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Examining the relationship between incidence and mortality for commonly diagnosed cancers in the USA: an observational study using population-based SEER database

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ABSTRACT

Objective Incidence and mortality are fundamental epidemiologic measures of cancer burden, yet few studies have examined individual cancers to determine how these measures correlate across place. We assessed the relationship between incidence and mortality for commonly diagnosed cancers in the USA.

Design Population-based observational study of US counties.

Setting and participants The Surveillance, Epidemiology and End Results (SEER) database was used to obtain incidence (2000–2016) and mortality (2002–2018) data for the 12 most commonly diagnosed non-haematologic cancers.

Outcome measures County-level correlation between cancer incidence and mortality. Cancers were grouped into terciles based on the population-weighted correlation coefficient (r). We also examined the 10 year risk of death, both from the diagnosed cancer and other causes.

Results County-level incidence and mortality were strongly correlated in some cancers, yet uncorrelated in others. Cancers in the high-correlation tercile (r range: 0.96 to 0.78) included lung, stomach, liver and pancreas. For patients with these cancers, the risk of death from the diagnosed cancer was >4-times the risk of death from other causes. The moderate-correlation tercile (r: 0.75 to 0.58) included cancers of the colon, bladder, kidney and uterus. There was little or no relationship between incidence and mortality for cancers in the low-correlation tercile (r: 0.33 to −0.10): melanoma, prostate, breast and thyroid. The risk of death from the diagnosed cancer for these patients was either lower or no different than their risk of death from other causes.

Conclusions For some cancers in the USA, the fundamental epidemiologic measure of disease frequency—incidence—now has little relationship with cancer death (mortality). Low correlations are most likely explained by differences in diagnostic practice leading to variable amounts of cancer overdiagnosis between different US counties.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ We systematically analysed incidence and mortality across US counties using population-level cancer registries reporting to Surveillance, Epidemiology and End Results.
⇒ We evaluated changes in relationship between county-level incidence and mortality over a 40 year period.
⇒ We could only analyse counties with at least 10 deaths across the analysed period and therefore some US counties were excluded from the analysis.

INTRODUCTION

Increasing cancer incidence is a concerning finding that requires investigation. Surges in cancer incidence in a geographic region (a 'cancer cluster') can cause considerable public concern and may even garner legislative attention.[1] For example: in the 1970s, reports of elevated melanoma incidence at the Lawrence Livermore National Laboratory[2] made national news[3] and triggered investigations from both the California State Legislature[4] and the US Department of Energy.[5] In the early 1990s, elevated breast cancer incidence in Long Island counties in New York State led to federal legislation and $30 million in funding to explore potential causes.[6] And more recently, the finding of 20–50 times higher than expected thyroid cancer incidence in children living near the tsunami-damaged Fukushima reactor[7] likely served as a motivating factor for a decade-long United Nations investigation.[8] In each case, the implicit assumption was that environmental causes explained much of the incidence rise and that a geographic cluster with high cancer occurrence (incidence) would be destined to experience high rates of the feared outcome of cancer (mortality).

There has been a growing recognition, however, that reported cancer incidence is not simply a reflection of true cancer

occurrence. It is also a reflection of diagnostic scrutiny: in simple terms, how hard doctors and the public are looking for cancer. Changes in diagnostic scrutiny have led to rapid, iatrogenic swings in the reported incidence of breast,[9 10] prostate,[11] thyroid[12] and even lung cancer.[13 14] Because incidence is considerably more sensitive to diagnostic scrutiny than is mortality, variable diagnostic scrutiny might be expected perturb the incidence–mortality relationship.

In prior work, examining the roles of UV radiation and diagnostic scrutiny in melanoma diagnosis, we were struck by the absence of a correlation between melanoma incidence and melanoma mortality across 727 US counties.[15] These findings piqued our interest to further explore the incidence–mortality relationship in other cancers. In this study, we examine the county-level incidence–mortality correlation for the 12 most commonly diagnosed non-haematologic cancers in the USA.

METHODS

Hypotheses

We hypothesised that there would be considerable variation in the correlation between incidence and mortality across cancer types. Cancers with high incidence–mortality correlations were expected to have high case-fatality rates and to be relatively unaffected by diagnostic scrutiny (eg, screening). On the other hand, we hypothesise cancers with low incidence–mortality correlations would have lower case-fatality rates, be more affected by diagnostic scrutiny and possibly have more effective treatments.

Overview

We assessed incidence and mortality of the most commonly diagnosed non-haematologic cancers in the USA (excluding non-melanoma skin cancer). As in prior published work, we focused on solid tumours which comprise approximately 90% of cancer diagnoses.[16] Common cancers were defined as those with at least 25 000 diagnoses in 2020 according to estimates by the American Cancer Society.[17] The 12 cancers that met these criteria in descending order of frequency were as follows: breast, lung, melanoma, prostate, colorectal, bladder, kidney, uterus, pancreas, thyroid, liver and stomach. Within each cancer site, we analysed the relationship between incidence and mortality across place—using the county as our unit of analysis.

Data and sample frame

County-level incidence data were from the Surveillance, Epidemiology and End Results (SEER) Programme of the National Cancer Institute (SEER 22 Registries, comprised of 1086 counties). County-level mortality data were from the National Vital Statistics System maintained by the National Center for Health Statistics. All ages were included, and all rates were age-adjusted to the 2000 US standard population.[18]

Our sample frame included incident cancers (in situ and invasive) diagnosed from 2000 through 2016. To allow for a delay between diagnosis and death, our ascertainment of mortality was delayed by 2 years (from 2002 through 2018). Because death from certain cancers is a rare event and US vital statistics suppress data from counties with less than 10 deaths over the study duration, the number of counties available for analysis differed by cancer type. For example, lung cancer (highest mortality) contributed 1071 counties to our analysis, whereas thyroid cancer (lowest mortality) only contributed 223 counties.

We further restricted our sample frame in selected cancers that disproportionally or exclusively affect certain demographic groups: breast and uterus cancer were restricted to females, prostate cancer was restricted to males and melanoma of the skin was restricted to non-Hispanic white Americans.

Analysis

To examine the strength of the relationship between incidence and mortality, we constructed scatterplots for each cancer. We calculated correlation coefficients using both parametric (Pearson's r) and non-parametric (Spearman's r) tests and performed population weighted analyses (for which the weight is the county population), as recommended by Solon *et al*.[19] Because the parametric and non-parametric correlations were virtually identical (online supplemental table 1), we report only the weighted Pearson's r the main text. Finally, we categorised the cancers into terciles based on the correlation coefficient (ie, high, moderate and low)—a categorisation that was consistent regardless of the correlation measure used.

For cancers in the low correlation tercile, we performed stage-specific analyses (online supplemental table 2) to determine if the incidence–mortality correlation would be strengthened if incidence was restricted to either regional and metastatic stages combined or metastatic disease alone, as categorised by SEER. To determine the effect of our decision to include in situ cancers in our calculation of incidence, we performed restricted incidence–mortality analyses (ie, invasive cancer only) for the two cancers in which in situ diagnoses are common: breast cancer and melanoma. For all cancers, we also examined how the incidence–mortality relationship changed across time using the subset of SEER registries that were initiated in the 1970s (SEER 9 Registries, comprised of 200 counties).

To explore how competing causes of death might contribute to the variability of the incidence–mortality relationship, we analysed the 10 year cause-specific case-fatality data available in SEER 22 registries (representing nearly half of the US population). We identified all patients diagnosed with cancer in the period 2005–2009 in a SEER*Stat survival session (N ≈ 2.5 million). Thus, all patients had 10 years of follow-up, and the final year of data (2019) was prior to the COVID pandemic. We determined two crude probabilities for patients with each of the 12 cancers: (1) the 10 year risk of death attributable

Table 1 Twelve most common non-haematologic cancers in the USA ordered by the strength of county-level incidence–mortality correlation

Correlation tercile	2020 estimated counts		Incidence–mortality correlation	10 year risks of death†		
	Diagnoses	Deaths	Population-weighted Pearson's r (95% CI)	Diagnosed cancer (%)	Other causes (%)	Ratio
High						
Lung	228 820	135 720	0.96 (0.95 to 0.96)	78	13	5.9
Stomach	27 600	11 010	0.89 (0.87 to 0.90)	66	14	4.6
Liver	42 810	30 160	0.87 (0.85 to 0.88)	77	13	5.9
Pancreas	57 600	47 050	0.78 (0.76 to 0.80)	89	7	13.6
Moderate						
Colorectal	147 950	53 200	0.75 (0.72 to 0.77)	36	21	1.7
Bladder	81 400	17 980	0.71 (0.67 to 0.74)	24	30	0.8
Kidney	73 750	14 830	0.68 (0.64 to 0.72)	29	19	1.5
Uterus	65 620	12 590	0.58 (0.52 to 0.63)	21	13	1.6
Low						
Melanoma	196 060*	6850	0.33 (0.26 to 0.40)	9	16	0.5
Prostate	191 930	33 330	0.27 (0.21 to 0.32)	9	21	0.4
Breast	325 010*	42 170	0.03 (–0.03 to 0.09)	14	13	1.0
Thyroid	52 890	2180	–0.10 (–0.23 to 0.04)	4	7	0.6

Estimated counts of the number of diagnoses and deaths in the USA come from the American Cancer Society.[17] The 10 year risks of death are for patients diagnosed with cancer in the SEER 22 registries (see Supplemental Methods).
*Includes in situ cancers.
†The absolute risks are rounded to the nearest per cent; the ratio is calculated using full precision.

to the diagnosed cancer and (2) the 10 year risk of death attributable to other causes (see online supplemental methods). To facilitate comparisons across cancer, we calculated the ratio of these two probabilities producing cancer/other cause case-fatality ratios. Ratios above 1 imply that patients are more likely to die from the diagnosed cancer than from other causes, ratios below 1 imply that patients are more likely to die from other causes than from the diagnosed cancer.

Analyses were conducted using Stata, V.15.1 (StataCorp LLC) and MATLAB 2022b (MathWorks). We followed the Strengthening the Reporting of Observational Studies in Epidemiology reporting guideline. This research project was considered by The University of Texas at Austin Institutional Review Board as non-human participant research, and approval was not required.

Patient and public involvement

None.

RESULTS

Among the 12 non-haematologic cancers analysed, county-level incidence and mortality were strongly correlated in some cancers, yet uncorrelated in others. The data for the correlation between incidence and mortality among individual tumour types are arranged in descending order of strength and grouped into terciles in the table 1 and in online supplemental table 1.

Incidence–mortality correlation terciles (SEER 22)

High-correlation tercile

Scatterplots of the four cancers in the high-correlation tercile reveal a strong relationship between incidence and mortality—lung cancer, in particular, has nearly a linear relationship (figure 1). The population weighted Pearson's correlation coefficients were as follows: lung (r=0.96 (95% CI: 0.95 to 0.96)), stomach (r=0.89 (95% CI: 0.87 to 0.90)), liver (r=0.87 (95% CI: 0.85 to 0.88)) and pancreas (r=0.78 (95% CI: 0.76 to 0.80)). Notably, the high-correlation tercile had more than twice the number of estimated cancer deaths than either the moderate or low correlation tercile (223 940 vs 98 600 and 84 530), despite having the fewest number of cancers diagnosed (356 830 vs 368 720 and 765 890).

Moderate correlation tercile

The moderate correlation tercile includes colorectal cancer (r=0.75 (95% CI: 0.72 to 0.77)) and cancers of the bladder (r=0.71 (95% CI: 0.67 to 0.74)), kidney (r=0.68 (95% CI: 0.64 to 0.72)) and uterus (r=0.58 (95% CI: 0.52 to 0.63)). Scatterplots highlight that colorectal cancer stands out from cancers of the kidney, uterus and bladder—with an incidence–mortality relationship closer

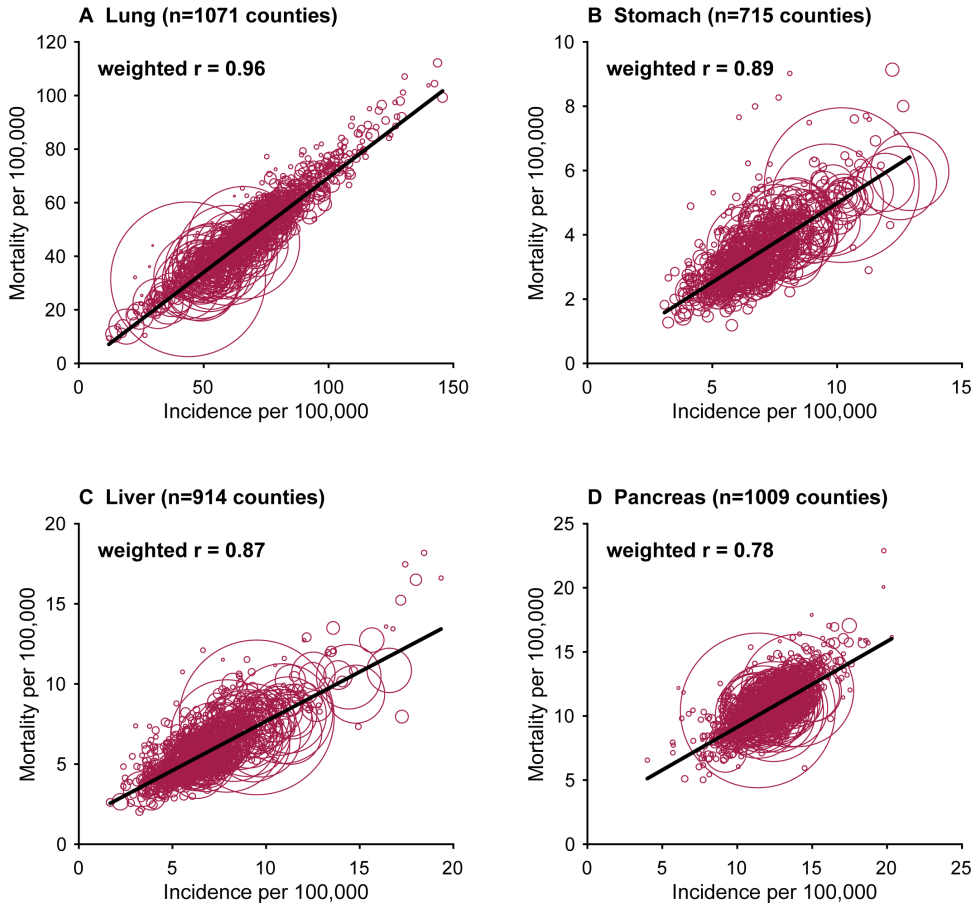

Figure 1 High-correlation tercile: common cancers in which incidence and mortality are tightly related across US counties. Incidence (2000–2016) and mortality (2002–2018) are both age-adjusted to the 2000 standard population and expressed per 100 000 person-years. Population-weighted correlation coefficients (Pearson's r) and simple linear regression lines are also shown. (A): Lung cancer. (B): Stomach cancer. (C): Liver cancer (D): Pancreas cancer.

to those of cancers in the high-correlation tercile (see online supplemental file 1).

Low correlation tercile

There was little or no relationship between incidence and mortality for cancers in the low correlation tercile: melanoma (r=0.33 (95% CI: 0.26 to 0.40)), prostate (r=0.27 (95% CI: 0.21 to 0.32)), breast (r=0.03 (95% CI: −0.03–0.09)) and thyroid (r=−0.10 (95% CI: −0.23–0.04)). This lack of correlation across counties is striking in the scatter plots of these cancers (figure 2), particularly for thyroid cancer in which incidence was negatively correlated with mortality. The low correlation tercile has double the number of diagnoses as the other terciles.

When incidence was restricted to regional and metastatic disease in stage-specific analyses, stronger incidence–mortality correlations were evident in breast cancer and melanoma, but not in prostate and thyroid cancer: breast (r=0.47 (95% CI: 0.42 to 0.53)), melanoma (r=0.42 (95% CI: 0.35 to 0.50)), prostate (r=0.33 (95% CI: 0.27 to 0.39)) and thyroid (r=0.08 (95% CI: −0.07 to −0.22)). When incidence was restricted to metastatic disease, stronger correlations were evident in all four cancers: breast (r=0.58 (95% CI: 0.53 to 0.64)), melanoma (r=0.48 (95% CI: 0.41 to 0.55)), prostate (r=0.49 (95% CI: 0.44 to 0.55)) and thyroid (r=0.64 (95% CI: 0.53 to 0.75)) (see online supplemental table 2).

Removing in situ melanomas and breast cancers strengthened the incidence–mortality correlation. In breast cancer, Pearson's correlation coefficient increased from 0.03 to 0.08 when restricted to the incidence of invasive cancer only; in melanoma, the increase was from 0.33 to 0.37. In 2020, an estimated 15% of all breast cancers were in situ as were more than 50% of all melanomas.[17]

Changes over time (SEER 9)

Figure 3 illustrates how the incidence–mortality relationship has changed over three periods for selected cancers that are considered candidates for screening (for all 12 cancers, see online supplemental figures 2–4). There has been little change in lung cancer (panel A), as might be expected given little or no screening in all three periods. Despite a shift from little or no screening in the earliest period to 60%–70% currently,[20] there has also been remarkably little change for colorectal cancer (panel B). The incidence–mortality relationship for prostate cancer has been more volatile: up then down (panel C)—possibly reflecting the volatility of diagnostic practice (ie, incidental detection following surgery to relieve

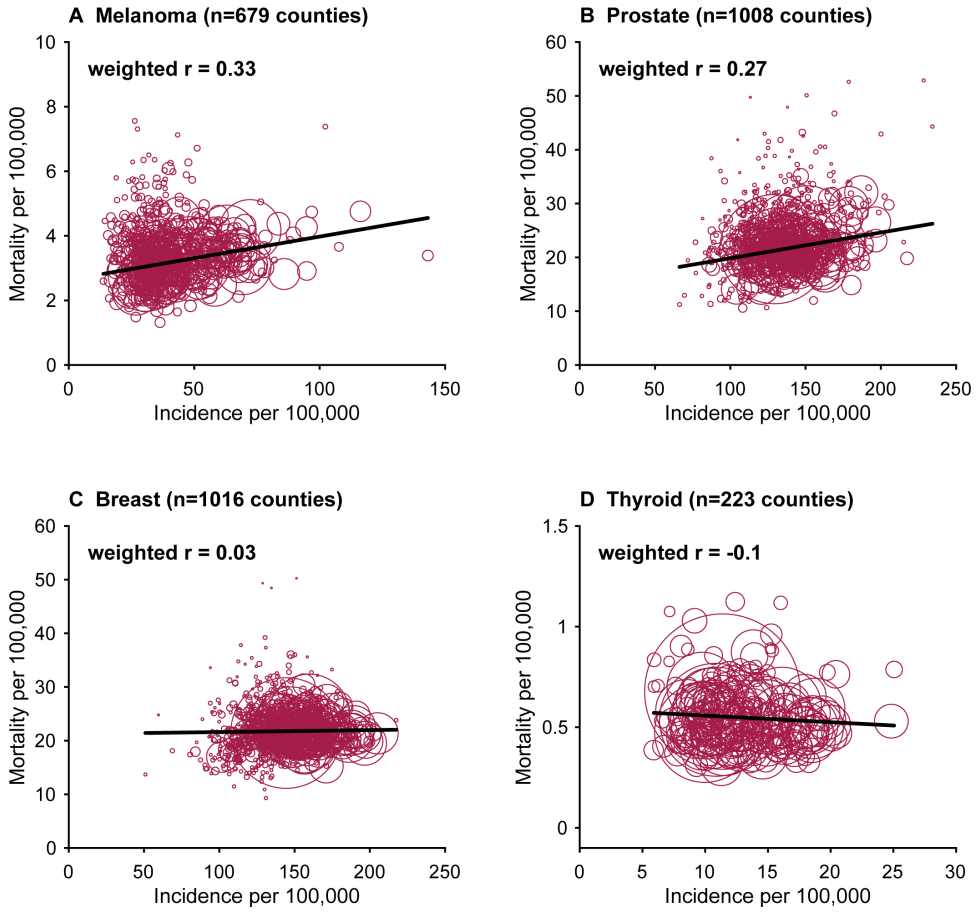

Figure 2 Low correlation tercile: common cancers in which incidence and mortality have little or no relationship across US counties. Incidence (2000–2016) and mortality (2002–2018) are both age-adjusted to the 2000 standard population and expressed per 100 000 person-years. Population-weighted correlation coefficients (Pearson's r) and simple linear regression lines are also shown. Breast cancer is restricted to females; melanoma is restricted to non-Hispanic white Americans. (A): Melanom. (B): Prostate cancer. (C): Breast cancer. (D): Thyroid cancer.

urinary obstruction and prostate-specific antigen (PSA) screening).

On the other hand, the incidence–mortality relationship has attenuated over time in breast cancer (panel D). The years 1976–1984 capture a period before screening mammography and the incidence–mortality correlation was strong (r=0.63). Plain film screening mammography was widespread during the 1988–1996 period and the correlation attenuated (r=0.45). The most recent period includes screening technologies in current use (digital, tomosynthesis, MRI, etc) and incidence–mortality correlation has disappeared (r=0.01).

Cancer/other cause case-fatality (SEER 22)

The ratio of the 10 year risk of death from the diagnosed cancer relative to the 10 year risk of death from other causes is shown in figure 4 and online supplemental table 3. The ratio is largest for patients with pancreatic cancer, who are more than 10 times as likely to die from their cancer as they are from other causes. The next largest ratio is approximately six for patients with lung cancer, a ratio likely attenuated by the increased risk of death from other causes (eg, cardiovascular, respiratory) associated with the major risk factor for lung cancer: cigarette smoking. For context, the ratio for all cancer sites combined is 2—meaning, for the average patient with cancer, the risk of death from the diagnosed cancer is twice that of other causes.

Figure 4 also illustrates the relationship between the cancer/other cause ratio and the incidence–mortality tercile. The ratios in the high tercile are all greater than 4. Among cancers in the moderate tercile, the ratios range from 1.7 to 0.8. Bladder cancer is the only cancer in this tercile with a ratio lower than one. Finally, in the low correlation tercile, the ratios are all 1 or lower—implying patients with these cancers are either more likely to die from other causes than they are from their diagnosed cancer (thyroid, melanoma and prostate) or equally likely (breast).

DISCUSSION

Among the 12 most commonly diagnosed cancers in the USA, however, we found striking variability in the incidence–mortality relationship—with correlation coefficients ranging essentially from 0 to 1. As hypothesised, cancers with higher case-fatality rates also had stronger

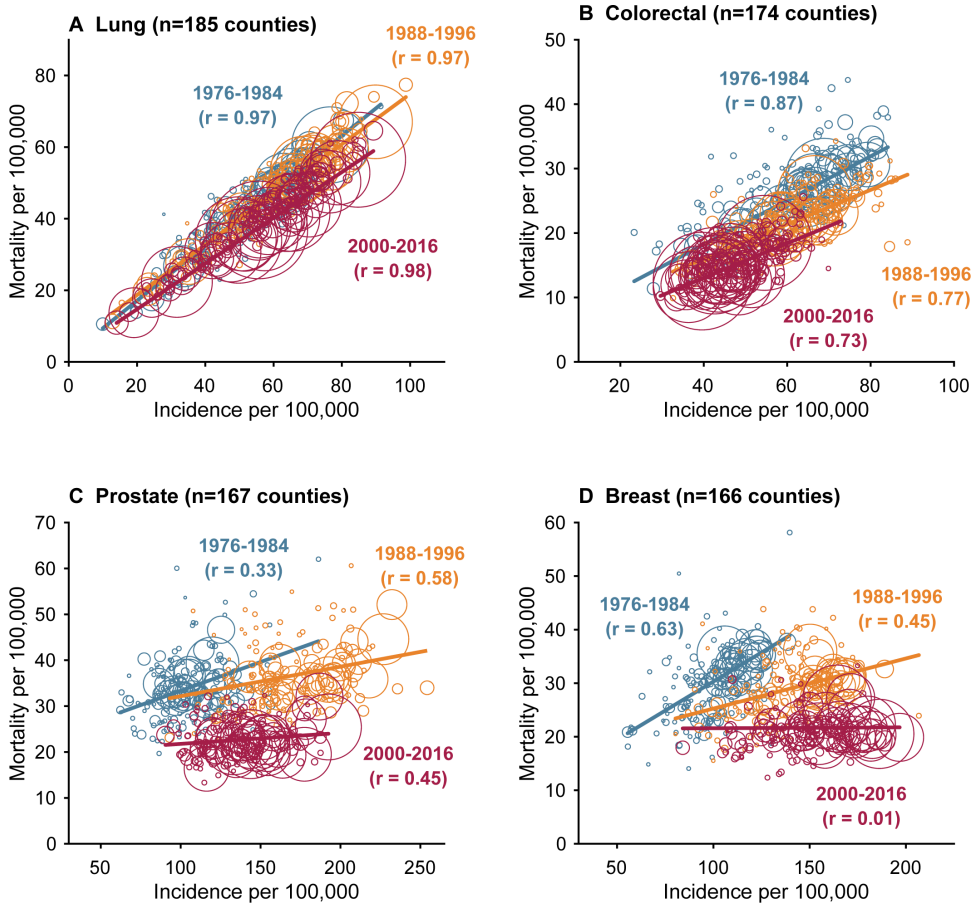

Figure 3 Changes in the incidence–mortality relationship over time for selected cancers in SEER 9 (200 counties). Labelled time periods correspond to incidence; mortality estimates are lagged by 2 years. Population-weighted correlation coefficients (Pearson's r) and simple linear regression lines are also shown. Panel A: lung cancer—little or no screening in all three periods. Panel B: colorectal cancer—little or no screening in 1976–1984, increasing to 60%–70% of target population currently. Panel C: prostate cancer—no screening/incidental detection from transurethral resection in 1976–1984, introduction of widespread PSA screening 1988–1996. Panel D: breast cancer (females)—premammography era (1976–1984), plain film mammography (1988–1996), digital mammography, tomosynthesis, MRI (2000–2016). PSA, prostate specific antigen; SEER, Surveillance, Epidemiology and End Results.

incidence–mortality correlation compared with cancers with lower case-fatality rates. Furthermore, most of the cancers in the lowest tercile have been targets for population wide screening (melanoma, breast and prostate) and had improvements in treatment.

While strong incidence–mortality relationships are readily explained (more clinically meaningful cancers=more deaths), what explains the weak incidence–mortality relationship for cancers in the low correlation tercile? This discordance could potentially be explained by considering two possible sources of variation across counties: (1) treatment and (2) diagnostic scrutiny.

Variation in treatment

Variable access to effective treatment could influence the incidence and mortality correlation across counties. For example, variations in social and economic drivers of health may restrict the delivery of cancer treatment affecting county-level incidence–mortality correlations. Therefore, our findings could in part be explained by substantial differences among counties in the quality of treatment for these particular cancers. Counties with high incidence rates of prostate cancer, melanoma, breast cancer and thyroid cancer might also be those with exceptionally effective treatment for these cancers—thus weakening the incidence–mortality relationship. Invoking this explanation, however, would require dramatic variations in the quality of cancer care for some cancers (eg, breast cancer), but not others (eg, colon cancer). Similarly, this explanation would require social drivers of health to influence the incidence and mortality correlation for some cancers but not others.

A related explanation might invoke changes in treatment effectiveness over time: that is, the more a cancer becomes curable, the less likely a correlation between incidence and mortality will exist. Without a doubt, the improvement in breast cancer treatment over the past 30 years has been a major success story of modern medicine. Perhaps, this explains the degradation in the breast cancer incidence–mortality relationship shown in

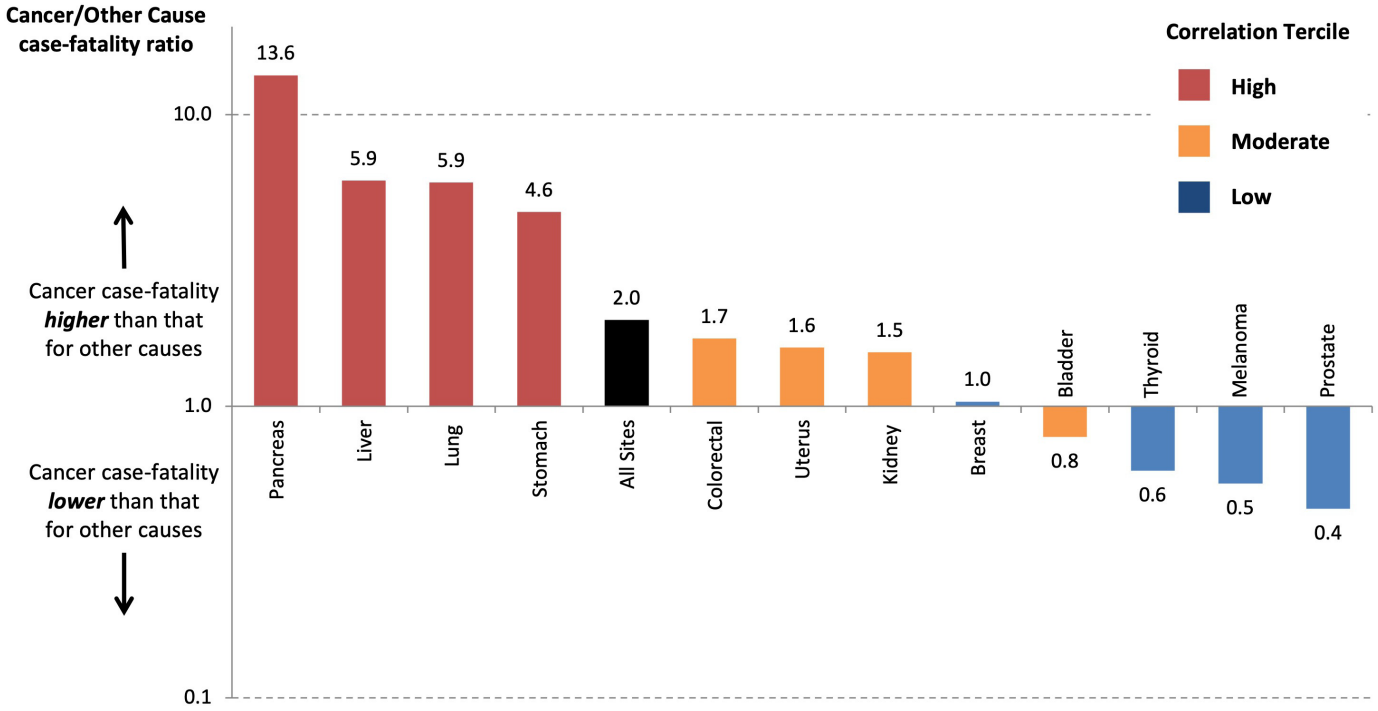

Figure 4 Cancer/other cause case-fatality ratios: 10 year risk of death from diagnosed cancer relative to the 10 year risk of death from other causes. Data are for patients diagnosed in 2005–2009 with one of the 12 most commonly diagnosed cancers in the USA. Each patient has 10 years of follow-up data (ie, no censoring). The correlation tercile for each cancer site is indicated with a distinct colour. For context, the ratio for all cancer sites combined is also shown.

figure 3. However, the treatments available for colorectal cancer today are also far better than they were 30 years ago: improved surgical technique, increasing reliance on high-volume providers and use of adjuvant chemotherapy for regional disease are all examples of changes that have reduced mortality. Yet the colorectal cancer incidence–mortality relationship has not exhibited a substantial degradation over time.

Variation in diagnostic scrutiny

The extent of diagnostic scrutiny is another possible explanation for weak incidence–mortality correlations across US counties. Some cancers are destined to metastasise and cause death, others are not. Increased diagnostic scrutiny disproportionately identifies the latter. As more cancers not destined to cause death are identified, the incidence–mortality correlation is weakened. This effect is more prominent in some cancers either because of biology or conventional diagnostic practice (eg, screening).

The low correlation tercile comprise a group of cancers in which diagnostic scrutiny—specifically screening and incidental detection—has been shown to influence the number of cancers diagnosed. The advent of PSA screening first alerted doctors how the degree of diagnostic scrutiny can affect prostate cancer incidence.[21 22] Melanoma incidence has increased sixfold over the past 40 years in the USA—in large part due to increasing rates of skin cancer screening.[23] Some combination of screening and incidental detection has also led to a tripling of thyroid cancer incidence, which notably also had the largest decline in incidence rate in 2020 as a result of the COVID-19 pandemic.[24 25] Finally, the prevalence of screening mammography in US counties has been strongly associated with county-level breast cancer incidence.[26]

While we expected low incidence–mortality correlations in these four cancers, we were struck by the extremely weak correlation in breast cancer (r=0.03 (95% CI: −0.03 to −0.09)). Unlike melanoma and thyroid cancer in which deaths are rare, breast cancer is a common cause of cancer death. Furthermore, the breast cancer incidence–mortality correlation has degraded markedly over time (in SEER 9, from r=0.47 (95% CI: 0.50 to 0.74) in 1976–1984 to r=0.15 (95% CI: −0.14–0.16) in 2000–2016). Either the substantial improvement in breast cancer treatment[27] has been dramatically, unevenly disseminated across US counties or variable screening practices have led to variable overdiagnosis.[28]

The relatively strong incidence–mortality relationship in colorectal cancer (r=0. 75 (95% CI: 0.72 to 0.77)) serves as an interesting counterexample. There is widespread screening for colorectal cancer (over half of the eligible population was up-to-date with screening during our analysis period),[20] yet this increased diagnostic scrutiny is not associated with frequent colorectal cancer overdiagnosis. Endoscopic screening (ie, sigmoidoscopy and colonoscopy) not only detects cancers early, but it also prevents others from developing, thus reducing cancer incidence. Instead overdiagnosis is confined to precursor lesions—non-malignant colorectal polyps.[29]

Despite a decline in both colorectal cancer incidence and mortality, the incidence of surgery for non-malignant colorectal polyps has been increasing.[30] Nevertheless, because these precursor lesions are not labelled as incident cancers, the incidence–mortality correlation is not perturbed (ie, they do not enter the equation).

Finally, it s important to emphasise that the frequency of overdiagnosis in a specific cancer is not simply a reflection of the cancer site, but also the existent screening strategies for that site. The high incidence–mortality correlation in lung cancer, for example, is less about lung cancer per se, more about the current conservative screening strategies in place. Were the US to promote the more aggressive strategies used in Taiwan,[13] China[14] and Korea,[31] we would expect a much weaker incidence–mortality correlation to soon appear.

Study limitations

In this study, we only analysed 12 cancers and did not include haematologic malignancies, which could be part of a subsequent investigation. Our data are observational. This is by necessity, however, as we cannot imagine an experimental design to examine the incidence mortality relationship. In addition, our data are undoubtedly subject to some measurement error: as some patients move from one county to another in the period between diagnosis and death. However, substantial migration between US counties after a cancer diagnosis is apparently relatively rare.[32] Nevertheless, in an effort to examine this possibility, we performed a sensitivity analysis on the lag time of 2 years. Testing a range from 0 to 5 years, however, had little effect on the reported correlations (see online supplemental table 4). Our study was also limited in that some US counties were excluded from the analysis, as mortality rates are repressed in those with less than 10 deaths during the period of analysis.

Finally, our suggestion that variable overdiagnosis is the primary explanation for low incidence–mortality correlations should be viewed as speculative. Indeed, kidney cancer stands out as a notable exception—a cancer in which incidence–mortality is moderately correlated, yet variable overdiagnosis is evident.[33]

CONCLUSIONS

For some cancers in the USA, the fundamental epidemiologic measure of disease frequency—incidence—now has little relationship with the feared outcome of cancer death. These weak incidence–mortality correlations likely reflect cancers subjected to high diagnostic scrutiny, variable local diagnostic practice and thus variable amounts of cancer overdiagnosis. Strong correlations, on the other hand, reflect more conservative and uniform diagnostic practice and less overdiagnosis. These findings should guide clinicians, researchers and policymakers in interpreting geographic variations in incidence for different cancers.

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Contributors ASA and HGW were responsible for the concept and design of the study. The acquisition, analysis and interpretation of data were performed by ASA, HGW and VP. Drafting of the manuscript was executed by ASA and HGW. Critical revision of the manuscript for important intellectual content was performed by ASA, HGW and VP. Statistical analysis was conducted by ASA, HGW and VP. Supervision of the study was carried out by ASA and HGW. ASA is responsible for the overall content of the manuscript as guarantor.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval The University of Texas at Austin deemed this work IRB exempt.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available in a public, open access repository. The data underlying this study are publicly available at www.seer.cancer.gov/data/.

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