Cancer Screening Problems: Lessons to be learned

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Cancer Screening Problems

- Breast Screening
  - Breast cancer expected population
  - Cost
  - Outcome
  - Biological behaviour
- Diagnosis
- Outcome of Screening and Problems in Breast Cancer
- Prostate Cancer
- Conclusion
Cancer Screening Problems

Age-standardized breast cancer incidence rates vary internationally by more than 13-fold. Disease diagnoses are more common in industrialized, Western countries that have high rates of screening, extremely low incidence rates in many developing countries in part reflect low screening rates and incomplete reporting.

**EUROPE**
High incidence rates of about 100 cases per 100,000 females occur in Belgium, France, Ireland, the Netherlands and Israel.

**EAST ASIA**
South Korea and Japan have low rates of breast cancer mortality (6.1 and 10.8 per 100,000) relative to other industrialized countries, but unlike elsewhere, those rates are rising.

**SCREENING**
Mammography screening rates vary widely, ranging from 12% in Turkey and 17% in Mexico, to more than 80% in Finland, the Netherlands and the United States.

**DEVELOPING COUNTRIES**
Rising rates of breast cancer diagnoses in many African and Asian countries might reflect increases in screening, and possibly rising rates of obesity, dietary changes and delayed childbirth.
Cancer Screening Problems

Growing Pains

Women in the United States have a roughly 12% chance of developing breast cancer at some point in their life. But that risk increases when breast cancer runs in the family. Hereditary mutations in the tumour-suppressor genes *BRCA1* and *BRCA2* raise an individual’s risks of developing breast cancer to 60% and 85%, respectively. Disregarding heritable factors, the likelihood of breast cancer through the decades is as follows:

- **Women age 30–39:** 1 in 233 people
- **Age 40–49:** 0.43% increase
- **Age 50–59:** 1.45% increase
- **Age 60–69:** 2.38% increase
- **Proportion of all cancer (men and women) that is breast cancer, second only to lung cancer (13%)**
Cancer Screening Problems

Many factors influence a woman's chance of survival, including how early the tumour is detected and the molecular profile of the tumour. Even so, women diagnosed now are much more likely to survive than women in decades past.

US DATA

By 2004 the overall survival rate had increased to 85.8%.

1944–54 saw a five-year overall survival rate of just 40%.

Patients are living longer each decade, because of improvements in surgery, screening, hormone and biologic therapies, and chemotherapies.

Doctors often detect cancer while the tumour resides in the breast alone. So-called localized tumours grant the patient the best prognosis. As the cancer spreads, it often becomes increasingly difficult to cure.

By splitting tumours into categories based on their molecular make-up, researchers can target therapies to the patient. Although mortality rates are relatively low for ER+ patients, the total number of breast cancer deaths from this type exceeds those for the HER2+ and triple-negative group, as they are much more common.
Cancer Screening Problems

BITTERSWEET SUCCESS

The cost of breast cancer is expected to rise as the population ages and patients live longer because of better — and more expensive — drugs. Because breast cancer is highly prevalent, it might have the highest price tag of any cancer by 2020. The chart projects the costs assuming a 2% increase in the initial treatment phase and a 2% increase in the final year of life.
Time Dependency of Outcome

**EBCTCG Lancet** 365, 1687–1717 (2005)
The Great Escape

If a cell leaves the primary tumour, it can circulate and lie dormant in other tissues for decades.

1. The seed is released
   - Invasive carcinoma
   - Tumour mass
   - Basement membrane
   - Blood and lymphatic vessels
   - Extracellular matrix
   - Blood-borne dissemination
   - Lymphatic dissemination

2. The seed enters the bloodstream and becomes a circulating tumour cell

3. The seed is planted: the most common sites are the bones, lungs, liver and brain
   - Cell death
   - Dormant solitary cell
   - Dormant micrometastasis
   - Growing micrometastasis
Cancer Screening Problems

Table 1: Relative survival rates by tumour site at 5, 10 and 15 years*

<table>
<thead>
<tr>
<th>Tumour site</th>
<th>5 years*</th>
<th>10 years*</th>
<th>15 years†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast (female)</td>
<td>90%</td>
<td>82%</td>
<td>75%</td>
</tr>
</tbody>
</table>

SEER data 89-2006

Dormant Cells

Cancer Screening Problems

# Table I Percentages of invasive cancers in categories of size, grade and node status by detection mode

<table>
<thead>
<tr>
<th>Factor/category</th>
<th>First screen</th>
<th>Later screens</th>
<th>Interval cases</th>
<th>Refusals</th>
<th>Control group</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size 1–9 mm</td>
<td>26.1</td>
<td>27.2</td>
<td>8.1</td>
<td>6.2</td>
<td>7.1</td>
<td>15.4</td>
</tr>
<tr>
<td>10–14 mm</td>
<td>29.6</td>
<td>26.4</td>
<td>21.0</td>
<td>8.6</td>
<td>15.4</td>
<td>21.1</td>
</tr>
<tr>
<td>15–19 mm</td>
<td>19.7</td>
<td>24.0</td>
<td>17.3</td>
<td>13.6</td>
<td>19.7</td>
<td>20.0</td>
</tr>
<tr>
<td>20–29 mm</td>
<td>14.1</td>
<td>16.5</td>
<td>31.5</td>
<td>28.4</td>
<td>29.0</td>
<td>23.7</td>
</tr>
<tr>
<td>30–49 mm</td>
<td>6.3</td>
<td>4.8</td>
<td>15.3</td>
<td>22.2</td>
<td>20.0</td>
<td>13.3</td>
</tr>
<tr>
<td>50 mm or more</td>
<td>4.2</td>
<td>1.1</td>
<td>6.8</td>
<td>21.0</td>
<td>8.8</td>
<td>6.5</td>
</tr>
<tr>
<td>Total cases</td>
<td>284</td>
<td>375</td>
<td>248</td>
<td>81</td>
<td>590</td>
<td>1578</td>
</tr>
<tr>
<td>Not known</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Node status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>78.6</td>
<td>83.9</td>
<td>53.6</td>
<td>37.5</td>
<td>54.5</td>
<td>65.0</td>
</tr>
<tr>
<td>Positive</td>
<td>21.4</td>
<td>15.5</td>
<td>41.8</td>
<td>41.7</td>
<td>39.8</td>
<td>30.9</td>
</tr>
<tr>
<td>Distant metastases</td>
<td>0.7</td>
<td>0.6</td>
<td>4.6</td>
<td>20.8</td>
<td>5.7</td>
<td>4.1</td>
</tr>
<tr>
<td>Total cases</td>
<td>271</td>
<td>361</td>
<td>237</td>
<td>72</td>
<td>558</td>
<td>1499</td>
</tr>
<tr>
<td>Not known</td>
<td>14</td>
<td>15</td>
<td>11</td>
<td>9</td>
<td>34</td>
<td>83</td>
</tr>
</tbody>
</table>

**Kopparberg**

- Grade 1: 25.2, 24.2, 11.5, 11.1, 12.6, 18.2
- Grade 2: 37.4, 52.7, 34.5, 40.7, 42.2, 42.7
- Grade 3: 37.4, 23.1, 54.0, 48.1, 45.2, 39.1
- Total cases: 139, 182, 113, 27, 199, 660
- Not known: 1, 1, 2, 2, 4, 10

**Östergötland**

- Grade 1: 44.5, 34.2, 16.3, 0.0, 19.7, 26.4
- Grade 2: 27.0, 31.0, 31.5, 29.0, 29.6, 29.6
- Grade 3: 28.5, 34.8, 52.2, 71.0, 50.8, 44.0
- Total cases: 137, 155, 92, 31, 294, 709
- Not known: 8, 38, 41, 21, 95, 203
Cancer Screening Problems (SE)

**Figure 1** Cumulative survival of breast cancer cases by detection mode. ●, Screen 1; +, Later screens; ×, Interval; □, Refusers; ×, Control.
# Cancer Screening Problems (SE)

## Table VIII

Results of multivariate analysis of effects of detection mode, size, node status and grade on survival, each factor adjusted for the others and for age and county.

<table>
<thead>
<tr>
<th>Factor/category</th>
<th>Hazard ratio</th>
<th>(95% CI)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detection mode</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>1.00</td>
<td></td>
<td>( P = 0.001 )</td>
</tr>
<tr>
<td>First screen</td>
<td>0.57</td>
<td>(0.38, 0.85)</td>
<td></td>
</tr>
<tr>
<td>Later screens</td>
<td>0.66</td>
<td>(0.43, 1.00)</td>
<td></td>
</tr>
<tr>
<td>Interval</td>
<td>0.77</td>
<td>(0.54, 1.09)</td>
<td></td>
</tr>
<tr>
<td>Refusers</td>
<td>1.64</td>
<td>(1.06, 2.53)</td>
<td></td>
</tr>
<tr>
<td>Size</td>
<td></td>
<td></td>
<td>( P &lt; 0.0001 )</td>
</tr>
<tr>
<td>1–9 mm</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10–14 mm</td>
<td>1.48</td>
<td>(0.69, 3.15)</td>
<td></td>
</tr>
<tr>
<td>15–19 mm</td>
<td>1.40</td>
<td>(0.65, 2.98)</td>
<td></td>
</tr>
<tr>
<td>20–29 mm</td>
<td>2.63</td>
<td>(1.28, 5.40)</td>
<td></td>
</tr>
<tr>
<td>30–49 mm</td>
<td>3.72</td>
<td>(1.78, 7.79)</td>
<td></td>
</tr>
<tr>
<td>50 + mm</td>
<td>4.98</td>
<td>(2.29, 10.79)</td>
<td></td>
</tr>
<tr>
<td>Node status</td>
<td></td>
<td></td>
<td>( P &lt; 0.0001 )</td>
</tr>
<tr>
<td>Negative</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>2.47</td>
<td>(1.85, 3.28)</td>
<td></td>
</tr>
<tr>
<td>Distant metastases</td>
<td>24.26</td>
<td>(14.96, 39.35)</td>
<td></td>
</tr>
<tr>
<td>Grade by county</td>
<td></td>
<td></td>
<td>( P &lt; 0.0001 )</td>
</tr>
<tr>
<td>Östergötland</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 1</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 2</td>
<td>2.17</td>
<td>(0.98, 4.77)</td>
<td></td>
</tr>
<tr>
<td>Grade 3</td>
<td>4.10</td>
<td>(1.96, 8.59)</td>
<td></td>
</tr>
<tr>
<td>Kopparberg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 1</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 2</td>
<td>2.27</td>
<td>(0.96, 5.35)</td>
<td></td>
</tr>
<tr>
<td>Grade 3</td>
<td>3.77</td>
<td>(1.62, 8.76)</td>
<td></td>
</tr>
</tbody>
</table>
Most of the size effect occurs in the difference between these tumours and those smaller than 2 cm in diameter, when detection by mammography is of greatest relevance.

Screening women over 50 years of age every 33 months reduces breast cancer mortality by some 40% (over a 10-year period, for the women screened).
Breast Cancer: 5-y Survival by pT

![Graph showing the survival rate by tumor size.](image)

- Observed
- ExpFit
Breast Cancer: 5-y Survival by number of pN

Breast Cancer: 5-y Survival by Grade

% survival at 5 year

Grade

Breast Cancer: 5-y Survival

- So if we have a breast tumor \( T1b = 10\text{mm}, \ N1=1 \text{ node} \) and \( G 1 \) the survival is: \( .86 \times .82 \times .85 = 60\% \) !!!

- Since we obtain 75-80\% for those patients the gain by the implementation is to be ascribed to ??

- Let’s look further.
Cancer Screening Problems (SE)

Figure 1: Breast cancer incidence and mortality per 100,000 in 1968–82 in women randomised to invited group and control group in Östergötland trial

Cancer Screening Problems (SE)

The advantageous effect of breast screening on breast cancer mortality persists after long-term follow-up. The recent criticism against the Swedish randomised controlled trials is misleading and scientifically unfounded.
Cancer Screening Problems (SE)

Cancer Screening Problems

![Graph showing age-adjusted breast cancer incidence and mortality in Swedish women aged 40 years and older in 1960–2009, and the cumulative proportion of women who received a first invitation to mammographic screening in 1974–1997.](image)

**Figure 3.** Age-adjusted breast cancer incidence and mortality in Swedish women aged 40 years and older in 1960–2009, and the cumulative proportion of women who received a first invitation to mammographic screening in 1974–1997.
Cancer Screening Problems

Group 1: Gävleborg, Dalarna and Östergötland

Group 2: Kalmar, Västmanland, Jönköping and Skåne

Group 3: Västra Götaland, Örebro, Uppsala and Blekinge

Group 4: Stockholm, Södermanland, Halland, Norrbotten, Kronoberg, Västernorrland and Värmland

Figure 5: Trends derived from Poisson regression models for observed age-adjusted breast cancer death rates (Null Model and Screening Model) and for the three theoretical scenarios in which mammographic screening was expected to result in 10%, 20%, or 30% reductions in breast cancer mortality, considering a lag time of 10 years between the start of screening and changes in trends, and a further period of 8 years after the inflexion year for reaching the 10%, 20%, or 30% mortality reduction. The open circles represent the observed annual mortality rates per 100 000 persons, and the vertical dashed line represents the average year of screening start. Continuous line: Null Model; thick dashed line: Screening Model with inflexion point; thin dashed line: Model with screening-associated 10% reduced mortality; thin dotted line: Model with screening-associated 20% reduced mortality; thick dotted line: Model with screening-associated 30% reduced mortality.
Cancer Screening Problems (SE)

Östergötland

Mortality ASR per 100,000 PY


0 20 40 60 80 100 120

Cancer Screening Problems

- In conclusion, Swedish mortality statistics show little evidence that the decrease in breast cancer mortality corresponds to the results of mammography trials and observational studies conducted in Sweden.

- In fact, the Swedish breast cancer mortality statistics are consistent with studies that show limited or no impact of screening on mortality from breast cancer

Cancer Screening Problems (N)

Figure 1. The Four Study Groups, According to Region and Year.

The 19 counties were grouped into six regions according to the date of introduction of the screening program, which was implemented throughout the country in a staggered fashion, starting in 1996. The screening group consisted of women who received a diagnosis of breast cancer after the introduction of the screening program. The nonscreening group consisted of women living in regions where screening was not offered in the same calendar period that screening was offered in other regions. The historical study groups consisted of women residing in the 19 counties in the 10-year period before screening was offered. A screening round lasted for 2 years, and the first year of the first round was included in both the screening and nonscreening groups (purple).
## Table 1. Rates of Death from Breast Cancer, According to Study Group and Age.*

<table>
<thead>
<tr>
<th>Age Group and Mortality Data</th>
<th>Nonscreening Groups</th>
<th>Screening Groups</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Historical Group</td>
<td>Current Group</td>
<td>Historical Group</td>
</tr>
<tr>
<td>50–69 Yr</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of deaths</td>
<td>494</td>
<td>396</td>
<td>555</td>
</tr>
<tr>
<td>No. of person-yr</td>
<td>1,898,989</td>
<td>1,866,741</td>
<td>2,197,469</td>
</tr>
<tr>
<td>No. of deaths/100,000 person-yr</td>
<td>26.0</td>
<td>21.2</td>
<td>25.3</td>
</tr>
<tr>
<td>Rate ratio for death (95% CI)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20–49 Yr</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of deaths</td>
<td>238</td>
<td>183</td>
<td>332</td>
</tr>
<tr>
<td>No. of person-yr</td>
<td>3,842,740</td>
<td>4,030,443</td>
<td>5,134,212</td>
</tr>
<tr>
<td>No. of deaths/100,000 person-yr</td>
<td>6.2</td>
<td>4.5</td>
<td>6.5</td>
</tr>
<tr>
<td>Rate ratio for death (95% CI)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>70–84 Yr</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of deaths</td>
<td>429</td>
<td>386</td>
<td>623</td>
</tr>
<tr>
<td>No. of person-yr</td>
<td>1,101,019</td>
<td>1,173,624</td>
<td>1,349,967</td>
</tr>
<tr>
<td>No. of deaths/100,000 person-yr</td>
<td>39.0</td>
<td>32.9</td>
<td>46.1</td>
</tr>
<tr>
<td>Rate ratio for death (95% CI)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Cancer Screening Problems (N)

Figure 2. Rates of Death among Women between the Ages of 50 and 69 Years in the Four Study Groups.

Among women in the nonscreening group, there was an 18% reduction in the rate of death from breast cancer, as compared with the preceding 10-year period, presumably as a result of increased breast-cancer awareness, improved therapy, and the use of more sensitive diagnostic tools. Among women in the screening group, there was a 28% reduction in mortality from breast cancer during the same period. Thus, the relative reduction in mortality that was causally related to the screening program alone was 10%.
Cancer Screening Problems (N)

Figure 3. Incidence-Based Rate Ratios for Death from Breast Cancer, According to Age Group.

Shown are the differences in breast-cancer mortality among women living in counties in which breast-cancer screening had been implemented, as compared with their historical counterparts, and corresponding values for women living in counties in which screening had not been implemented, as compared with their historical counterparts. Only women between the ages of 50 and 69 years were invited to participate in mammographic screening.

Thus, the difference in the reduction in mortality between the current and historical groups that could be attributed to screening alone was 2.4 deaths per 100,000 person-years, or a third of the total reduction of 7.2 deaths.

We conclude that our results support the evidence that screening mammography reduces the rate of death from breast cancer.

However, the magnitude of this benefit seems modest in the high attendance, nation wide screening program we evaluated.

Most important, the apparent benefit conveyed by optimized patient care may be missed unless breast-cancer screening is integrated into a well-functioning health care system that is available to the entire population.
Table 1: Woman years of observation, number of breast cancer deaths, and average rates per 100,000 women in screened and non-screened areas

<table>
<thead>
<tr>
<th></th>
<th>Screened areas</th>
<th>Non-screened areas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of woman years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>35-54 years</td>
<td>1,174,997</td>
<td>640,700</td>
</tr>
<tr>
<td>55-74 years</td>
<td>1,218,157</td>
<td>492,081</td>
</tr>
<tr>
<td>75-84 years</td>
<td>478,800</td>
<td>223,441</td>
</tr>
<tr>
<td>Number of breast cancer deaths</td>
<td></td>
<td></td>
</tr>
<tr>
<td>35-54 years</td>
<td>457</td>
<td>257</td>
</tr>
<tr>
<td>55-74 years</td>
<td>1,478</td>
<td>658</td>
</tr>
<tr>
<td>75-84 years</td>
<td>937</td>
<td>429</td>
</tr>
<tr>
<td>Average number of breast cancer deaths per 100,000 women</td>
<td></td>
<td></td>
</tr>
<tr>
<td>35-54 years</td>
<td>39</td>
<td>40</td>
</tr>
<tr>
<td>55-74 years</td>
<td>121</td>
<td>134</td>
</tr>
<tr>
<td>75-84 years</td>
<td>196</td>
<td>192</td>
</tr>
</tbody>
</table>
Conclusions: *We were unable to find an effect of the Danish screening program on breast cancer mortality.* The reductions in breast cancer mortality we observed in screening regions were similar or less than those in non-screened areas and in age groups too young to benefit from screening, *and are more likely explained by changes in risk factors and improved treatment than by screening mammography.*
Cancer Screening Problems

Breast cancer growth with a doubling time of 130 days and probability of M+ spread

Michaelson JS 2008
"One year after the single screening experience, the cancers found among these women will be just as large and just as lethal as the cancers found among women who never use screening."
Cancer Screening Problems

Michaelson JS 2008
Cancer Screening Problems

Marginal Cost

$700,000

$600,000

$500,000

$400,000

$300,000

$200,000

$100,000

$0

Screening Interval

0

365

730

1095

Doubling Time 130 Days

Doubling Time 260 Days

Doubling Time 65 Days
Breast Cancer: Shift in Stage


- $pT_1 = 14$ mm*
- $= 13$ mm**
- $= 12$ mm***
- $pT_2 = 30$ mm*
- $= 30$ mm**
- $= 28$ mm***
Breast Cancer: 3-Y Survival

1988 (ALL:12480)  1997 (ALL:14812)

T1: 5581/5999    T1: 7626/8197
T2: 2572/3055    T2: 2940/3492
Total 10525/12480
Total 12748/14812
84.33%  86.06%
Breast Cancer: 3 year survival

1988 (ALL:12480)  1997 (ALL:14812)

84.33%  86.06%

Taking into account the differences of median size of pT1 14 vs 12 mm, pT2 30 vs 28 mm and the relative impact of 3.4%/mm relative survival benefit (RSB)(1), the expected survival for 1997 is 85.28% 

\[(2 \times 3.4\%) \times 0.14 = 0.95\%; \quad 84.33\% + 0.95\% = 85.28\%\]

There is a gain due to whatever of 86.06%-85.2%=0.78%
Breast Cancer: Is RX making the difference?

Cancer Screening Problems (CN)

Registered volunteers who signed consent form and received physical examination (n=39,459)

Randomly assigned (39,459)

Received mammography plus physical examination as allocated (19,711)

Excluded from analysis: 24
(Did not receive intervention as allocated: 7
Initially ineligible: 5
Total refusal: 12)

Followed up (19,711)

Outcome: death from breast cancer over 11-16 years: (107)

Available for analysis (19,711)

Received physical examination alone as allocated (19,694)

Excluded from analysis: 30
( Did not receive intervention as allocated: 15
Initially ineligible: 5
Total refusal: 8
Lost file: 2)

Followed up (19,694)

Outcome: death from breast cancer over 11-16 years: (105)

Available for analysis (19,694)

Cumulative numbers of invasive breast cancers ascertained, by year after entry into the Canadian National Breast Screening Study-2.

Miller AB et al. JNCI J Natl Cancer Inst 2000; 92:1490-1499
CONCLUSIONS: Despite substantial increases in the number of cases of early-stage breast cancer detected, *screening mammography has only marginally reduced the rate at which women present with advanced cancer*. Although it is not certain which women have been affected, the *imbalance suggests that there is substantial overdiagnosis*, accounting for nearly a third of all newly diagnosed breast cancers, and *that screening is having, at best, only a small effect* on the rate of death from breast cancer.

Breast Cancer

Breast cancer seems also a “Will Rogers” phenomenon: “If the Okies left Oklahoma and moved to California, they raised the average intelligence level in both states”

Feinstein, I et al NEJM 312:1604-1608, 1985
Prostate Screening (USA)

Table 4. Causes of Death at 10-Year Follow-up. *

<table>
<thead>
<tr>
<th>Cause</th>
<th>Screening Group</th>
<th>Control Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any†</td>
<td>3953 (100.0)</td>
<td>4058 (100.0)</td>
</tr>
<tr>
<td>Cancer†</td>
<td>916 (23.2)</td>
<td>918 (22.6)</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>857 (21.7)</td>
<td>843 (20.8)</td>
</tr>
<tr>
<td>Stroke</td>
<td>107 (2.7)</td>
<td>109 (2.7)</td>
</tr>
<tr>
<td>Other circulatory disease</td>
<td>684 (17.3)</td>
<td>723 (17.8)</td>
</tr>
<tr>
<td>Respiratory disease</td>
<td>415 (10.5)</td>
<td>416 (10.3)</td>
</tr>
<tr>
<td>Digestive disease</td>
<td>141 (3.6)</td>
<td>133 (3.3)</td>
</tr>
<tr>
<td>Infectious disease</td>
<td>74 (1.9)</td>
<td>85 (2.1)</td>
</tr>
<tr>
<td>Endocrine or metabolic disease or immune disorder</td>
<td>155 (3.9)</td>
<td>188 (4.6)</td>
</tr>
<tr>
<td>Nervous system disease</td>
<td>128 (3.2)</td>
<td>113 (2.8)</td>
</tr>
<tr>
<td>Accident</td>
<td>238 (6.0)</td>
<td>235 (5.8)</td>
</tr>
<tr>
<td>Other</td>
<td>238 (6.0)</td>
<td>295 (7.3)</td>
</tr>
</tbody>
</table>

* Causes of death were determined by death certificate.
† Causes of death from any cause and cancer do not include prostate, lung, and colorectal cancer.
Prostate Screening (USA)

- After 7-10 years of FU, the rate of death from prostate cancer was very low and did not differ significantly between the two study groups (1)

- Recent update: After 13 years of follow-up, there was no evidence of a mortality benefit for organized annual screening in the PLCO trial compared with opportunistic screening, which forms part of usual care, and there was no apparent interaction with age, baseline comorbidity, or pretrial PSA testing (2).

The study involved 182,160 men between the ages of 50 and 74 years at entry, with a predefined core age group of 162,388 men 55 to 69 years of age. The trial was conducted in eight European countries. Men who were randomly assigned to the screening group were offered PSA-based screening, whereas those in the control group were not offered such screening. The primary outcome was mortality from prostate cancer.
Prostate Cancer Screening

Prostate Cancer Screening

To *prevent one death* from prostate cancer at 11 years of follow-up, *1055 men would need to be invited* for screening and *37 cancers* would need to be detected. There was no significant between-group difference in all-cause mortality.

The benefit of PSA screening was diminished by loss of QALYs owing to post-diagnosis long-term effects. Longer follow-up data from both the ERSPC and quality-of-life analyses are essential before universal recommendations regarding screening can be made.
Prostate Cancer: Over-treatment?

The authors conclude to the favourable impact of PSA screening expressed by the downward trend in mortality.

However, the trend is less sharp to the sharp rise in incidence. Also improvement in treatment can account for it.

An even acceptable explanation is that patients are diagnosed who don’t need a treatment.
Cancer Screening Problems: Conclusions

- Breast Cancer Screening:
  → Is more likely a personal advantage than a societal: who needs to pay for it?
  → Physical examination seems as good as mammographic screening!!

- Prostate cancer Screening:
  → Again it’s a personal advantage in a negligible amount.

*Is screening worthwhile the cost, anxiety, QoL?*