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What is the current evidence for progress against cancer?

Bruce Trock, PhD
"As far as the laws of mathematics refer to reality, they are not certain; as far as they are certain, they do not refer to reality."

--Albert Einstein
Change in the US Death Rates* by Cause, 1950 & 2003

* Age-adjusted to 2000 US standard population.

Sources: 1950 Mortality Data - CDC/NCHS, NVSS, Mortality Revised.
## Lifetime Probability of Developing Cancer, by Site, 1998-2000

<table>
<thead>
<tr>
<th>Site</th>
<th>Male Risk</th>
<th>Female Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>All sites</td>
<td>1 in 2</td>
<td>1 in 3</td>
</tr>
<tr>
<td>Prostate</td>
<td>1 in 6</td>
<td>n.a.</td>
</tr>
<tr>
<td>Breast</td>
<td>1 in 833</td>
<td>1 in 7</td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>1 in 13</td>
<td>1 in 17</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>1 in 17</td>
<td>1 in 18</td>
</tr>
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</table>

565,000 deaths from cancer annually

Progress Against Cancer

• NCI Goal in 1985: 50% decrease in cancer mortality by year 2000*:
  - 1985: 171 per 100,000
  - 2000: 158 per 100,000 (7.6% decrease)
  - 2004: 147 per 100,000 (14.0% decrease)

• How do you define progress against cancer?

• What has influenced progress?

• What will influence future progress?

* age-adjusted to 1970 population
Is overall mortality the best way to define progress?

• **Advantage:**
  - clinically most relevant; indicates biologic behavior
  - less subject to artifact

• **Disadvantage:**
  - obscures effects by age or tumor type
  - have to balance against true increases in incidence

• Is the most important issue whether decreases in mortality are due to improved treatment? Should the measure of progress reflect government spending?
Measures of Progress

• **Incidence – affected by:**
  - changes in risk factors
  - increase in detection, treatment of premalignant lesions
  - changes in definition of cancer

• **Survival – affected by:**
  - changes in early detection
  - changes in treatment

• **Mortality – affected by:**
  - changes in incidence
  - changes in survival
Mortality from All Malignant Neoplasms 1950 - 1982, by Race and Sex*

* Bailar, NEJM 1986; 314:1226
*Age-adjusted to the 2000 US standard population and adjusted for delay in reporting.
Data from American Cancer Society website, www.cancer.org:  Cancer_Statistics_2006_Presentation.ppt
Bailar's Arguments (1950-1982)

Failures:

- increase in overall mortality, and in most race-sex groups.
- no decrease in breast, prostate or lung cancer mortality
- some decreases not due to treatment or to programmatic efforts at prevention (stomach, colorectum, cervix)
- should some cancers be excluded from the evaluation? Even excluding lung, stomach, cervix, < 1% decrease in overall cancer mortality (in 1986), i.e. not “progress”
Cancer Death Rates* in US Men 1930-2002
(1950-1982 period covered by Bailar)

*Age-adjusted to the 2000 US standard population and adjusted for delay in reporting.
Data from American Cancer Society website, www.cancer.org: Cancer_Statistics_2006_Presentation.ppt
Cancer Incidence Rates* US Men, 1975-2002

*Age-adjusted to the 2000 US standard population and adjusted for delay in reporting.
Data from American Cancer Society website, www.cancer.org: Cancer_Statistics_2006_Presentation.ppt
Cancer Death Rates* in US Women 1930-2002
(1950-1982 period covered by Bailar)

*Age-adjusted to the 2000 US standard population and adjusted for delay in reporting.
Data from American Cancer Society website, www.cancer.org: Cancer_Statistics_2006_Presentation.ppt
Cancer Incidence Rates* US Women, 1975-2002

*Age-adjusted to the 2000 US standard population and adjusted for delay in reporting.
Data from American Cancer Society website, www.cancer.org: Cancer_Statistics_2006_Presentation.ppt
US Tobacco Use vs. Lung Cancer Deaths, 1900-2000

Per capita cigarette consumption

Year

Per Capita Cigarette Consumption

Male lung cancer death rate

Female lung cancer death rate

Lung Cancer Death Rates (age-adjusted, per 100,000)

Mortality from All Malignant Neoplasms
1970 - 1994, by Race and Sex*

* vertical lines: last years of data in 1986 and 1997 Bailar papers

NCI, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2004
Mortality from All Malignant Neoplasms 1970 - 2004, by Race and Sex*

Death Rate (per 100,000)

- Black Males
- White Males
- Total
- Black Females
- White Females

* dotted lines: last years of data in 1986 and 1997 Bailar papers

NCI, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2004
Mortality from All Cancers except Lung, Oral/Larynx, Stomach, Cervix, 1970-2000*

NCI, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2004
### Annual percentage change in overall cancer mortality rates (1975-2004) *

<table>
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<tr>
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<tbody>
<tr>
<td><strong>Both Sexes</strong></td>
<td>0.5 %</td>
<td>-0.3% **</td>
<td>-1.1%</td>
<td>-2.1%</td>
</tr>
<tr>
<td><strong>Males</strong></td>
<td>0.9 %</td>
<td>0.3%</td>
<td>-1.5%</td>
<td>-2.6%</td>
</tr>
<tr>
<td><strong>Females</strong></td>
<td>0.6 %</td>
<td>-0.2%</td>
<td>-0.8%</td>
<td>-1.8%</td>
</tr>
</tbody>
</table>
**Mortality from All Cancers 1970-2000, by Age & Sex**
(extends Figure 2 from Bailar, NEJM 1997)

NCI, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2004
Mortality from Lung Cancer 1970-2000, by Age & Sex*
(extends Figure 4 from Bailar, NEJM 1997)

NCI, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2004
Breast cancer mortality trends in countries that have introduced screening*

Mortality from Breast Cancer 1970-2000, by Age & Sex*
(extends Figure 3 from Bailar, NEJM 1997)

NCI, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2004
Cancer Incidence Rates* US Women, 1975-2004

*American Cancer Society website:
Age-adjusted to 2000 US standard population (Source: SEER 2004).
Breast cancer incidence rates 1999-2004*

* SEER data
Breast cancer incidence 1975-2004, by age group

Adapted by CTLT from Ravdin, NEJM 2007.
Breast cancer incidence vs. HRT prescriptions 2000-2004*

Adapted by CTLT from Ravdin, NEJM 2007.
Bailar’s claims of failure (1986-1994) vs. updated mortality data

- Large increases in breast and prostate 1974-1990 are overdiagnosis so don’t balance mortality [mortality now decreasing faster than incidence: treatment, early detection]


- 1970-1994 decreases in stomach, cervical and colorectal mortality due to decreased risk factors, early detection, but not to treatment or prevention programs [mortality continues to decrease without major treatment advances]
What Bailar Ignores

• Mortality decreased dramatically in ages < 55 (1973-90) or < 65 (1991-2004), not all due to early detection or cohort effects (breast).

• Different trends by age group represents a statistical interaction - in such a setting, overall age-adjusted rates are misleading

• Treatment advances (chemotherapy) slower to occur in elderly (other illnesses, less aggressive treatment, cohort effects).

• Since 1991, decreases in all of 10 biggest cancer killers
Where are we Now?

• Mortality was increasing through early 1990’s, is now decreasing or flat in all major cancers except liver (males), lung (females - may be starting to decrease)

• Annual percentage changes in mortality: 2000-2004 (2.1% decrease) vs. 1970-1990 (0.5% increase)

• Decreases in mortality have been influenced more by risk factor reduction and early detection than treatment

• Some mortality increases have clearly identifiable risk factors (melanoma, non-Hodgkin’s lymphoma, liver)

• Some increases are unexplained (testis, esophageal adenocarcinoma, multiple myeloma)

Cancer in the absence of screening

Birth

cancer appears clinically

Death

Survival Time
Appropriate diagnosis due to screening

Birth

cancer detected by screen

Pre-clinical Phase

cancer appears clinically

Survival Time
Screening effective, life extended

Birth → cancer detected by screen → increased survival time → death

Death
Lead-time bias, life not extended: treatment doesn't cure screened cancers.
Overdiagnosis, life not extended: screening identifies tumors of low lethality