Is there an upper age limit in screening?

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Is there an upper age limit in screening?

YES!

The question: WHERE (which age)?
Current screening practice

- NL, France, Israel: p 50-74/75
- Sweden: p (40-) 50-69 (-74)
- UK: p 50-69, 70+ self-invitation
- Finland: p 50-59 (-69 recommended)
- Most other European countries: p 50-69
- Canada: p 50-69
  (40-49 and 70+: “talk to your doctor about how often you should be tested”)  
- Australia: p 40+ (focus 50-69)
- Japan, Singapore: p 40+

- US: life-expectancy > 4-5 years (needs recommendation physician)

p = BC screening programme
Evidence efficacy?

Cumulative breast cancer mortality per 1000 in invited group (___) and control group (……..) by year since randomisation and by age at randomisation.

Nyström et al., Lancet 1993
Evidence efficacy?


Mean follow-up time: 15.8 years (5.8-20.2)

<table>
<thead>
<tr>
<th></th>
<th>RR</th>
<th>95% C.I.</th>
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<tbody>
<tr>
<td>Overall (40-74 years)</td>
<td>0.79*</td>
<td>0.70-0.89</td>
</tr>
<tr>
<td>Age 65-74 years</td>
<td>0.81</td>
<td>0.61-1.07</td>
</tr>
<tr>
<td>Age 65-69 years</td>
<td>0.69*</td>
<td>0.49-0.96</td>
</tr>
<tr>
<td>Age 70-74 years</td>
<td>1.18</td>
<td>0.71-1.97</td>
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Breast cancer mortality reduction

Randomized controlled mammography screening trials (RCT):

< 50 years: UK trial non-significant 17%
(earlier trials: if effect, probably due to mammography examinations undergone after age 50)

50-69 years: significant 25-30%

70-74 years: subgroup analyses not possible

75+ years: no RCTs
What do we know on breast cancer in elderly women?

- Higher incidence and mortality
- Decreasing life expectancy
- Possibly clinically less important breast cancers
- Co-morbidity / competing causes of death
Main causes of death by age category (% distribution)

(breast and non-breast) cancer, CVD and other mortality, NL 1989-2006
Review

Routine screening mammography in women older than 74 years: A review of the available data

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1) Four studies on screening performance and BC incidence.

2) Three studies on screening performance and BC mortality reduction:
   in 2 of them lower BC death risk in “users mammography” > 75 years.

   *But in all three selection bias and other limitations (no distinguishing between screening and diagnostic mammogram); no information on harms*

→ **Contradictory conclusions:**

   “Regular mammography screening in older women may be associated with an earlier-stage disease and lower breast cancer mortality.

   These data support the use of screening mammography above age 75 years based on individual evaluations, rather than setting an upper age limit for breast cancer screening.”
Screening – a question of balance

BENEFITS
- Lower mortality
- Life-years gained
- Improvement quality of life
- No undertreatment

HARMS
- No gain in life-years
- Overdetection / overtreatment
- More years living with disease (loose quality of life)
Theoretical considerations

Mean sojourn time preclinical detectable period:

1. continuous increase with age (= slower tumour growth at higher ages)
   - more additional BC incidence, but proportionally less additional life-years gained, more years living (in lead-time) with disease,
   - = ‘pessimistic’ model variant for screening

2. constant sojourn time (no further increase) after the age of 65
   - less additional BC incidence, less years living with disease, more additional life-years gained than 1)
   - = ‘optimistic’ model variant for screening
Sojourn time and life-years gained

‘Optimistic’ variant

sojourn time constant after age 65

‘Pessimistic’ variant

sojourn time continues increasing after age 65

QALYs gained (5% discounted, thousands)

last screening age

[Boer et al., Eur J Cancer 1995]
The Dutch breast cancer screening programme

- 1989-1997: for women aged 50-69
  since 1998: women aged 50-75
- Biennial invitation for free mammography (reminder if non-attendance)
- 65 dedicated screening units (mostly mobile)
- Initial screen: 2-view, subsequent screen: 2nd view on indication (± 35%)
- Double reading
- Referral screen-positive women to GP
Age-specific participation

all screening rounds 2001-2005

invited
screened
participation %
### Results Dutch BCSP 1998-2005

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<thead>
<tr>
<th></th>
<th>70-75</th>
<th>50-69</th>
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</thead>
<tbody>
<tr>
<td>Screen examinations (N)</td>
<td>711,029</td>
<td>5,430,915</td>
</tr>
<tr>
<td>Referrals (per 1000)</td>
<td>16.4</td>
<td>12.4</td>
</tr>
<tr>
<td>(Needle) Biopsies (per 1000)</td>
<td>10.0</td>
<td>6.6</td>
</tr>
<tr>
<td>Breast cancers (per 1000)</td>
<td>7.9</td>
<td>4.5</td>
</tr>
<tr>
<td>PPV referral (%)</td>
<td>48</td>
<td>36</td>
</tr>
<tr>
<td>PPV biopsy (%)</td>
<td>79</td>
<td>68</td>
</tr>
<tr>
<td>% DCIS (of all)</td>
<td>76.3</td>
<td>10.5</td>
</tr>
<tr>
<td>% T1 (of all)</td>
<td>65.8</td>
<td>61.2</td>
</tr>
<tr>
<td>% N- (of invasive)</td>
<td>71.8</td>
<td>67.2</td>
</tr>
<tr>
<td>% N+ (of invasive)</td>
<td>23.1</td>
<td>28.9</td>
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Breast cancer mortality NL 1986/1988 – 2005, 75-84 years

75-84 years

breast cancer mortality per 100,000 vro


MISCAN no screening observed

reduction obs -14.4%
obst -exp -16.0%
Summary and conclusions

- No RCT evidence on benefit mammography screening 75+
- Results 1998-2005 Dutch BCSP 70-75 years
  - justify the extension from 69 to 75 (good attendance and screening performance)
  - probably contribute to further BC mortality reduction > 69 years
  - confirm lower tumour growth rate → more overtreatment
- For (high-quality) mammography screening programmes 75 years of age still best upper age limit
- Screening mammograms > 75 need QA and evaluation
Modelled and observed cancer detection rates
(update, preliminary data 1998-2005)

3a model: no previous screen
observed: initial screens

3b model: previous screen 2 years before
observed: subsequent screens interval < 2.5 yrs

3c model: previous screen 4 years before
observed: subsequent screens interval >= 2.5 yrs

3d model: previous screen 6 years before
observed: subsequent screens interval >= 2.5 yrs

Modified from Fracheboud et al., Br J Cancer 2006