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

Cancer Survival Group

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

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## The mortality-to-incidence ratio (M/I ratio) – 20th century

*"Cancer Incidence in Five Continents, Vol. III" (1976)*

- "Deaths in period"
- *If* no. of deaths *exceeds* no. of cases, suggests incomplete registration
- Deaths from an independent data source
- Indicator of the completeness of cancer registration (M/I %)

## The mortality-to-incidence ratio (M/I ratio) – 20th century

*"Cancer Incidence in Five Continents, Vol. VI" (1993)*

- 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."

## Increasingly mis-used as a proxy for survival (or anything)

- 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)*

## (1-M/I ratio) is <u>not</u> a valid proxy for survival

### 1 – 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

## 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?

**3 – Empirical evaluation of trends, by single year 1981-2009**
**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?

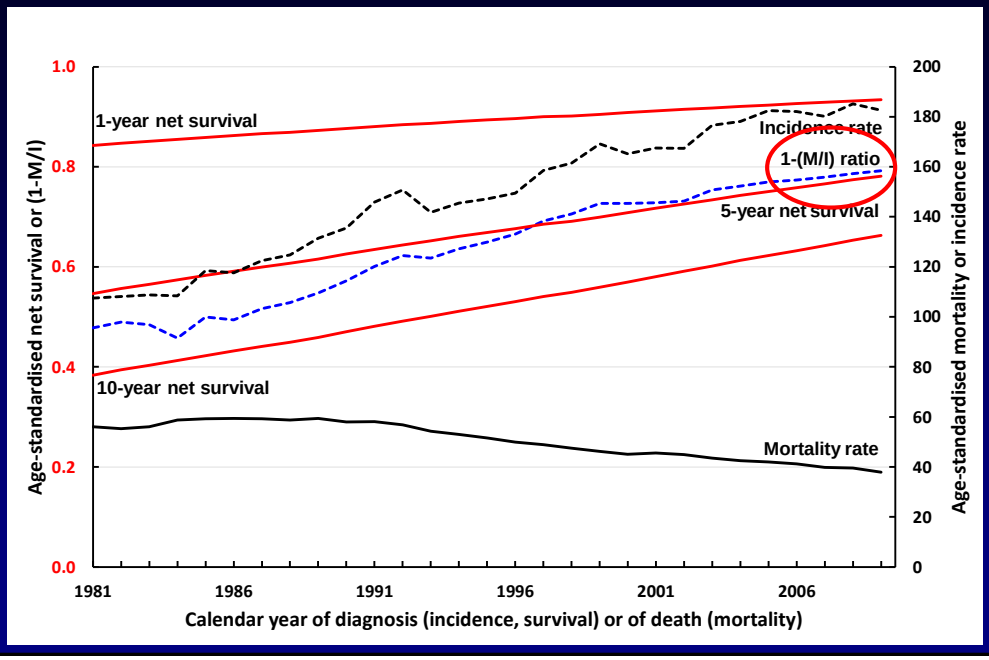
**4 - Absolute difference from 5-year net survival, *for 2009*:**

- **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

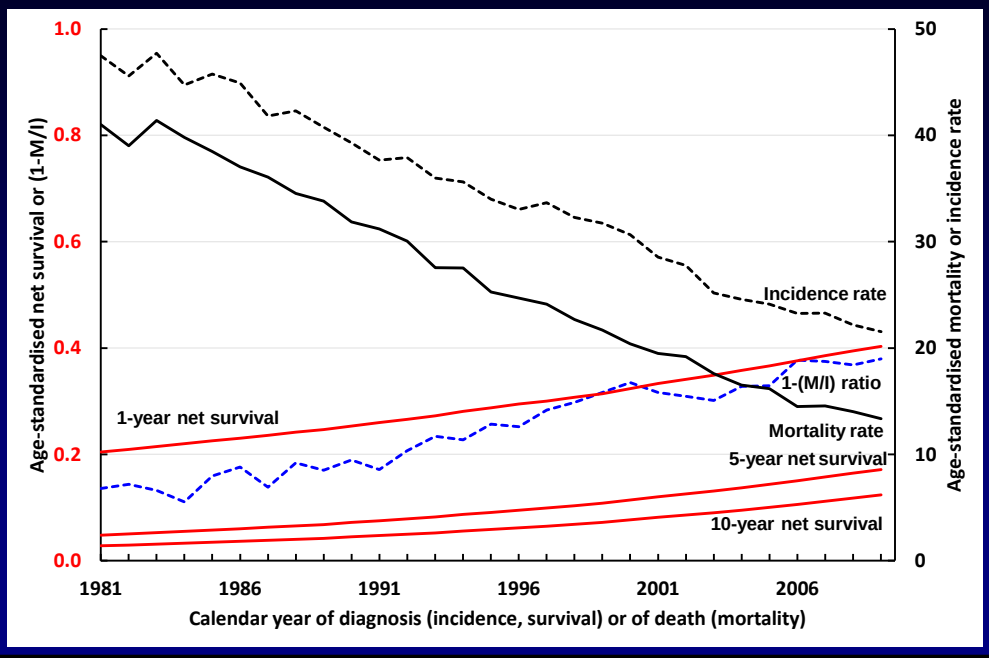
**Dramatic changes in this difference between 1981 and 2009 – most cancers**

**Difference from 1-year or 10-year survival generally even wider**

## Less than 5% difference in 2009 – breast cancer




## More than 15% difference in 2009 – stomach cancer (men)



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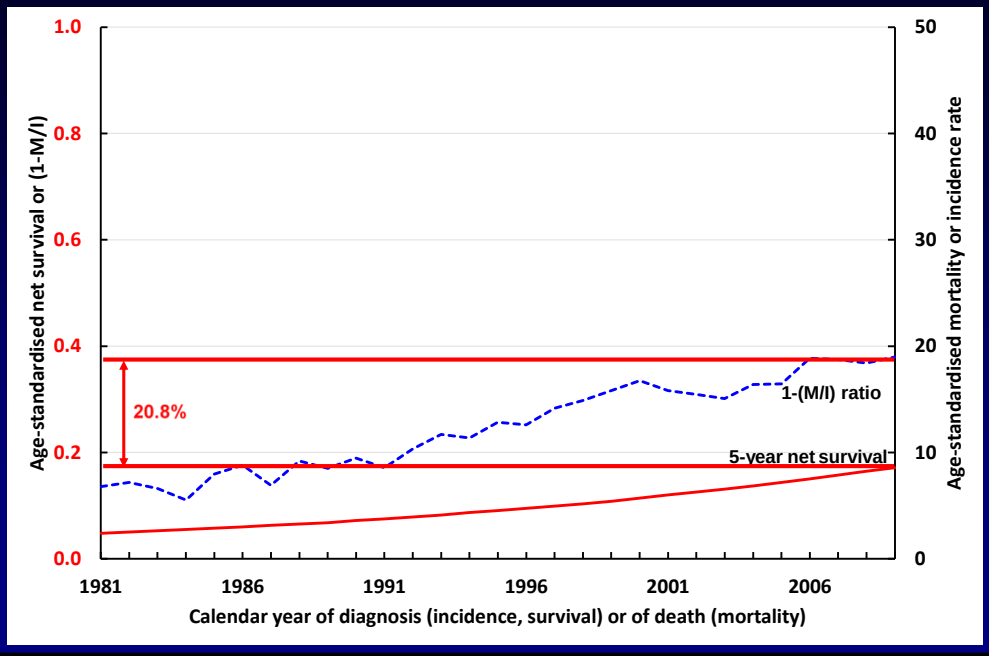



## 1-M/I ratio is *invalid* as a survival metric …

**… 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

## Increasingly mis-used as a proxy for survival (or anything)

**"Mortality-to-incidence ratio is calculated by dividing the mortality rate by the incidence rate. It presents a population-based indicator of survival and is a good approximation of the 5-year relative survival rate for most but not all tumor sites [25]."**

*Cancer Control in Central and Eastern Europe: Current Situation and Recommendations for Improvement. Vrdoljak et al., Oncologist 2016*

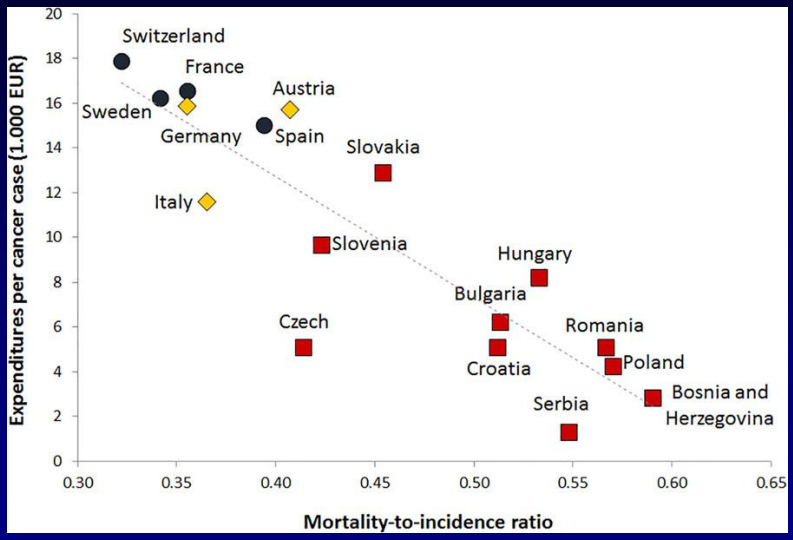
## Increasingly mis-used as a proxy for survival (or anything)

**The M/I ratio, which is significantly worse in CEE, is correlated with the expenditures on oncology drugs. Consequently, more investment in oncology drugs most likely will result in better M/I ratios in CEE countries.**

**Policy makers should also be aware that expenditure on oncology drugs makes up only about 11% of total cancer costs, and that novel treatments increase survival and lower the costs associated with morbidity and mortality.**

*Expenditures on Oncology Drugs and Cancer Mortality-to-Incidence Ratio in Central and Eastern Europe. Vrdoljak et al. Oncologist 2018*

# Mortality-to-incidence ratio and expenditure on cancer drugs in 17 countries




**Age-standardised national incidence and mortality rates in each country**
**All cancers combined**
**in 2012**

**National expenditure per incident cancer patient on 35 antineoplastic and immunomodulatory drugs [ATC L01]**
**in 2015**

*Vrdoljak et al., Oncologist 2018*

# Increasingly mis-used as a proxy for survival (or anything)

**Conclusion. There is a financial threshold for oncology drugs per cancer case needed to increase survival. Based on significantly lower expenditures for oncology drugs in CEE in comparison with WE, more investment for drugs as well as better, more organized, value-oriented consumption is needed.**

*Expenditures on Oncology Drugs and Cancer Mortality-to-Incidence Ratio in Central and Eastern Europe. Vrdoljak et al. Oncologist 2018*

# The Mortality-to-Incidence Ratio Is Not a Valid Proxy for Cancer Survival

Libby Ellis, PhD[1]; Aurélien Belot, PhD[1]; Bernard Rachet, PhD, MD[1]; and Michel P. Coleman, BM, BCh[1]

**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.

*Ellis L, Belot A, Rachet B, Coleman MP. J Global Oncol 2019*