Overdiagnosis in Mammography Screening

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Outline

• Mammographic Screening for Breast Cancer

• Fallacy on Overdiagnosis

• Overdiagnosis in Taiwanese Randomized Controlled Trial

• Methodology for Estimating Overdiagnosis

• Personalized Probabilistic Cost-Effectiveness Analysis
Meta-analyses: UK Independent

The benefits and harms of breast cancer screening: an independent review

2012 Lancet

Average effect: 20% mortality reduction
Fallacy in BC mass screening

1. Short follow-up time: without lead-time consideration

2. Breast Cancer mixed: diagnosed before screening program, but died after program implementation

With an average follow-up of 2.2 years

Mixed up lead-time and over-detection

Overdiagnosis with mammography in Taiwan

based on the Taiwanese randomized controlled trial for young women

Overdiagnosis in publically organised mammography screening programmes: systematic review of incidence trends

Jørgensen et al., 2009

Eligible Population

Randomization

N=20,040  M  U  M  U

N=20,087  U  M  U  M

N=39,563  Control Arm

M: Mammography
U: Ultrasound

RR=1.13 (0.94-1.35)
Overdiagnosis with mammography in Taiwan based on the Taiwanese Population-based service screening

Total Incidence of breast cancer

Mammography vs CBE:
RR=1.13 (95% CI: 1.08-1.18)

Over-detection: 13%
Methodology for Estimating Overdiagnosis

1. Graphic method
2. Zero-inflated model
3. Coxian Phase-Type Markov Process

1. Graphic method

Curved method by comparing cumulative incidence of cancer

Chen et al., 2017
Assessing overdetection in breast cancer screening using data on randomized controlled trial

Chen et al., 2017 *Medicine*

**2. Zero-inflated model**

*Survival of Breast Cancer, Darlana, Sweden*

Without consideration of over-diagnosis

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Follow-up time
Zero-inflated Poisson regression model and overdiagnosis rate

<table>
<thead>
<tr>
<th>Variable</th>
<th>Count part RR/OR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Size, mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10-14 vs. 1-9</td>
<td>3.69(0.76-18.01)</td>
<td>0.015</td>
</tr>
<tr>
<td>15-19 vs. 1-9</td>
<td>3.85(0.80-18.53)</td>
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<tr>
<td>20-29 vs. 1-9</td>
<td>10.26(2.27-46.33)</td>
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<tr>
<td>30+ vs. 1-9</td>
<td>9.45(2.01-44.49)</td>
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<tr>
<td>Node (+) vs. (-)</td>
<td>2.40(1.30-4.45)</td>
<td>0.005</td>
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<tr>
<td>Grade 3 vs 1/2</td>
<td>1.62(0.94-2.79)</td>
<td>0.080</td>
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<tr>
<td>Surgery MA vs. BCS</td>
<td>1.92(0.95-3.88)</td>
<td>0.071</td>
</tr>
<tr>
<td>Triple Negative Yes vs No</td>
<td>2.49(1.36-4.59)</td>
<td>0.003</td>
</tr>
<tr>
<td>Chemotherapy Yes vs No</td>
<td>0.79(0.42-1.47)</td>
<td>0.456</td>
</tr>
<tr>
<td>Radiotherapy Yes vs. No</td>
<td>1.23(0.60-2.53)</td>
<td>0.568</td>
</tr>
<tr>
<td>Tamoxifen Yes vs. No</td>
<td>0.95(0.94-1.64)</td>
<td>0.847</td>
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<thead>
<tr>
<th>Variable</th>
<th>Zero part OR</th>
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</thead>
<tbody>
<tr>
<td>Intercept</td>
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<td></td>
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<tr>
<td>Detection mode</td>
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<td>0.041</td>
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<tr>
<td>SD vs. RF</td>
<td>2.38(0.97-5.85)</td>
<td></td>
</tr>
<tr>
<td>IC vs. RF</td>
<td>1.23(0.48-3.17)</td>
<td></td>
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</table>

\[ \pi = 56.14\% \]

\[ \text{SD: 66.4\% } \uparrow \text{ Overdiagnosis, 8.9\% } \]

\[ \text{IC: 50.5\% } \uparrow \text{ Awareness, 2.9\% } \]

\[ \text{RE: 45.4\% } \rightarrow \text{ Treatment effect } \]

3. Coxian Phase-Type Markov Process

Applying the concept of cured model:

\[ S(t) = S^P(t) \cdot \pi + S^{NP}(t) \cdot \pi^0 \]

For exponentially distributed random variable

\[ \exp(-\alpha_1 \cdot t) = \pi \cdot \left[ \exp(-\alpha_1^P \cdot t) \right] + \pi^0 \]

\[ \pi^0 = \frac{\exp(-\alpha_1 \cdot t) - \exp(-\alpha_1^P \cdot t)}{1 - \exp(-\alpha_1^P \cdot t)} \]
Estimated natural history of breast cancer with and without consideration of over-detection, Swedish Two-County Trial (Kopparberg) 1977-1985

\[ \pi^0 = 2.6\% \]

Probabilistic CEA of Personalized Breast Cancer Screening

- Population risk stratification for trade-off between harm and benefit
- Time preference for screening policy and outcome
Risk stratification:
The recommend age to begin screening and inter-screening interval for screening by percentiles of risk score

Economic Evaluation
Acceptability curve of primary and secondary breast cancer prevention for non-BRCA Carrier
Acceptability curve of primary and secondary prevention of breast cancer for BRCA-carrier women

Conclusion

• The estimated proportion of over-diagnosis cases is affected by lead-time, sensitivity, and follow-up time, which causes the large disparity of over-detection across studies.

  - Methodological flaws

• Use high-quality design-based study and model-based approach

• Probabilistic CEA for personalized screening policy is strongly recommended
Thanks for your attention!