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 not 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?

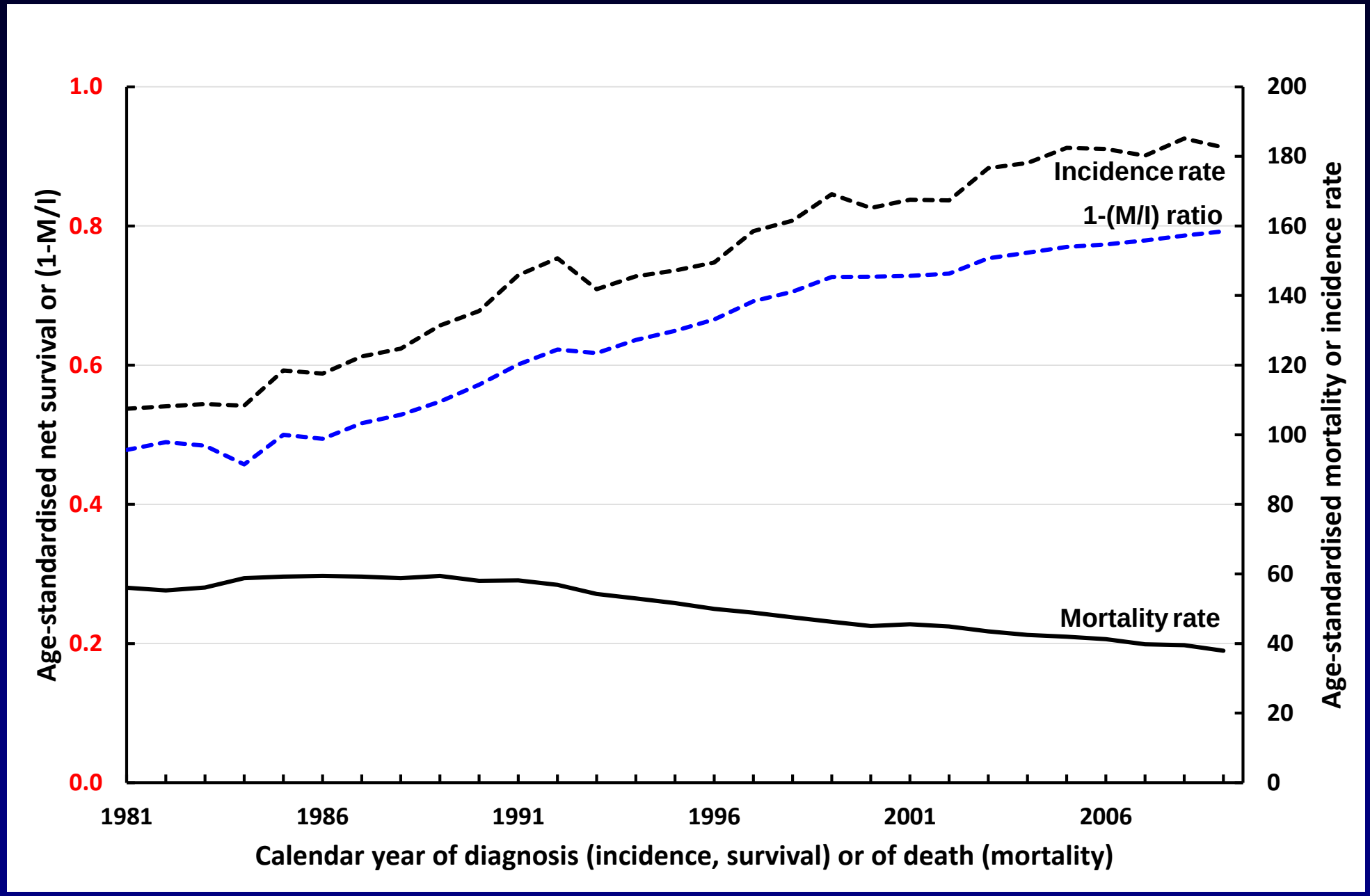
4 - Absolute difference from 5-year net survival, *for 2009*:

- **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

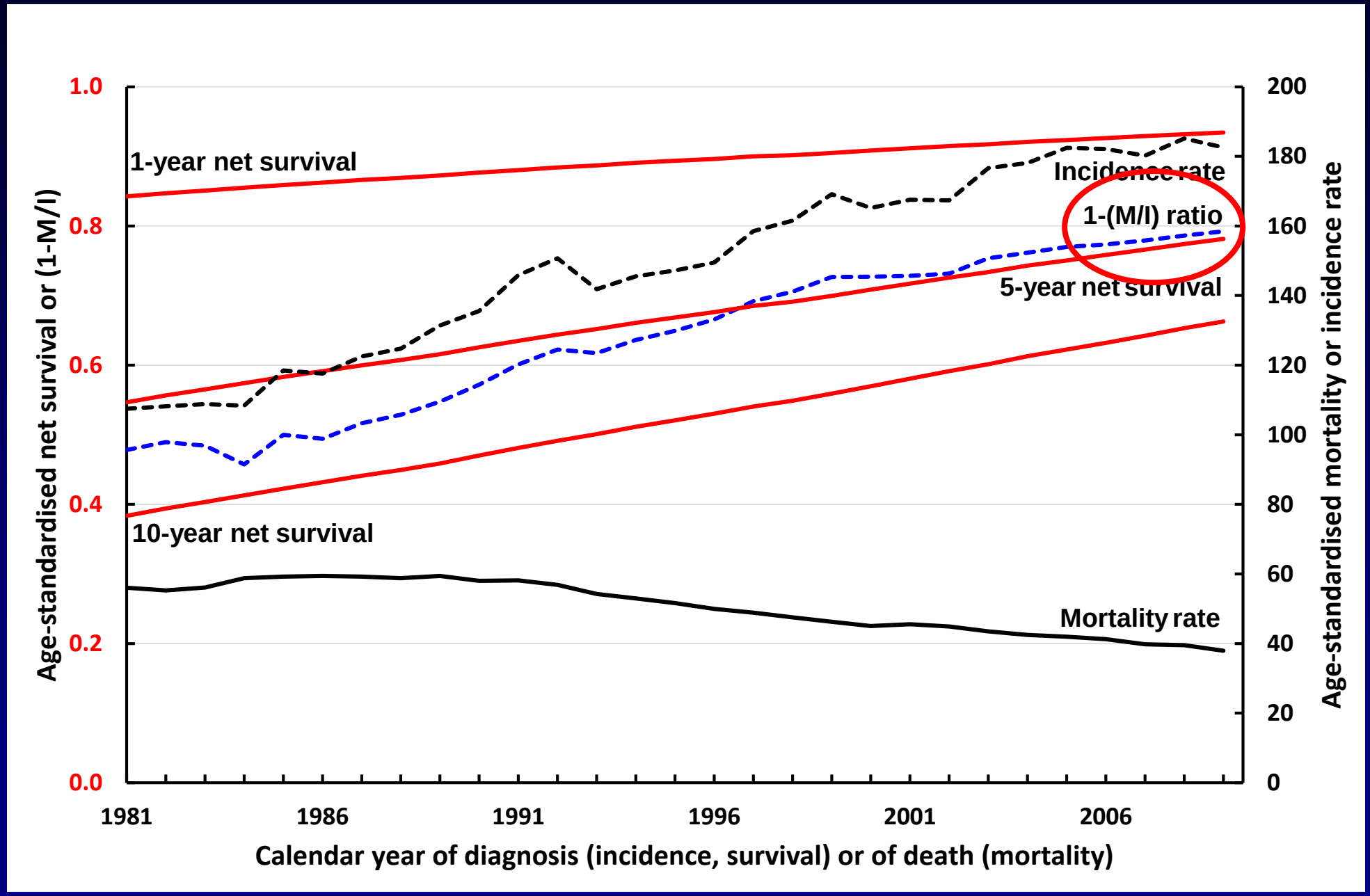
Dramatic changes in this difference between 1981 and 2009 – most cancers

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

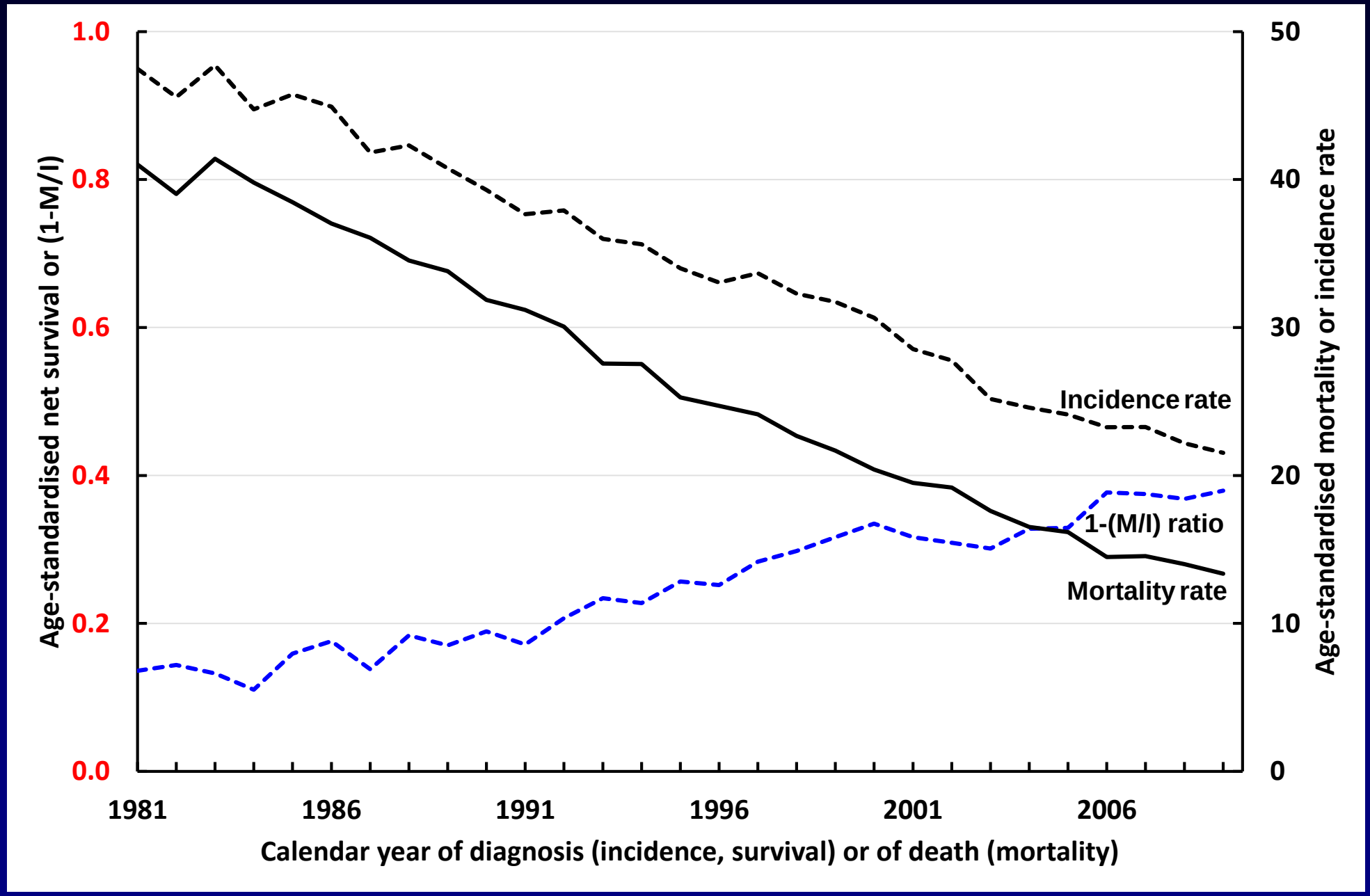
Less than 5% difference in 2009 – breast cancer



Less than 5% difference in 2009 – breast cancer



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



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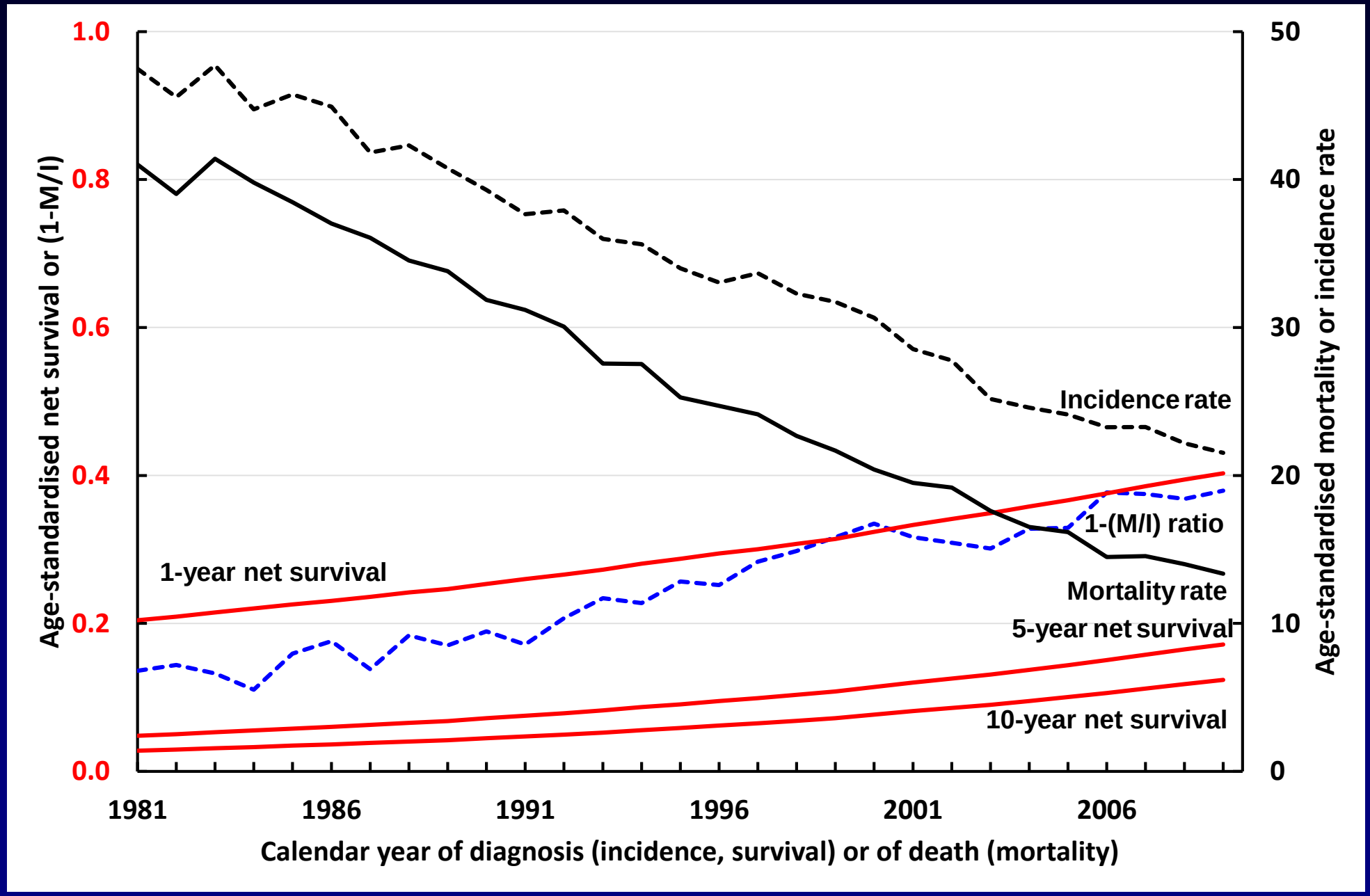

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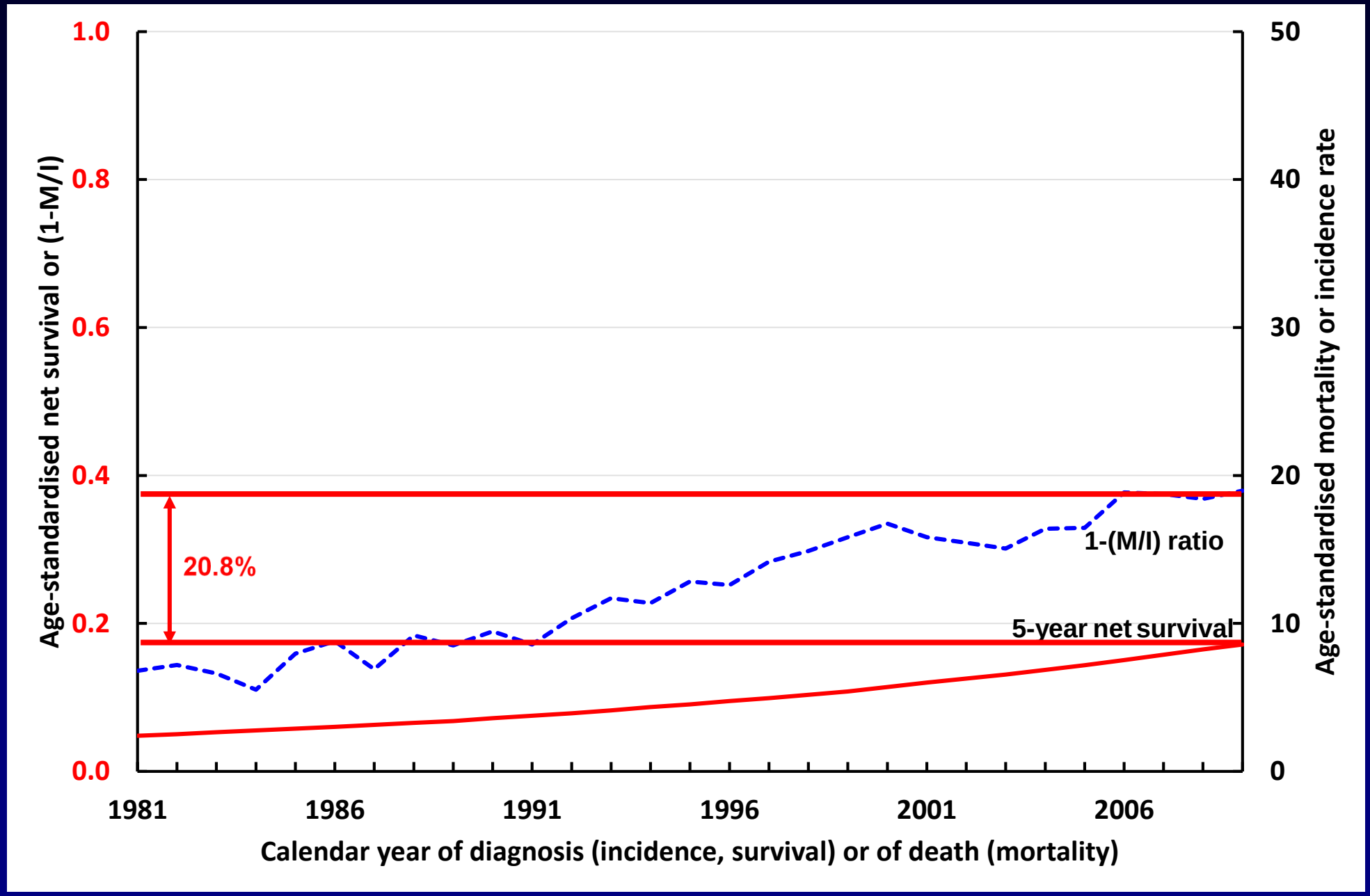

1-M/I ratio is *invalid* as a survival metric …

… 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**

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

TABLE 1. Absolute Difference (%) Between the 1-M/I Ratio (%) in 2009 and Age-Standardized 5-Year Net Survival (%) for Patients Diagnosed in 2009, by Cancer and Sex

	Men			Women		
Absolute Difference	**1-M/I Ratio**	**5-year NS**	**Difference**	**1-M/I Ratio**	**5-year NS**	**Difference**
Less than 5% difference*						
Esophagus	8.4	13.3	–4.9	13.4	15.6	–2.2
Pancreas	7.4	4.4	3.1	6.7	4.7	2.0
Melanoma	84.8	77.7	7.0	89.5	85.6	3.9
Breast (women)	.	.	.	79.2	78.1	1.1
Ovary	.	.	.	43.1	43.9	–0.8
Testis	96.6	95.3	1.3	.	.	.
Thyroid	77.6	74.4	3.2	88.9	81.8	7.1
Hodgkin disease	79.8	79.7	0.1	84.4	82.9	1.5
Non-Hodgkin lymphoma	61.3	55.4	5.9	65.2	61.0	4.2
5%-14.9% difference						
Larynx (men)	68.4	58.2	10.2	.	.	.
Lung	15.5	9.5	6.1	21.0	12.3	8.7
Uterus	.	.	.	78.8	71.4	7.4
Prostate	73.2	66.8	6.4	.	.	.
Kidney	62.9	48.7	14.3	61.9	51.7	10.2
Multiple myeloma	49.7	37.7	12.1	46.0	37.9	8.2
Leukemia	47.5	40.1	7.4	48.0	40.7	7.3
Difference of 15% or more †						
Stomach	37.9	17.2	20.8	37.7	18.6	19.1
Colon	64.9	45.6	19.3	66.1	47.6	18.5
Rectum	63.7	48.5	15.2	63.4	51.4	12.0
Liver	38.7	11.2	27.5	41.7	10.2	31.5
Cervix	.	.	.	97.4	64.9	32.6
Bladder	75.7	48.4	27.3	70.3	43.1	27.3
Brain	35.3	18.9	16.5	39.2	21.3	17.9