The mortality-to-incidence ratio is not a valid proxy for cancer survival

Cancer Survival Group

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The mortality-to-incidence ratio (M/I ratio) – 20\textsuperscript{th} century


- “Deaths in period”
- \textit{If} no. of deaths \textit{exceeds} no. of cases, suggests incomplete registration
- Deaths from an independent data source
- \textit{Indicator of the completeness of cancer registration (M/I \%)}

• M/I ratio “bears strong inverse association to survival”, and …

• “… taken in conjunction with known average survival rates, should give some indication as to completeness.”

• M/I ratio was not being proposed as a surrogate for cancer survival
The mortality-to-incidence ratio (M/I ratio) – 20th century

“Cancer Registration: Principles and Methods” (1991)

- *If* the registry cannot estimate survival, the M/I ratio [*case-fatality ratio*] …
- “… can be used as an *indicator* of survival.” [*duration not specified*]

But

- Registered patients and persons certified as having died of cancer *not* the same
- M/I ratio only “an indirect description of the general survival experience.”
M/I ratio is the “case-fatality ratio”, or the “case-fatality rate”

(1-M/I ratio) is the survival [rate] [duration not specified!]

Global Burden of Cancer (Economist Intelligence Unit, 2009)

M/I ratio approximates the percentage of people who die of cancer
M/I ratio approximates the cancer-specific mortality rate

Disease Control Priorities: Cancer (World Bank, 2015)

M/I ratio estimates cancer prevalence, as a surrogate for access to care

Global Burden of Disease (IHME, 2018)
Mistaken in principle

• Mortality and incidence rates do not refer to the same persons

• Inaccurate cancer mortality rates
  – Incomplete death registration
  – Inaccuracy in certification of cause(s) of death
  – Inaccuracy in selecting the underlying cause of death

• Death certificate less precise than registry diagnosis

• No mathematical relationship between (1-M/I ratio) and survival

(1-M/I ratio) is not a valid proxy for survival
Mortality rates – questionable validity

56 million deaths every year: two-thirds are not registered

Of 115 WHO Member States reporting mortality data in 2003:

• Only 64 had high-quality vital registration with cause of death
• Excl. N America, Europe – one-third with usable mortality statistics
• Africa, Southeast Asia – half do not record cause of death
(1-M/I ratio) is **not** a valid proxy for survival

2 – Misleading in practice

- M/I ratio calculated with numbers *or* rates
- Rates either crude *or* age-standardised (standard not stated)
- Survival declines with time since diagnosis …
- No intrinsic reason why (1-M/I ratio) should estimate **five**-year survival
(1-M/I ratio) is not a valid proxy for survival – or is it?


   England, 19 cancers in men, 20 in women
   Diagnosed 1981-2009, followed up to 2013

   • Age-standardised mortality rates/10^5 p-yr (2013 European standard)
   • Age-standardised incidence rates/10^5 p-yr (2013 European standard)
   • (1-M/I ratio)
   • Age-standardised net survival up to 10 years (ICSS standard)
   • Flexible excess hazard regression model, age and year of diagnosis
(1-M/I ratio) is not a valid proxy for survival – or is it?

4 - Absolute difference from 5-year net survival, for 2009:

- Less than 5% for 12 cancer-sex combinations
- 5% to 14.9% for 15 cancer-sex combinations
- 15% or more for 12 cancer-sex combinations

Dramatic changes in this difference between 1981 and 2009 – most cancers

Difference from 1-year or 10-year survival generally even wider
Less than 5% difference in 2009 – breast cancer

Age-standardised net survival or (1-M/I)

1-(M/I) ratio

Mortality rate

Incidence rate

Calendar year of diagnosis (incidence, survival) or of death (mortality)
Less than 5% difference in 2009 – breast cancer

- 1-year net survival
- 5-year net survival
- 10-year net survival
- Incidence rate
- 1-(M/I) ratio
- Mortality rate

Age-standardised net survival or (1-M/I)

Calendar year of diagnosis (incidence, survival) or of death (mortality)
More than 15% difference in 2009 – stomach cancer (men)
More than 15% difference in 2009 – stomach cancer (men)
More than 15% difference in 2009 – stomach cancer (men)
1-M/I ratio is *invalid* as a survival metric …

… that would be robust for

- all cancers
- all countries
- all calendar periods
- any particular time since diagnosis
(1-M/I ratio) is indefensible as a proxy for survival

- No theoretical basis
- Not an observation of survival in a cohort of cancer patients
- Inconsistent between cancers (sexes, countries…)
- Relationship not stable over time, for any cancer
- Public health interest wider than “5-year survival league tables”
(1-M/I ratio) is indefensible as a proxy for survival

The (1-M/I ratio) does not:

• Enable quality control of individual records
• Reflect survival by time since diagnosis (survival curve)
• Reflect survival by age, stage, SES, race/ethnicity, region, …
• Take account of background mortality
• Enable evaluation of health service effectiveness
• Enable derivation of “cure”, avoidable deaths, …
• Enable robust comparison between countries
The Mortality-to-Incidence Ratio Is Not a Valid Proxy for Cancer Survival

Libby Ellis, PhD; Aurélien Belot, PhD; Bernard Rachet, PhD, MD; and Michel P. Coleman, BM, BCh

PURPOSE The ratio of cancer mortality and cancer incidence rates in a population has conventionally been used as an indicator of the completeness of cancer registration. More recently, the complement of the mortality-to-incidence ratio (1-M/I) has increasingly been presented as a surrogate for cancer survival. We discuss why this is mistaken in principle and misleading in practice.

METHODS We provide an empirical assessment of the extent to which trends in the 1-M/I ratio reflect trends in cancer survival. We used national cancer incidence, mortality and survival data in England to compare trends in both the 1-M/I ratio and net survival at 1, 5, and 10 years for 19 cancers in men and 20 cancers in women over the 29-year period from 1981 to 2009.
<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Men Absolute Difference</th>
<th>Men 1-M/1 Ratio</th>
<th>Men 5-year NS</th>
<th>Men Difference</th>
<th>Women Absolute Difference</th>
<th>Women 1-M/1 Ratio</th>
<th>Women 5-year NS</th>
<th>Women Difference</th>
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<td>7.0</td>
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<td><strong>5%-14.9% difference</strong></td>
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<td>Larynx (men)</td>
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<td>Lung</td>
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<td>9.5</td>
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<td>6.1</td>
<td>21.0</td>
<td>12.3</td>
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<td><strong>Difference of 15% or more</strong></td>
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