BREAST CANCER SCREENING IN OLDER WOMEN

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No disclosures
Worse breast cancer prognosis

- Breast cancer mortality increases with age
  - < 65 years (reference group)
  - 65-74 years HR 1.25 (95%CI 1.01-1.54)
  - ≥ 75 years HR 1.63 (95%CI 1.23-2.16)

Role for screening?

Van de Water et al. JAMA 2012
Benefits and harms of screening

Benefits
- Better survival: regular screening can reduce the risk of dying from breast cancer

Harms
- Overdiagnosis and overtreatment
- More extensive surgery and adjuvant therapy
- False alarm
- Pain at examination
- False reassurance

Gotzsche 2008
Risk of overtreatment of older patients

- Increased risk of postoperative complications
- Increased risk of toxicity of chemotherapy
- Increased risk of adverse events and nonpersistence of endocrine therapy
Evidence for screening in older women

- Randomized clinical trials rarely included patients over the age of 68

- Some observational studies suggest improved survival for screen-detected tumours

- However: several types of bias may be present in these studies
Observational research in screening

Cohort breast cancer patients

Screen-detected

Survival vs Survival

Interval tumours

Several forms of bias
Lead-time bias

Without screening
- Cancer starts
- Cancer diagnosed because of symptoms at age 67 y
- 5-year survival = 0%
- Dead at age 70 y

With screening
- Cancer starts
- Cancer diagnosed because of screening at age 60 y
- 5-year survival = 100%
- Dead at age 70 y

Wegwarth Ann Intern Med 2012
Length-time bias

Figure 3. Screen Detection Capability Based on Tumor Biology and Growth Rates

Esserman JAMA 2009
Selection bias

• Generally, women who attend screening programs are
  • “Healthy”
  • Of high socio-economic status
  • Etc

• Even more important in older patients!
  • Comorbidity
  • Institutionalization (nursing home)
  • Mobility

Aarts BCRT 2011; Badgwell JCO 2008
## Selection bias in older patients

### Table 4. Multivariate Analysis of Effect of Mammography Use on Survival

<table>
<thead>
<tr>
<th>Factor</th>
<th>No. of Patients</th>
<th>All-Cause Mortality</th>
<th>Breast Cancer-Specific Mortality</th>
<th>Mortality From Other Diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>HR</td>
<td>95% CI</td>
<td>HR</td>
</tr>
<tr>
<td>Adjusted without comorbidity*</td>
<td>12,358</td>
<td>0.87</td>
<td>0.85 to 0.90</td>
<td>0.89</td>
</tr>
<tr>
<td>Adjusted including comorbidity†</td>
<td>12,358</td>
<td>0.86</td>
<td>0.85 to 0.90</td>
<td>0.88</td>
</tr>
<tr>
<td>Comorbidity score</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>10,455</td>
<td>0.88</td>
<td>0.85 to 0.91</td>
<td>0.89</td>
</tr>
<tr>
<td>1</td>
<td>1100</td>
<td>0.83</td>
<td>0.78 to 0.91</td>
<td>0.82</td>
</tr>
<tr>
<td>2+</td>
<td>803</td>
<td>0.89</td>
<td>0.81 to 0.97</td>
<td>0.93</td>
</tr>
</tbody>
</table>

Abbreviation: HR, hazard ratio.
*Adjusted by diagnosis year, age at diagnosis, race/ethnicity, region, marital status, socioeconomic status, stage, grade, estrogen receptor status, surgery, radiation, and chemotherapy.
†Adjusted by all of the above predictor variables and comorbidity.
Alternative - Hypothetical Screening Scenarios

Esserman JAMA 2009
Example

Our analysis suggests that whatever the mortality benefit, breast-cancer screening involved a substantial harm of excess detection of additional early-stage cancers that was not matched by a reduction in late-stage cancers. This imbalance indicates a considerable amount of overdiagnosis.
Aim of the study

• Despite limited evidence: in the Netherlands, the upper age limit of the mass screening program was extended from 70 to 75 in 1998

• If a screening program is effective, the incidence of early stage tumours increases, while the incidence of advanced stage tumours decreases

To assess the incidence rates of early stage and advanced stage tumours after implementation of mass screening in patients aged 70-75 years in the Netherlands
Methods

- Calculation of incidence rates per years of
  - Early stage breast cancer (Stage I-II and in situ)
  - Advanced stage breast cancer (Stage III-IV)

- Calculation of Incidence Rate Ratio’s (IRR’s) in three time periods
  - 1995-1997 (before screening), reference
  - 1998-2003 (transition period)
  - 2004-2011 (after screening)

- Adjustment for changing incidence rates by including control group of women aged 76-80 years

- Calculation ratio early stage / advanced stage after screening
Results
Results - 2

Table 2 | Breast cancer incidence before and after implementation of screening in the Netherlands

<table>
<thead>
<tr>
<th>Time period</th>
<th>70-75 years</th>
<th>76-80 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Incidence*</td>
<td>IRR (95% CI)</td>
</tr>
<tr>
<td>Early stage:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prescreening (1995-97)</td>
<td>248.7</td>
<td>1.0 (ref)</td>
</tr>
<tr>
<td>Screening uptake period</td>
<td>383.1</td>
<td>1.54 (1.47 to 1.61)</td>
</tr>
<tr>
<td>Active screening (2003-11)</td>
<td>362.9</td>
<td>1.46 (1.40 to 1.52)</td>
</tr>
<tr>
<td>Advanced stage:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Period:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prescreening (1995-97)</td>
<td>58.6</td>
<td>1.0 (ref)</td>
</tr>
<tr>
<td>Screening uptake period</td>
<td>46.3</td>
<td>0.79 (0.71 to 0.87)</td>
</tr>
<tr>
<td>Active screening (2003-11)</td>
<td>51.8</td>
<td>0.88 (0.81 to 0.97)</td>
</tr>
</tbody>
</table>

IRR = incidence rate ratio.
*Cases per 100,000 women per year.
†Calculated by dividing incidence rate ratio for age 70-75 by incidence rate ratio for age 76-80

Ratio early stage / advanced stage = (362.9-248.7)/(51.8-58.6) = 17 “extra” early stage tumours per prevented advanced stage tumour
Conclusion

• Implementation of mass screening in women aged 70-75 years of age has lead to
  • Strong increase of early stage breast cancer
  • Limited decrease of advanced stage tumours
Implications

• Screening in older women leads to a large proportion of overdiagnosis

• Older patients are at risk of adverse events of breast cancer treatment

• Increase risk of competing mortality with increasing age → even if breast cancer is diagnosed in an earlier stage this will possibly result in a very small survival benefit

• Tremendous health expenditure with few beneficial effects
Future perspectives

• Personalized screening based on
  • Remaining life expectancy
  • Breast cancer risk
  • Patients’ preferences

• Improving treatment strategies in older patients, rather than implementing mass screening programs in older women
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