>
<th>2 One lifetime CBE age 40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of screen tests performed</td>
<td>212,008</td>
<td>275,735</td>
</tr>
<tr>
<td>Number of cancers detected by screening</td>
<td>217</td>
<td>97</td>
</tr>
<tr>
<td>Number of deaths averted</td>
<td>45</td>
<td>21</td>
</tr>
<tr>
<td>Number of life years gained</td>
<td>625</td>
<td>359</td>
</tr>
<tr>
<td>Steady state mortality reduction (%)</td>
<td>2.0</td>
<td>0.9</td>
</tr>
<tr>
<td>Number of screen tests per death averted</td>
<td>4,734</td>
<td>13,394</td>
</tr>
<tr>
<td>Number of screen tests per life year gained</td>
<td>339</td>
<td>769</td>
</tr>
<tr>
<td>Net costs of screening (Million Int.$)</td>
<td>0.5</td>
<td>0.6</td>
</tr>
<tr>
<td>Cost Effectiveness</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost per death prevented (Int.$)</td>
<td>11,054</td>
<td>28,878</td>
</tr>
<tr>
<td>Cost per life year gained (Int.$)</td>
<td>793</td>
<td>1,657</td>
</tr>
<tr>
<td>Incremental cost per life year gained ($) compared to program (x)</td>
<td>Dominated</td>
<td></td>
</tr>
</tbody>
</table>
## 5-year interval CBE ages 50-70

<table>
<thead>
<tr>
<th>Parameter</th>
<th>1 One lifetime CBE age 50</th>
<th>2 One lifetime CBE age 40</th>
<th>3 5 yr interval CBE age 50-70</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of screen tests performed</td>
<td>212,008</td>
<td>275,735</td>
<td>740,227</td>
</tr>
<tr>
<td>Number of cancers detected by screening</td>
<td>217</td>
<td>97</td>
<td>1,004</td>
</tr>
<tr>
<td>Number of deaths averted</td>
<td>45</td>
<td>21</td>
<td>172</td>
</tr>
<tr>
<td>Number of life years gained</td>
<td>625</td>
<td>359</td>
<td>1,913</td>
</tr>
<tr>
<td>Steady state mortality reduction (%)</td>
<td>2.0</td>
<td>0.9</td>
<td>7.8</td>
</tr>
<tr>
<td>Number of screen tests per death averted</td>
<td>4,734</td>
<td>13,394</td>
<td>4,298</td>
</tr>
<tr>
<td>Number of screen tests per life year gained</td>
<td>339</td>
<td>769</td>
<td>387</td>
</tr>
<tr>
<td>Net costs of screening (Million Int.$)</td>
<td>0.5</td>
<td>0.6</td>
<td>2.3</td>
</tr>
<tr>
<td>Cost Effectiveness</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost per death prevented (Int.$)</td>
<td>11,054</td>
<td>28,878</td>
<td>13,532</td>
</tr>
<tr>
<td>Cost per life year gained (Int.$)</td>
<td>793</td>
<td>1,657</td>
<td>1,218</td>
</tr>
<tr>
<td>Incremental cost per life year gained ($) compared to program (x)</td>
<td>Dominated</td>
<td>Dominated</td>
<td></td>
</tr>
</tbody>
</table>
Cost-effectiveness breast screening (India)
Conclusions for breast screen in India

- Estimated mortality reduction was greatest for screening programs targeting women between the ages of 40 and 60.
- Clinical breast examination (CBE) performed annually from ages 40 to 60 was predicted to be nearly as efficacious as biennial mammography screening for reducing breast cancer deaths (23-26%).
- Biennial CBE screening (40-60) is a cost-effective programme.

Limitations

- The study relied on a number of assumptions concerning the efficacy of CBE in reducing breast cancer mortality in India that have not been verified in randomized trials, and realistic cost estimates are essential.
Screening programme for non-communicable diseases in India

- Hypertension, diabetes, and common cancers
- Ages 30-65

- Oral cancer; oral visual examination; once in 5 years

- Cervical cancer; visual inspection with Acetic acid; once in 5 years

- Breast cancer; CBE; once in 5 years
Breast cancer control Ghana (SG Zelle 2012)

- GHANA
  - Low awareness
  - Late stage treatment
  - Poor survival

- Biennial screening CBE 40-69 most cost-effective strategy
  - (1,299 USD/DALY averted)
- Mass Media awareness raising second best option
  - (1,364 USD/DALY averted)

- MMG screening NOT cost-effective (12,908 USD/DALY averted)
<table>
<thead>
<tr>
<th></th>
<th>Stage I (%)</th>
<th>Stage II (%)</th>
<th>Stage III (%)</th>
<th>Stage IV (%)</th>
<th>ACE (USD/DALY)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current</td>
<td>2</td>
<td>21</td>
<td>50</td>
<td>27</td>
<td>3,745</td>
</tr>
<tr>
<td>Awareness raising</td>
<td>10</td>
<td>20</td>
<td>45</td>
<td>25</td>
<td>2,298</td>
</tr>
<tr>
<td>Mass media</td>
<td>40</td>
<td>30</td>
<td>19</td>
<td>11</td>
<td>1,364</td>
</tr>
<tr>
<td>CBE (2)</td>
<td>40</td>
<td>30</td>
<td>19</td>
<td>11</td>
<td>1,299</td>
</tr>
<tr>
<td>MMG 50+</td>
<td>42</td>
<td>32</td>
<td>16</td>
<td>9</td>
<td>2,163</td>
</tr>
<tr>
<td>MMG 40+</td>
<td>48</td>
<td>37</td>
<td>10</td>
<td>6</td>
<td>2,907</td>
</tr>
<tr>
<td>Treatment IV</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>16,824</td>
</tr>
<tr>
<td>Treatment II</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5,012</td>
</tr>
</tbody>
</table>
Structure of the MiSCAN model for breast cancer

- No breast cancer
- Preclinical DCIS
  - Preclinical breast cancer $\leq 5$ mm (T1a)
  - Preclinical breast cancer 6-10 mm (T1b)
  - Preclinical breast cancer 11-20 mm (T1c)
  - Preclinical breast cancer $> 20$ mm (T2+)
- Clinically diagnosed DCIS
  - Clinically diagnosed breast cancer $\leq 5$ mm (T1a)
  - Clinically diagnosed breast cancer 6-10 mm (T1b)
  - Clinically diagnosed breast cancer 11-20 mm (T1c)
  - Clinically diagnosed breast cancer $> 20$ mm (T2+)

Mass screening

- False positive test result
- Screen-detected DCIS
  - Screen-detected breast cancer $\leq 5$ mm (T1a)
  - Screen-detected breast cancer 6-10 mm (T1b)
  - Screen-detected breast cancer 11-20 mm (T1c)
  - Screen-detected breast cancer $> 20$ mm (T2+)

Death from breast cancer
Death from other cause

Figure A1: Structure of the MiSCAN model for breast cancer.
PERU

- Fixed and mobile MMG 45-69 (every 3 years)
  - (4,125 USD/DALY averted)

- RURAL: CBE (3) 40-69
- URBAN: CBE (40-49) & fixed MMG (50-69)

- Total cost 63-72 million USD per year !! (triennial programs)

- Current BC programme is 8,426 USD/DALY (so should be improved)
  - (Zelle et al., PLOS One 2013)
Conclusions

There is not one strategy that will apply to all countries.
Detailed assessment of expected effects and cost are crucial for policy decision making.

Information on quality of screening, and referred or not-referred women is crucial.

Do not perform breast screening more often than every 2-3 years.

Debate the possibility of CBE screening & awareness campaigns.
Monitoring and evaluation of the three Slovenian cancer screening programmes

Urska Ivanus
MD, Public health specialist
Director of national cervical cancer screening programme ZORA
Head of cancer screening department, Epidemiology and cancer registry
Institute of Oncology Ljubljana, Slovenia

Disclosure of interest: None declared
Slovenia

- 20.253 km²
- Population:
  - 2.06 million
  - 1.04 million women
  - 4.6% foreigners
- Slovene language
- Bilingual areas
  - Italian
  - Hungarian
Cancer screening in Slovenia

• Three population-based, organised screening programmes
• Established by MoH and Health Insurance Institute of Slovenia
• European recommendations and guidelines
Cervical cancer screening - ZORA

Pilot in 1998
National in 2003
Women, 20–64 years
Pap / 3 years
72 % coverage

NEW CERVICAL CANCER CASES
60% non-responders
80 % FIGO II+
40% screened
80% FIGO I

2nd most common cancer in women in early 1960’s

APC=-2.6
APC=4.4
APC = -5.8
(2003–2015)

OPPORTUNISTIC SCREENING
ZORA pilot
ZORA national
Breast cancer screening - DORA

Roll-out started in 2008
National in 2017
Women, 50–69 years
Dig. mammography / 2 years

1st most common cancer in women

Stage of breast cancer at diagnosis

- Localized
- Regional
- Distant

<table>
<thead>
<tr>
<th>Year</th>
<th>Localized</th>
<th>Regional</th>
<th>Distant</th>
</tr>
</thead>
<tbody>
<tr>
<td>1990-95</td>
<td>0.5</td>
<td>0.3</td>
<td>0.2</td>
</tr>
<tr>
<td>1996-99</td>
<td>0.4</td>
<td>0.3</td>
<td>0.3</td>
</tr>
<tr>
<td>2000-3</td>
<td>0.5</td>
<td>0.4</td>
<td>0.1</td>
</tr>
<tr>
<td>2004-7</td>
<td>0.5</td>
<td>0.4</td>
<td>0.1</td>
</tr>
<tr>
<td>2008-11</td>
<td>0.5</td>
<td>0.4</td>
<td>0.1</td>
</tr>
<tr>
<td>2012-15</td>
<td>0.5</td>
<td>0.4</td>
<td>0.1</td>
</tr>
</tbody>
</table>
Colorectal cancer screening - SVIT

National in 2008
Women and men
50–74 years (69 untill 2014)
FIT / 2 years

svit@nijz.si
http://www.program-svit.si/

2nd most common cancer in women and 3rd in men

- Crude incidence rate
- Crude incidence rate men
- Crude incidence rate women

Trend 1999-2009

SLORA, Cancer register, Institute of Oncology
uivanus@onko-i.si
Track #2 Advances in screening early detection
World Cancer Congress, Kuala Lumpur, Malaysia, 1–4 October 2018
Screening registries

- National, centralised

- Providers have legal obligation for reporting all screening and diagnostic procedures and results, also treatment to some extent (two legal acts)

- Data can be exchanged between different national registries (legal act, unique PIN)

Central population registry (1970, 1980 PIN)

National cancer registry (1950)

CERVICAL (2003)

BREAST (2008)

COLORECTAL (2009)

MONITORING and EVALUATION

Reporting

Planning

Implementing changes

Feedback (provider’s personal quality indicators)

Providers of screening, diagnostics, follow up and treatment

CERVICAL (2003)

BREAST (2008)

COLORECTAL (2009)
Cervical cancer screening – referral rate challenge

<table>
<thead>
<tr>
<th>Cervical cancer</th>
<th>1962</th>
<th>2003 implementation of ZORA programme</th>
<th>2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence</td>
<td>286</td>
<td>↓ 211</td>
<td>↓ 131</td>
</tr>
<tr>
<td>100.000 Crude</td>
<td>32.1</td>
<td>↓ 20.7</td>
<td>↓ 12.7</td>
</tr>
<tr>
<td>ASR (W) / 100.000</td>
<td>27.5</td>
<td>↓ 15.3</td>
<td>↓ 8.8</td>
</tr>
<tr>
<td>Mortality ASR (W) / 100.000</td>
<td>no data</td>
<td>(↓) 3.0</td>
<td>↓ 2.7</td>
</tr>
<tr>
<td>3-year coverage by Pap</td>
<td>no data</td>
<td>67.1</td>
<td>↑ 71.8</td>
</tr>
<tr>
<td>Referral rate (repeat Pap or colposcopy)</td>
<td>no data</td>
<td>16.7</td>
<td>≈ 16.8</td>
</tr>
</tbody>
</table>

Year 2003 = 16.7 %
- Unsatisfactory = 5.6 %
- Reactive changes = 2.0 %
- Pathological changes = 8.2 %

School for cervical screening

Year 2010 = 16.8 %
- Unsatisfactory = 5.2 %
- Reactive changes = 5.6 %
- Pathological changes = 5.9 %
Decision 2010

Based on literature review – implementation of the Bethesda classification

• Revision of criteria for unsatisfactory smears
  lack of endocervical cells (only) is not the reason for labelling smear as unsatisfactory

• Revision of clinical guidelines for reactive changes
  non-neoplastic changes (except keratotic changes) do not need to be followed up sooner than in three years (women can be returned to regular screening)

• Adding HPV triage test (with Pap co-testing) for low-grade changes and follow up after CIN treatment

→ New guidelines for cytology laboratories and clinicians planned in 2011

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Track #2 Advances in screening early detection
World Cancer Congress, Kuala Lumpur, Malaysia, 1–4 October 2018
Doubts of clinicians and laboratories – is it safe?

At that time we were facing the decrease in CIN 3 incidence.

Are we were missing important lesions?

Will we miss even more lesions, if we implement changes?
Extensive analysis of screening and cancer registry data – conclusions:

- **Decrease of CIN 3 incidence is probably too large:** age-specific, region-specific analyses, background incidence, results of revision of negative smears of women diagnosed with cervical carcinoma.

- **It is safe to implement planned changes:** linkage of screening and cancer registry data to analyse the burden of cervical cancer in four years after the unsatisfactory screening smear due to the lack of the endocervical cells or reactive changes.

- We didn’t have any national-specific data on HPV testing.

Changes implemented:

- **Revisited guidelines** for cytology laboratories and clinicians as planned – implemented at the end of 2011 (application to the Health Council)

- In depth refreshment course with foreign experts (Great Britain in 2010 and Canada in 2015 and 2016) for all cytoscreeners and cytologists

- 29/30 cytoscreeners obtained QUATE certificate by the European Federation of Cytology Societies by the end of 2017

- In depth education for clinicians regarding the benefits of **HPV triage test** if used according to the guidelines and harms of opportunistic screening
## Observations in the following years

<table>
<thead>
<tr>
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<td>↓12.7</td>
<td>↓11.6</td>
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<td>no data</td>
<td>67.1</td>
<td>↑71.8</td>
<td>↑72.3</td>
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<tr>
<td><strong>Referral rate</strong></td>
<td>no data</td>
<td>16.7</td>
<td>≈16.8</td>
<td>5.0</td>
</tr>
</tbody>
</table>

(→ repeat Pap or colposcopy)
Observations in the following years

However – we now face a new challenge – **how to build trust in HPV testing:**

- in year 2012 HPV triage test was used only in 60% of all women with the indication
- although 90% of women had Pap test in appropriate time window
Lessons learned

• Good **quality data** is necessary for monitoring and evaluation of benefits and harms of the screening programmes.

• Data is necessary, but not enough. Any change in the screening policy has to be accepted by the providers and target population if we want to:
  • gain benefits from new recommendations and
  • prevent harms from an underuse of new recommendations or spread of an opportunistic screening.
Future challenges of Slovenian screening programmes

CERVICAL – revision of a screening policy and new recommendations by 2021
- HPV primary screening
- HPV self-sampling for non-responders
- Screening of vaccinated cohorts (50% coverage with HPV vaccine)
- Renewal of the cervical screening registry IT system (2017–2020)

ALL SCREENING PROGRAMMES
- target age for screening (lower, upper)
- risk-stratified screening and management of screen positive women

Slovenian screening models are under the development as regional models in the EU-TOPIA project

uivanus@onko-i.si

Track #2 Advances in screening early detection
World Cancer Congress, Kuala Lumpur, Malaysia, 1–4 October 2018
The role of modeling in shaping lung cancer screening in the US

Rafael Meza, University of Michigan
Cancer Intervention and Surveillance Modeling Network (CISNET)
rmeza@umich.edu; @meza_rafa
Lung Cancer Globally

Globocan (2018):

- 2,093,976 cases (11.6%)
- 1,761,007 deaths (18%)

Bray et al, Cancer 2018
### Estimated New Cases

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>164,690</td>
<td>Prostate</td>
<td>266,120</td>
</tr>
<tr>
<td>121,680</td>
<td>Lung &amp; bronchus</td>
<td>112,350</td>
</tr>
<tr>
<td>75,610</td>
<td>Colon &amp; rectum</td>
<td>64,640</td>
</tr>
<tr>
<td>62,380</td>
<td>Urinary bladder</td>
<td>63,230</td>
</tr>
<tr>
<td>55,150</td>
<td>Melanoma of the skin</td>
<td>40,900</td>
</tr>
<tr>
<td>42,680</td>
<td>Kidney &amp; renal pelvis</td>
<td>36,120</td>
</tr>
<tr>
<td>41,730</td>
<td>Non-Hodgkin lymphoma</td>
<td>32,950</td>
</tr>
<tr>
<td>37,160</td>
<td>Oral cavity &amp; pharynx</td>
<td>26,240</td>
</tr>
<tr>
<td>35,030</td>
<td>Leukemia</td>
<td>25,270</td>
</tr>
<tr>
<td>30,610</td>
<td>Liver &amp; intrahepatic bile duct</td>
<td>22,660</td>
</tr>
<tr>
<td><strong>All Sites</strong></td>
<td><strong>856,370</strong></td>
<td><strong>All Sites</strong></td>
</tr>
</tbody>
</table>

### Estimated Deaths

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>83,550</td>
<td>Lung &amp; bronchus</td>
<td>70,500</td>
</tr>
<tr>
<td>29,430</td>
<td>Prostate</td>
<td>40,920</td>
</tr>
<tr>
<td>27,390</td>
<td>Colon &amp; rectum</td>
<td>23,240</td>
</tr>
<tr>
<td>23,020</td>
<td>Pancreas</td>
<td>21,310</td>
</tr>
<tr>
<td>20,540</td>
<td>Liver &amp; intrahepatic bile duct</td>
<td>14,070</td>
</tr>
<tr>
<td>14,270</td>
<td>Leukemia</td>
<td>11,350</td>
</tr>
<tr>
<td>12,850</td>
<td>Esophagus</td>
<td>10,100</td>
</tr>
<tr>
<td>12,520</td>
<td>Urinary bladder</td>
<td>9,660</td>
</tr>
<tr>
<td>11,510</td>
<td>Non-Hodgkin lymphoma</td>
<td>8,400</td>
</tr>
<tr>
<td>10,010</td>
<td>Kidney &amp; renal pelvis</td>
<td>7,340</td>
</tr>
<tr>
<td><strong>All Sites</strong></td>
<td><strong>323,630</strong></td>
<td><strong>All Sites</strong></td>
</tr>
</tbody>
</table>

**Lung Cancer in the US**

ACS (2018):

- 234,030 cases (13.5%)
- 154,050 deaths (25%)

Siegel et al, Cancer 2018
Lung Cancer & Smoking in the US

• It’s been more than 50 years since the relationship between smoking and lung cancer was established
• **Smoking rates have dropped significantly**
  – ~40% in 1960 → ~15.5% in 2016
• **Lung cancer rates have followed**

But

• **Smoking rates still ~ 15%**

• **Smoking remains as the top preventable cause of cancer and death- 2014 Surgeon General Report**

• **Lung cancer remains as the top cancer killer**
Lung Cancer Screening

• A potential preventive tool to reduce lung cancer mortality
• Debated for many years …
• Low-dose CT screening finally shown to be effective

• **National Lung Cancer Screening Trial – US 2011**
  – Eligibility: >30 pack years, ages 55-74, no more than 15 years since quitting
  – Observed 20% lung cancer mortality reduction in CT vs CXR arm after 6 years of follow-up

• **Nelson Trial – Netherlands and Belgium 2018**
  – Eligibility: smoking history of ≥15 cigarettes per day for ≥25 years or ≥10 cigarettes for ≥30 years, ages 55-75, no more than 10 years since quitting
  – Observed 26% (men) and 39% (women) mortality reduction in CT vs Control arm after 10 years of follow-up
Uses of modeling in shaping lung cancer screening in the US (and elsewhere)

- Support in guidelines/recommendations development
  - Identification of optimal strategies

- Extrapolation of trial results and other studies to the whole population
  - Synthetization of available information/data

- Projection of future burden, eligibility and impact
  - Important for decision makers and to help shape promotion messages

- Understanding interaction and synergies with other interventions
CISNET

Cancer Intervention and Surveillance Modeling Network

NCI-sponsored collaborative consortium of simulation modelers in breast, cervical, colorectal, esophageal, lung, and prostate cancers formed in 2000

Use surveillance, epidemiology, clinical data and simulation modeling to guide public health research and priorities

http://cisnet.cancer.gov
CISNET Lung Group

- Six lung cancer models:
  - Erasmus, Georgetown, MGH, Michigan, Stanford and Yale

- Smoking and lung cancer
  - Reconstruction of smoking histories in the US
  - Impact of tobacco control on lung cancer outcomes and overall mortality

- Lung cancer screening
CISNET Lung Group Screening Work

Five lung cancer and screening models:

**Erasmus, MGH, Michigan (FHCRC) and Stanford**

Calibrated models to NLST and PLCO lung screening trials

Evaluated hundreds (576) of alternative screening strategies on a “virtual” US population

Worked with the US Preventive Services Task Force (USPSTF) to generate additional evidence to support their update of LC screening recommendations
Extrapolation and Guidelines
Models well calibrated to data

Meza et al, Cancer 2014
Lung cancer deaths prevented per # of screens
576 competing scenarios

McMahon et al, Plos One 2014
Consensus-efficient scenarios

identified optimal scenarios
USPSTF selected final scenario

de Koning et al, Ann Intern Med 2014
Screening for Lung Cancer: Recommendations from the USPSTF

- USPSTF Recommendations
- Background modeling study
- Editorial by Peter Bach
- Editorial by Michael Unger & Frank Detterbeck
Screening for Lung Cancer: U.S. Preventive Services Task Force Recommendation Statement

Virginia A. Moyer, MD, MPH, on behalf of the U.S. Preventive Services Task Force*

Description: Update of the 2004 U.S. Preventive Services Task Force (USPSTF) recommendation on screening for lung cancer.

Methods: The USPSTF reviewed the evidence on the efficacy of low-dose computed tomography, chest radiography, and sputum cytologic evaluation for lung cancer screening in asymptomatic persons who are at average or high risk for lung cancer (current or former smokers) and the benefits and harms of these screening tests and of surgical resection of early-stage non–small cell lung cancer. The USPSTF also commissioned modeling studies to provide information about the optimum age at which to begin and end screening, the optimum screening interval, and the relative benefits and harms of different screening strategies.

Population: This recommendation applies to asymptomatic adults aged 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years.

Recommendation: The USPSTF recommends annual screening for lung cancer with low-dose computed tomography in adults aged 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery. (B recommendation)

Ann Intern Med.

For author affiliation, see end of text.
*$ For a list of the members of the USPSTF, see the Appendix (available at www.annals.org).

This article was published online first at www.annals.org on 31 December 2013.
### Table. Screening Scenarios From CISNET Models*

<table>
<thead>
<tr>
<th>Minimum Pack-Years at Screening, ( n )</th>
<th>Minimum Age at Which to Begin Screening, y</th>
<th>Time Since Last Cigarette, y</th>
<th>Population Ever Screened, %</th>
<th>Benefit: Lung Cancer Deaths Averted, %</th>
<th>Benefit: Lung Cancer Deaths Averted, n</th>
<th>Harm: Total CT Screens, ( n )</th>
<th>Harm: Radiation-Induced Lung Cancer Deaths, ( n )</th>
<th>Harm: Overdiagnosis, %§</th>
<th>Harm: CT Screens per Lung Cancer Death Averted, n</th>
</tr>
</thead>
<tbody>
<tr>
<td>40</td>
<td>60</td>
<td>25</td>
<td>13.0</td>
<td>11.0</td>
<td>410</td>
<td>17,192,4</td>
<td>17</td>
<td>11.2</td>
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<td>40</td>
<td>55</td>
<td>25</td>
<td>13.9</td>
<td>12.3</td>
<td>458</td>
<td>221,606</td>
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<td>30</td>
<td>60</td>
<td>25</td>
<td>18.8</td>
<td>13.3</td>
<td>495</td>
<td>253,095</td>
<td>21</td>
<td>11.9</td>
<td>534</td>
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<tr>
<td><strong>30</strong></td>
<td><strong>55</strong></td>
<td><strong>15</strong></td>
<td><strong>19.3</strong></td>
<td><strong>14.0</strong></td>
<td><strong>521</strong></td>
<td><strong>286,813</strong></td>
<td><strong>24</strong></td>
<td><strong>9.9</strong></td>
<td><strong>577</strong></td>
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<td>20</td>
<td>60</td>
<td>25</td>
<td>24.8</td>
<td>15.4</td>
<td>573</td>
<td>321,024</td>
<td>29</td>
<td>9.8</td>
<td>597</td>
</tr>
<tr>
<td>30</td>
<td>55</td>
<td>25</td>
<td>20.4</td>
<td>15.8</td>
<td>588</td>
<td>342,880</td>
<td>25</td>
<td>10.0</td>
<td>609</td>
</tr>
<tr>
<td>20</td>
<td>55</td>
<td>25</td>
<td>27.4</td>
<td>17.9</td>
<td>664</td>
<td>455,381</td>
<td>31</td>
<td>10.4</td>
<td>719</td>
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<td>10</td>
<td>55</td>
<td>25</td>
<td>36.0</td>
<td>19.4</td>
<td>721</td>
<td>561,744</td>
<td>35</td>
<td>9.5</td>
<td>819</td>
</tr>
</tbody>
</table>

*CISNET = Cancer Intervention and Surveillance Modeling Network; CT = computed tomography.
* All scenarios model the results of following a cohort of 100,000 persons from age 45 to 90 y or until death from any cause, with a varying number of smokers and former smokers screened on the basis of smoking history, age, and years since stopping smoking. Bold text indicates the screening scenario with a reasonable balance of benefits and harms that is recommended by the U.S. Preventive Services Task Force.
† In all scenarios, screening is continued through age 80 y.
‡ Number of CT screenings is a measure of harm because it relates to the number of patients who will have risk for overdiagnosis and potential consequences from false-positive results.
§ Percentage of screen-detected cancer that is overdiagnosis; that is, cancer that would not have been diagnosed in the patient’s lifetime without screening.

Projection of future burden, eligibility, impact
Screening Eligibility

Number and percentage of eligible individuals will decrease considerably
Projected Lung Cancer Burden

Number of lung cancer deaths overall and in current/former smokers will decrease.

Number in never smokers will increase.

Please do not share/tweet/distribute.

Joint impact of screening and cessation
Smoking Cessation within the Context of Lung Screening

• NCI Smoking in the Context of Lung Screening (SCALE) collaboration

• Impact of cessation programs at the point of screening

• 8 ongoing trials

• Modeling impact and cost-effectiveness
  • As part of the Georgetown trial
  • Collaboration with the whole scale consortium
Additional lung cancer mortality reduction benefits
Total Life-Years Gained (LYG)

Big potential impact of cessation programs within the context of lung screening
Conclusions – Take home message

- Lung cancer screening is an effective way to reduce lung cancer mortality

- Modeling has played a key role in the adoption/implementation of lung cancer screening in the US
  - Canada, Netherlands, UK

- Multiple areas:
  - Extrapolation of trial results to the whole population
  - Projection of burden, eligibility, impact
  - Interaction with cessation interventions
  - Cost-effectiveness (not shown)

- Need for country-specific analyses to translate impact to the local context
Acknowledgments

CISNET
- Erasmus – Harry de Koning
- Georgetown – David Levy
- MGH-ITA – Joey Kong
- Stanford – Sylvia Plevritis
- U Michigan
- Yale – Ted Holford

Organizers
- Iris Lansdorp-Vogelaar

US NCI
- Eric J. (Rocky) Feuer

University of Michigan
- Jihyoun Jeon
- Pianpian Cao

Contact Information
Rafael Meza, Ph.D.
Department of Epidemiology, University of Michigan
rmeza@umich.edu; @meza_rafa
How will transitioning from cytology to HPV testing change the balance between the benefits and harms of cervical cancer screening?

Dr Eleonora Feletto
Research Fellow, Cancer Research Division, Cancer Council NSW
Figure 9.7(a): Incidence and mortality ASRs of cervical cancer, 1982–2018
Australian Cervical Cancer Screening and Vaccination: 1991-2013

- National Cervical Screening Program (NCSP) began in 1991.
- NCSP Renewal process began in 2011.
- National HPV Vaccination Program (NHVP) extended to boys in 2013.

National HPV Vaccination Program (NHVP)
What did this mean for cervical screening?

A woman’s lifetime risk of cervical cancer now depends on vaccination...

- If vaccinated, what type of vaccine?
- How many doses?
- Vaccinated after HPV exposure?
- Unvaccinated but benefiting from herd immunity?

....how should this be factored into cervical screening decisions?
Key elements of transformation

1. Evidence
2. Catalyst
3. Evaluation
4. Sentinel experience
5. Implementation
1. Evidence

Pooled data from RCTs on invasive cervical cancer outcomes from four European trials - 176,000 women

Ronco et al, Lancet 2014
2. Catalyst

Prevalence of high grade pre-cancerous abnormalities

~34%↓ in 20-24 year olds; 17%↓ in 25-29 year olds in Victoria to 2014

Brotherton et al., MJA 2016.
3. Evaluation

**NOVEMBER 2011**
- Renewal of the National Cervical Screening Program
- **Aim:** *To ensure that all Australian women, HPV vaccinated and unvaccinated, have access to a cervical screening program that is acceptable, effective, efficient and based on current evidence.*
- The government commissioned a systematic review of the international evidence & modelled evaluation of health outcomes and costs

**APRIL 2014**
- Evidence report released
Cancer microsimulation model.

- Describe events and outcomes at the person-level
- Results are aggregated to give population outcomes.

www.policy1.org
• Dynamic model of sexual behaviour, HPV transmission, HPV type-specific natural history and cervical screening\textsuperscript{1-17}

• Extensively validated against screening and cancer outcomes.\textsuperscript{6,11}

• Screening uptake informed by analysis of Victorian Cervical Cytology Service.

• Vaccine uptake informed by National HPV Vaccination Register data.

Cytology
• 2-yearly
• Age 18-20 to 69 years
• 26 tests in a lifetime

HPV DNA testing
• 5-yearly
• Age 25-74 years
• 10 tests in a lifetime
Predicted impact on outcomes & costs

<table>
<thead>
<tr>
<th></th>
<th>Current practice</th>
<th>HPV: final guidelines*</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>If HPV vaccination had not been introduced</td>
<td>If HPV vaccination had not been introduced</td>
</tr>
<tr>
<td></td>
<td>Cohort offered vaccination at age 12 years</td>
<td>Cohort offered vaccination at age 12 years</td>
</tr>
<tr>
<td>Cervical cancer incidence†</td>
<td>6.92</td>
<td>4.73 (-31%)</td>
</tr>
<tr>
<td>Cervical cancer mortality†</td>
<td>1.80</td>
<td>1.15 (-36%)</td>
</tr>
<tr>
<td>Cervical cancer cases (n)‡</td>
<td>850</td>
<td>584 (-26%; -31%)</td>
</tr>
<tr>
<td>Cervical cancer deaths (n)‡</td>
<td>227</td>
<td>145 (-82%; -36%)</td>
</tr>
<tr>
<td>Colposcopies (n)‡</td>
<td>85795</td>
<td>116889 (31094; 36%)</td>
</tr>
<tr>
<td>Treatments (n)‡</td>
<td>22661</td>
<td>23963 (1302; 6%)</td>
</tr>
<tr>
<td>Annual cost‡ of screening programme (AUSS)</td>
<td>$223 million</td>
<td>$182 million (-41 million; -19%)</td>
</tr>
<tr>
<td>Average discounted cost per woman‡ (AUSS)</td>
<td>$383</td>
<td>$304</td>
</tr>
<tr>
<td>Average discounted life-year per woman§</td>
<td>21.6219</td>
<td>21.6229</td>
</tr>
</tbody>
</table>
Clinical management guidelines for the HPV-based screening

National Cervical Screening Program: Guidelines for the Management of Screen Detected Abnormalities, Screening in Specific Populations and Investigation of Abnormal Vaginal Bleeding.

Released 2017

**Cumulative Lifetime Risk (CLR): cervical cancer case/death and excisional treatment**

<table>
<thead>
<tr>
<th></th>
<th>Unvaccinated</th>
<th>Unvaccinated in cohort offered vaccination as 12- to 13-years old</th>
<th>Vaccinated as 12- to 13-years old</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cytology</td>
<td>HPV DNA</td>
<td>Cytology</td>
</tr>
<tr>
<td>CLR cervical cancer</td>
<td>0.65%</td>
<td>0.44%</td>
<td>0.52%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.36%</td>
</tr>
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<td></td>
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<td>0.18%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.14%</td>
</tr>
<tr>
<td>CLR cervical death</td>
<td>0.2%</td>
<td>0.12%</td>
<td>0.16%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.1%</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td>0.06%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.04%</td>
</tr>
<tr>
<td>CLR excisional treatment</td>
<td>13.4%</td>
<td>13.9%</td>
<td>11.9%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>12%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>6.8%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5.9%</td>
</tr>
</tbody>
</table>

*Velentzis L et al., Int J Cancer 2017*
## Obstetric outcomes: 5-yearly primary HPV screening

<table>
<thead>
<tr>
<th></th>
<th>Unvaccinated</th>
<th>Unvaccinated in cohort offered vaccination as 12- to 13-years old</th>
<th>Vaccinated as 12- to 13-years old</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of births</td>
<td>187,600</td>
<td>187,600</td>
<td>187,600</td>
</tr>
<tr>
<td>Pre-term delivery (PTD) events</td>
<td>13,880</td>
<td>13,830</td>
<td>13,570</td>
</tr>
<tr>
<td>PTD rate</td>
<td>7.4%</td>
<td>7.37%</td>
<td>7.23%</td>
</tr>
<tr>
<td>Low birth weight (LBW) events</td>
<td>11,570</td>
<td>11,520</td>
<td>11,270</td>
</tr>
<tr>
<td>LBW rate</td>
<td>6.17%</td>
<td>6.14%</td>
<td>6.01%</td>
</tr>
</tbody>
</table>

Velentzis L et al., *Int J Cancer* 2017
Key elements of transformation

1. Evidence
2. Catalyst
3. Evaluation
4. Sentinel experience
5. Implementation
The renewed National Cervical Screening Program started on December 1st 2017
Continuing national and international work in cervical cancer control.

- Awarded and leading a $2.5M Centre of Research Excellence Grant from the Australia’s National Health and Medical Research Council in Cervical Cancer Control
- Following changes to Australia’s National Cervical Screening program, our research is now informing similar program changes in New Zealand in 2019
- Ongoing work funded by NCI (USA), to underpin future changes to screening in the USA.
- World Health Organisation using Policy1-Cervix results to inform global targets for cervical cancer elimination
Acknowledgements and Funding

Medical Services Advisory Committee

**MSAC Application No. 1276. November 2013.**


National Cervical Screening Program: Guidelines for the management of screen-detected abnormalities, screening in specific populations and investigation of abnormal vaginal bleeding.

**Guidelines Working Party:** Prof Ian Hammond (chair), A/Prof Marion Saville (Deputy Chair)

**Cancer Council Australia Guidelines Project Team:** Ms Jutta von Dincklage, Ms Laura Wueellner.

**Cancer Council New South Wales Technical Team:** Prof Karen Canfell, Jessica Darlington-Brown, Michaela Hall, Suzanne Hughes, Harriet Hui, Chloë Jennett, Jie Bin-Lew, Megan Smith, Dr Kate Simms, Dr Louiza Velentzis, Dr Susan Yuill.


Cancer Council NSW in collaboration with VCS Ltd

**Co-Principal Investigators:** Prof Karen Canfell, A/Prof Marion Saville

**Chief Investigators:** Dr Philip Castle, Dr Michael Caruana, Prof Val Gebski, Jessica Darlington-Brown, Dr Stella Heley, A/Prof Julia Brotherton, Prof Dorota Gertig, A/Prof Marion Saville

The VCS have received equipment and a funding contribution for the Compass trial from Roche Molecular Systems and Ventana Inc USA.

Website www.compasstrial.org.au

Pilot Study Registration ACTRN12613001207707

Main Trial Registration: Clinicaltrials.gov NCT02328872

Associated grants:

**Project Grant APP1109121**

Prof Karen Canfell, Prof You-Lin Qiao, Dr Philip Castle, Dr Kate Simms, Dr Ju-Fang Shi, Dr Jose Jeronimo

**Project Grant APP1065892**

Prof Karen Canfell, Dr Michael Caruana, Dr Kate Simms, Jie-Bin Lew

**Career Development Fellowship APP1082989**

Prof Karen Canfell
Thank-you

eleonoraf@nswcc.org.au
Modelling and improving cancer screening programmes in Europe
Objective EU-TOPIA

• Improve outcomes of breast, cervical and colorectal cancer screening programmes across Europe

HOW?

• by providing national, regional, and local policymakers with TOOLS to evaluate and quantify their cancer screening programmes.
  – Monitoring
  – Evaluation
  – Barrier assessment
Two workshops (100+ participants from 29 countries):
- monitoring in September 2017 in Budapest
- Evaluation in September 2018 in Malmö

Monitoring tool
Prototype of evaluation tool
Introduced workshop participants to both tools
Need for modelling tools

Impact of indicators on benefits (e.g. mortality reduction) and harms (e.g. overdiagnosis) cannot be observed directly:

• Outcomes in the situations – with and without screening - are not known at the same time for the same population

• Changes to screening programmes often accumulate over time, making it impossible to disentangle the impact of one change from the other.

→ Modelling tools
Data sent from the partners

Calibrated MISCAN models
  Exemplary countries: NL, I, FI, and SLO

1a

Review literature
  Evidence on mortality reduction due to cancer screening in Europe

1b

Validated models
  Countries: NL, I, FI, and SLO

2

EU-TOPIA: Evaluation tool

3
Developing a model for other countries
Two steps in model development

- **Model Calibration**: estimating model parameters to get good fit with observed data in a country

- **Model validation**: using model to predict outcomes for dataset not used for calibration without changing parameters → establishing that model gives valid predictions
Developing a model for other countries

Model NL

- Population
- Survival by stage
- Programme characteristics:
  - Ages
  - Test
  - Interval
  - Attendance
  - Referral
  - Triage
  - etc

Directly adjustable model inputs

- Incidence of disease
- Stage distribution
- Sensitivity
- Specificity
- (Progression)

Model inputs to be estimated

Success?
- Yes
  - New model
- No
  - Check and re-validate

Validation country B model

New model country B
How successful was this approach? Calibration of the CRC model to Italy

I. Italy, CRC rates

II. Italy, CRC Stage distribution
How successful was this approach?

Calibration of the CRC model to Slovenia

III. Slovenia, CRC rates

IV. Slovenia, CRC Stage distribution
How successful was this approach?
Calibration of the CRC model to Finland
How successful was this approach? Validation of the CRC model for Italy
How successful was this approach?
Validation of the CRC model for Finland

I. Controls

II. Screening
Web-based tool for cancer screening evaluation in 30+ countries
Webtool: adjustments should be automatic

<table>
<thead>
<tr>
<th>Original model</th>
<th>Adjusting model inputs based on data from country B</th>
<th>Calibration targets based on data from country B</th>
<th>Calibration model</th>
<th>Validation country B model</th>
<th>New model country B</th>
</tr>
</thead>
</table>

### Clinical background situation
- **Demographic assumptions**
  - Birth tables
  - Life tables
  - [Organ removal tables]

### Natural history assumptions
- Relative survival by stage

### Test Characteristics
- Referral criteria

### Programme characteristics
- Starting age
- Stopping age
- Screening interval
- Screening test
- Attendance
- Referral procedure
- Surveillance
- Vaccination

Parameters in blue are cervical cancer specific

Parameters in black are general for all cancer sites

Search for most plausible reason for validation fail. Check if the model inputs represent the study setting well. Validation success?

Validation:
1. Visual inspection of the following key outcomes:
   - Incidence
   - Mortality
2. Outcomes are within the 95% confidence interval ranges of the best evidence of the systematic review on:
   - Mortality reduction after screening
   - Age and/or time specific incidence
   - Stage distribution
3. Mortality reduction outcomes are within the 95% confidence interval ranges of the remaining studies of the systematic review.
Webtool: adjustments should be automatic

• Use model from exemplary country for their region

• Basic adjustments to
  – background incidence level
  – overall participation rates
  – detection rates
  – etc...

• Try to make as many adjustments to their situation as possible, but in less accurate way
## Scenarios

Define the scenarios you want to simulate and the settings of each scenario.

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Screening Test</th>
<th>Age target</th>
<th>Screening Interval</th>
<th>Coverage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Current Screening</td>
<td>Current Screening</td>
<td>Current Screening</td>
<td>Current Screening</td>
</tr>
<tr>
<td>2.</td>
<td>FIT</td>
<td>50-74</td>
<td>2 years</td>
<td>Current Screening</td>
</tr>
<tr>
<td>3.</td>
<td>FIT</td>
<td>60-75</td>
<td>1 year</td>
<td>Current Screening</td>
</tr>
<tr>
<td>4.</td>
<td>FIT</td>
<td>55-74</td>
<td>1 year</td>
<td>Current Screening</td>
</tr>
</tbody>
</table>
Next steps EU-TOPIA

• Further develop barrier assessment tool
• April 2019: workshop on barrier assessment
• Winter 2019/2020: workshop on developing road maps to improve local screening programmes