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Temporal trends in net and crude probability of death from cancer and other causes in the Australian population, 1984–2013

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ABSTRACT

Background: While net probabilities of death in the relative survival framework ignore competing causes of death, crude probabilities allow estimation of the real risk of cancer deaths. This study quantifies temporal trends in net and crude probabilities of death.

Methods: Australian population-based cohort of 2,015,903 people aged 15-89 years, diagnosed with a single primary invasive cancer from 1984 to 2013 with mortality follow-up to 31 December 2014. Survival was analyzed with the cohort method. Flexible parametric relative survival models were used to estimate both probability measures by diagnosis year for all cancers and selected leading sites.

Results: For each site, excess mortality rates reduced over time, especially for prostate cancer. While both the 10-year net and crude probability of cancer deaths decreased over time, specific patterns varied. For example, the crude probability of lung cancer deaths for males aged 50 years decreased from 0.90 (1984) to 0.79 (2013); whereas the corresponding probabilities for kidney cancer were 0.64 and 0.18 respectively. Patterns for crude probabilities of competing deaths were relatively constant. Although for younger patients, both net and crude measures were similar, crude probability of competing deaths increased with age, hence for older ages net and crude measures were different except for lung and pancreas cancers.

Conclusions: The observed reductions in probabilities of death over three decades for Australian cancer patients are encouraging. However, this study also highlights the ongoing mortality burden following a cancer diagnosis, and the need for continuing efforts to improve cancer prevention, diagnosis and treatment.

1. Introduction

As more people are diagnosed with and survive cancer [1], the ability of clinicians to convey useful prognostic information to patients at diagnosis and during follow-up is critical. Typically, newly diagnosed patients are informed of their prognosis based on population-based estimates of net survival [2].

Standard net survival in the relative survival framework allows estimation of the net probability of death in a hypothetical situation where the diagnosed cancer is the only cause of death [2]. However, this measure can be difficult to interpret in the real-world, where cancer patients can also die from other (competing) causes. In contrast, crude probability estimates quantify the more real-world probability of cancer deaths while accounting for competing causes [3], and are thus potentially more relevant for risk-communication and clinical decision-making [3,4].

While several population-based studies have reported crude probability estimates [3–8], these were mainly limited to breast [7,8] or prostate cancer [3,4,7] and only one [7] examined temporal changes in these estimates. Here we quantify, for the first time, crude probabilities of death for a population-based cohort of Australians diagnosed with 13 cancers and quantify changes in these measures over three decades.

Abbreviations: ACD, Australian Cancer Database; ACT, Australian Capital Territory; HRE, Human Research Ethics Committee; NSW, New South Wales; NHL, non-Hodgkin lymphoma

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Greater understanding of the burden of crude probabilities of cancer and competing deaths and temporal changes in these measures could provide additional insight into the impact that advances in early detection and treatment have had on these real-world prognostic measures.

2. Methods

Ethical approval was obtained from the Queensland University of Technology Human Research Ethics Committee (HREC) (1600000868), NSW Population & Health Services Research Committee (2016/HRE1203) and ACT HREC (ETHLR.16.228). All cancer registries provided approval to access de-identified data from the Australian Cancer Database (ACD) [9]. Notification of all invasive cancers (excluding keratinocyte cancers) to these cancer registries is a statutory requirement and the ACD is considered to cover all Australians diagnosed with cancer [9].

2.1. Cohort

Data was obtained for all persons from 1984-2013 with mortality follow-up to 31 December 2014, allowing a minimum of one year's follow-up. Vital status is determined through routine annual linkage of cancer records with the Australian National Death Index [9] Only single primary invasive cancer cases (n = 2,120,231) were considered, given the difficulty assessing which cancer impacted mortality when multiple cancers were diagnosed, and is consistent with other studies [5,6,10]. Only those aged 15-89 years at diagnosis (n = 2,055,880) were included due to different classification of childhood cancers [11] and since the bias in net survival estimatesis highest among older people [12]. Cases identified at death (27,749, 1%), or with negative survival times (12,228, 0.5%) were excluded.

Analyses are presented for all cancers combined and 13 leading individual sites (Table 1)

2.2. Survival

Survival was measured in days from the date of diagnosis to one of: death, 10 years after diagnosis, or the study endpoint (31 December 2014), whichever came first. Cases alive at the end of follow-up were censored.

Survival analyses were carried out in the framework of relative survival, a measure of net survival, defined as the ratio of the observed survival for the cancer cohort to the expected survival in a cancer-free population [3]. The cohort method was used as this study was designed to assess temporal trends in survival [13]. However, for comparison, survival estimates were also calculated with the period [13] method, with cancer patients considered at risk between 1 January 2008 and 31 December 2014.

2.3. Statistical analysis

All analyses were performed with Stata/SE version 15 (StataCorp, TX, USA).

2.3.1. Outcome measures

The first of the three considered outcome measures, excess mortality rate, represents the increased mortality among cancer patients compared to the expected mortality (general population) [3]. The second, net probability of death (1-net survival), quantifies the probability of death among cancer patients in a hypothetical scenario where they can only die of their cancer. The third measure, crude probability of death, partitions the total excess mortality among individual patients into cancer and other deaths without requiring cause of death information [3].

2.3.2. Modelling

Survival was modeled with flexible parametric relative survival models that use restricted cubic splines for the baseline cumulative excess hazard to obtain smooth estimates of the excess mortality rates [14,15]. This approach enables inclusion of individual-level continuous covariates and time-varying effects with additional splines and the estimation of both net [14] and crude probability measures [3] from the same model. Age and year were included as continuous time-varying covariates, with second-order interactions between the spline terms for age and year. Models were stratified by sex (Appendix A).

Population life tables were generated from published national all-cause mortality data [16]. All models were fitted with stpm2 package [14,15] and excess mortality rates estimated through the predict command.

Crude probabilities of cancer and competing deaths were estimated by transforming the fitted model parameters as described by Lambert et al [3]. Probabilities were predicted till 10 years after diagnosis, consistent with previous studies [3,4,6,7] and required extrapolation of the survival functions for patients diagnosed from 2005 onwards. We used the fitted models to extrapolate the observed survival for the cancer cohort and utilised life tables based on published actual mortality rates until 2017 [16] and projected mortality rates assuming high life expectancy from 2018 onwards [17].

Sensitivity analyses were performed by looking at the impact of changing the projected mortality rates by ± 2 to ± 5% and using projections derived with various assumptions (for life expectancy) [17] on the trends in crude probabilities of death for lung cancer and melanoma.

Table 1
Characteristics of study cohort, by site, Australia.,1984–2013

Cancer (ICD-10 codes)	Cases	% all cases	Median age (years) and IQR	% females	% died (within 10 years after diagnosis)
Stomach (C16)	45,614	2	70 [60-78]	35	82
Colorectal (C18-C20)	259,386	13	69 [59-77]	47	54
Pancreas (C25)	45,269	2	71 [62-78]	48	94
Lung (C33-C34)	200,692	10	69 [61-76]	34	91
Melanoma (C43)	196,748	10	57 [43-70]	46	20
Female Breast (C50)	271,077	14	58 [49-69]	100	27
Cervical (C53)	22,701	1	46 [36-72]	100	35
Uterine (C54-C55)	35,709	2	63 [55-72]	100	29
Prostate (C61)	286,446	14	69 [62-76]	0	34
Kidney (C64)	41,635	2	64 [54-73]	37	46
Non-Hodgkin lymphoma (C82-C86)	75,563	4	65 [53-75]	46	50
Leukaemia (C91-C95)	52,064	3	67 [54-76]	42	62
Head and neck (C00-C14, C30-C32)	73,389	4	62 [52-71]	27	47
All cancers (C00-C97, D45, D46, D47.1, D47.3-D47.5)	2,015,903	100	66 [55-75]	46	51

ICD-10 International Statistical Classification of Diseases and related health problems, Tenth revision, IQR Interquartile range.

Results are presented as 10-year estimated sex-specific net probabilities of deaths and the crude probabilities of cancer and competing deaths. Since age and year were modelled continuously, we selected ages 50, 65 and 80 years for reporting purposes. Except for cervical cancer and melanoma, at least 80% of patients were within this age range. Estimates are predicted for five specific years of diagnosis: 1984, 1994, 2004, 2009 and 2013 to provide an overview of the temporal changes over three decades.

The stmp2-standsurv [18] and stpm2cm commands [3] were used for predicting net and crude probabilities of death with 95% confidence intervals (CI) respectively.

3. Results

The final cohort included 2,015,903 persons, of whom almost half had died within 10 years of diagnosis (Table 1).

3.1. Trends by year of diagnosis

3.1.1. Excess mortality rates

Estimated sex and age-specific excess mortality rates reduced over calendar time for each site, particularly prostate cancer (Appendix Figs. B.1–B.2. Rates also increased with age and tended to be highest immediately after diagnosis before declining with increasing follow-up interval, although patterns varied by demographics and site (Figs. B.3–B.4).

3.1.2. Net probabilities of death

The net probability of death decreased over calendar time for both males and females (Fig. 1) at each of the selected ages, however the magnitude of the decrease varied by site, sex and age. For example, the 10-year net probability of death for 50-year old males decreased from 0.91 if diagnosed with lung cancer in 1984 to 0.80 in 2013; whereas the corresponding probabilities for 50-year old male kidney cancer patients were 0.65 (1984) and 0.18 (2013) (Appendix Table C.1).

3.1.3. Crude probabilities of death

3.1.3.1. Cancer deaths. The estimated age and sex-specific 10-year crude probabilities of cancer deaths decreased over calendar time for most cancers, but the decrease was particularly pronounced for non-Hodgkin lymphoma (NHL), leukaemia, prostate, kidney, colorectal, uterine and breast cancers. However, the crude probabilities of cancer deaths for lung and pancreatic cancer remained high, while for cervical cancer it was lower, but still relatively stable (Fig. 2, Appendix Tables C.2–C.5). Patterns varied by site, sex and age. As an illustrative example, for males aged 50 years the crude probability of lung cancer deaths decreased from 0.90 in 1984 to 0.79 (2013) and for kidney cancer from 0.64 to 0.18 respectively.

3.1.3.2. Competing causes. Compared to the pattern among younger patients, a key feature of the time trends for crude probability of competing causes was the higher and generally increasing trend among people aged 80 years (Fig. 2). For 65-year-olds, these probabilities were relatively constant, especially for females, but among males there was some evidence of a decrease over time for melanoma, head and neck, colorectal and prostate cancers. Patterns were also relatively stable at age 50 for both sexes (Appendix Tables C.2–C.5). For example, the 10-year crude probability of competing deaths for male kidney cancer patients in 1984 were 0.03, 0.11 and 0.28 at ages 50, 65 and 80 respectively with the corresponding probabilities in 2013 being 0.03, 0.11 and 0.42.

3.1.3.3. Net versus crude probabilities. While the predicted 10-year net and crude probability of being alive were relatively similar for 50-year-olds, regardless of calendar time, the risk of competing deaths increased with age. Hence with advancing age, estimates of net mortality began to diverge from the corresponding values for the crude probability. Exceptions were lung and pancreas cancer where both these measures indicated that most deaths were from the diagnosed cancer over all ages (Appendix Tables C.2–C.3).

Five and 10-year net and crude survival estimates for patients diagnosed in 2013 (Table 2) highlighted the increasing difference between these measures with age and the importance of considering competing mortality especially from the perspective of long-term risk communication. Competing causes are also likely to be the main contributor to deaths after 10-years among currently diagnosed older cancer patients (except lung or pancreas). Moreover, the difference between the estimated measures for 2013 using the cohort (Table 2) and period methods (Appendix Table C.6) was relatively small, although the magnitude varied by site, sex, age and follow-up time.

3.1.4. Sensitivity analysis

Sensitivity analyses (results not shown) suggested little quantifiable difference between the estimated crude probabilities of death using varying assumptions for projected mortality rates. Model-based predictions were also not sensitive to the number of knots.

4. Discussion

While the probability of cancer deaths has decreased over the past three decades for Australian cancer patients, this study also highlighted that the magnitude of that decrease varied by site, sex and age. However, the risk of competing deaths remained relatively stable over time among younger ages, whereas for older patients it typically increased particularly among males.

The commonly reported net survival measure refers to the hypothetical situation when people can only die of cancer. This can be misleading when communicating these estimates to patients, because a 10-year net survival of 60% does not mean 60% of patients will survive ten years. In comparison, by incorporating competing mortality causes, the crude probabilities of death provide important advantages from the perspective of risk communication to patients and the public [4]. By estimating crude probabilities, we can report that for every 100 people diagnosed with a specific cancer, how many would die from their cancer, how many would die from other causes and how many are alive after a given period of time. The difference between net and crude survival is relatively small among younger people, reflecting the low rate of competing mortality in those age groups. However, as people age, and the risk of competing mortality increases, correctly communicating the differing prognosis for cancer and competing causes becomes critical when conveying the implications of a cancer diagnosis to them. To the best of our knowledge, our study provides the most comprehensive comparison of these estimates across major cancer sites and by year of diagnosis and is the first to report them for Australia.

While the specific causes of the decrease in crude probability of cancer deaths described here are probably multifactorial and beyond the scope of this study, they are consistent with current knowledge about advances in diagnosis and treatment. For example, incidental detection and diagnosis of early-stage kidney cancers during imaging procedures would include tumours with better prognosis in the survival estimates [19,20]. In addition, improved treatments for NHL [21,22], leukaemia [21,23], stomach [24], uterus [25], colorectal [21,26] and head and neck cancers [27] would likely increase the survival time between diagnosis and cancer death.

Complicating the interpretation of these survival trends is the role of screening, and the likely over-diagnosis of tumours that would not have progressed or would have progressed too slowly to impact a patient's longevity [28]. By definition, the detection of these tumours through screening would increase the observed survival rate [29,30]; if screening prevalence has also changed over time, this would also influence observed survival although the extent of this effect is unknown. This is particularly relevant for prostate cancer through prostate

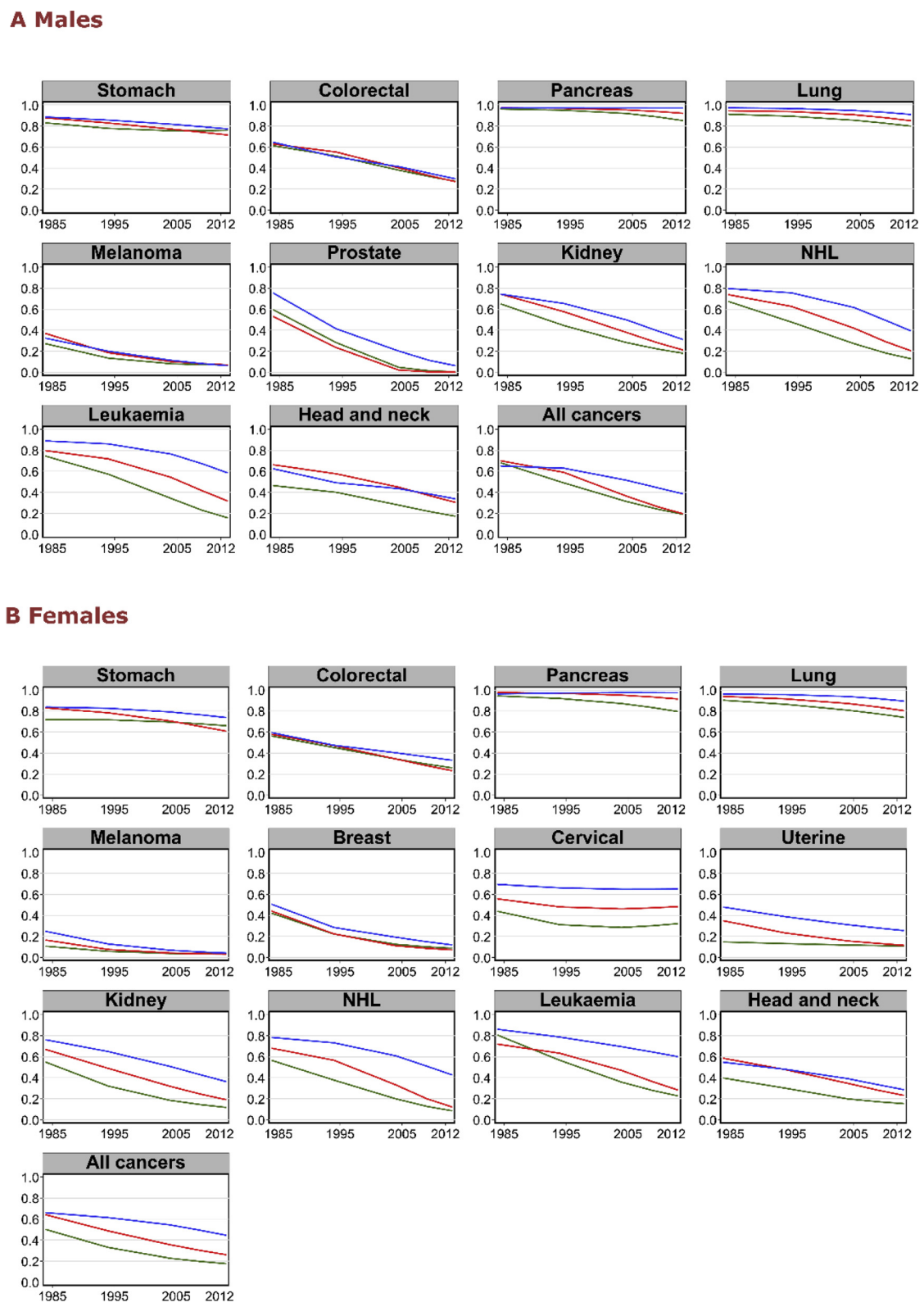

Fig. 1. Temporal trends in the predicted 10-year net probability of death (1-net survival) at selected ages, for males (A) and females (B), Australia 1984-2013. *The x axis in each plot is the 'Year of Diagnosis' and the y axis the 'Net probability of death'. Dark green, red and light blue lines indicate estimates at age 50, 65 and 80 years respectively.*

specific antigen (PSA) testing [31], and breast cancer through mammograms [32]. Moreover, while there is no formal screening program, clinical skin examinations for early melanoma detection are widespread [33,34]. The impact of organised or *ad-hoc* screening would be to reduce the crude probability of cancer deaths, consistent with observed temporal patterns for these cancers. While screening does not directly influence non-cancer deaths, it could have an indirect impact by changing the characteristics of the cancer cohort. For example,

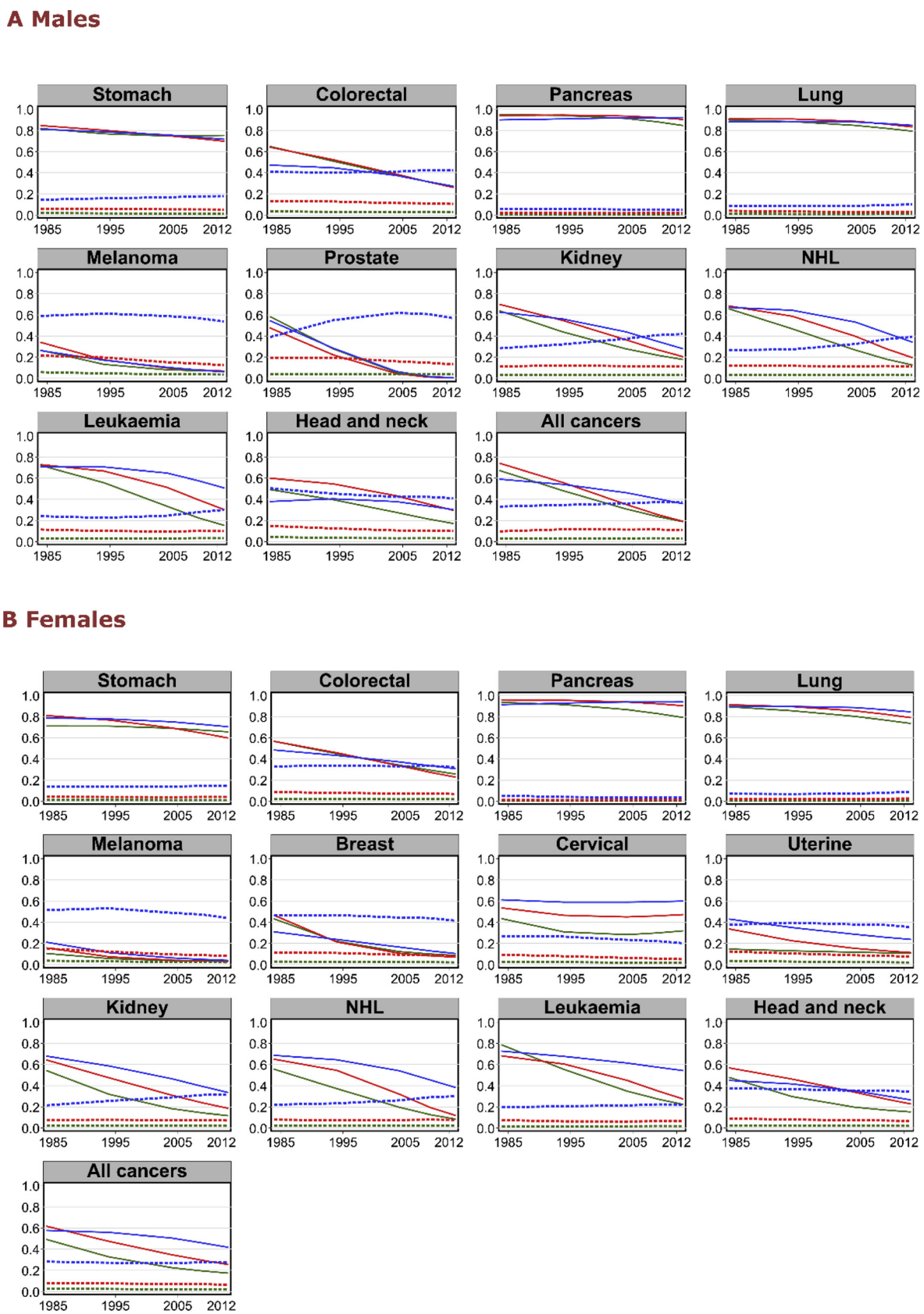

Fig. 2. Temporal trends in the predicted 10-year crude probability of deaths due to cancer and other causes at selected ages for males (A) and females (B), Australia 1984-2013. *The x axis in each graph is the 'Year of Diagnosis' and the y axis the 'Crude probability of death'. Dark green represents estimates at age 50, red at age 65 and light blue at age 80 years.*

Table 2
Predicted net and crude survival with 95% confidence intervals [brackets], at five and ten years after diagnosis, based on cohort method for patients diagnosed in 2013 by sex for selected ages, Australia.

		Males				Females			
		5 year		10-year		5-year		10-year	
Cancer	Age (years)	net survival	crude survival	net survival	crude survival	net survival	crude survival	net survival	crude survival
Stomach	50	0.31 [0.28, 0.35]	0.31 [0.28, 0.34]	0.24 [0.21, 0.27]	0.24 [0.20, 0.27]	0.40 [0.36, 0.45]	0.40 [0.35, 0.44]	0.34 [0.29, 0.39]	0.33 [0.28, 0.38]
	65	0.35 [0.33, 0.38]	0.33 [0.31, 0.36]	0.28 [0.26, 0.31]	0.25 [0.22, 0.28]	0.44 [0.41, 0.48]	0.43 [0.39, 0.46]	0.39 [0.35, 0.43]	0.36 [0.32, 0.40]
	80	0.26 [0.24, 0.29]	0.19 [0.16, 0.23]	0.23 [0.20, 0.26]	0.10 [0.06, 0.15]	0.28 [0.24, 0.33]	0.23 [0.18, 0.28]	0.26 [0.22, 0.31]	0.15 [0.09, 0.21]
Colorectal	50	0.78 [0.77, 0.79]	0.77 [0.75, 0.78]	0.72 [0.71, 0.74]	0.70 [0.68, 0.71]	0.79 [0.77, 0.80]	0.78 [0.77, 0.79]	0.74 [0.72, 0.76]	0.72 [0.71, 0.74]
	65	0.78 [0.77, 0.79]	0.74 [0.72, 0.75]	0.73 [0.71, 0.74]	0.64 [0.62, 0.65]	0.81 [0.79, 0.82]	0.78 [0.77, 0.79]	0.77 [0.75, 0.78]	0.70 [0.69, 0.72]
	80	0.71 [0.70, 0.73]	0.52 [0.50, 0.54]	0.70 [0.68, 0.72]	0.31 [0.29, 0.33]	0.69 [0.67, 0.70]	0.56 [0.54, 0.58]	0.67 [0.65, 0.69]	0.37 [0.34, 0.39]
Pancreas	50	0.19 [0.17, 0.23]	0.19 [0.16, 0.22]	0.15 [0.12, 0.18]	0.14 [0.11, 0.18]	0.27 [0.23, 0.31]	0.26 [0.23, 0.30]	0.20 [0.17, 0.25]	0.20 [0.16, 0.24]
	65	0.12 [0.10, 0.14]	0.11 [0.09, 0.13]	0.08 [0.06, 0.10]	0.08 [0.05, 0.10]	0.13 [0.12, 0.15]	0.13 [0.11, 0.15]	0.09 [0.07, 0.11]	0.08 [0.06, 0.10]
	80	0.05 [0.04, 0.06]	0.04 [0.02, 0.06]	0.03 [0.02, 0.04]	0.03 [0.01, 0.05]	0.05 [0.03, 0.06]	0.04 [0.02, 0.06]	0.03 [0.02, 0.04]	0.03 [0.01, 0.04]
Lung	50	0.23 [0.22, 0.25]	0.23 [0.21, 0.24]	0.20 [0.18, 0.22]	0.20 [0.18, 0.21]	0.31 [0.29, 0.33]	0.31 [0.29, 0.33]	0.26 [0.24, 0.28]	0.25 [0.23, 0.28]
	65	0.19 [0.18, 0.20]	0.18 [0.17, 0.19]	0.15 [0.14, 0.16]	0.14 [0.12, 0.15]	0.26 [0.24, 0.27]	0.25 [0.24, 0.27]	0.20 [0.18, 0.21]	0.18 [0.17, 0.20]
	80	0.13 [0.12, 0.14]	0.10 [0.08, 0.11]	0.09 [0.08, 0.10]	0.05 [0.04, 0.07]	0.16 [0.14, 0.17]	0.13 [0.11, 0.15]	0.10 [0.09, 0.12]	0.06 [0.05, 0.09]
Melanoma	50	0.94 [0.93, 0.94]	0.92 [0.91, 0.93]	0.93 [0.92, 0.94]	0.89 [0.89, 0.91]	0.97 [0.96, 0.97]	0.96 [0.95, 0.96]	0.96 [0.96, 0.97]	0.95 [0.93, 0.95]
	65	0.93 [0.92, 0.94]	0.88 [0.87, 0.89]	0.93 [0.92, 0.94]	0.81 [0.80, 0.82]	0.97 [0.96, 0.98]	0.93 [0.93, 0.94]	0.97 [0.96, 0.98]	0.89 [0.88, 0.90]
	80	0.93 [0.92, 0.94]	0.67 [0.66, 0.69]	0.94 [0.92, 0.95]	0.40 [0.38, 0.42]	0.96 [0.94, 0.97]	0.77 [0.76, 0.79]	0.96 [0.94, 0.97]	0.52 [0.50, 0.54]
Female breast	50					0.94 [0.94, 0.95]	0.93 [0.93, 0.94]	0.91 [0.91, 0.92]	0.89 [0.88, 0.90]
	65					0.94 [0.94, 0.95]	0.92 [0.91, 0.92]	0.93 [0.92, 0.93]	0.85 [0.84, 0.86]
	80					0.91 [0.90, 0.91]	0.73 [0.72, 0.74]	0.88 [0.87, 0.89]	0.47 [0.46, 0.50]
Cervical	50					0.73 [0.71, 0.76]	0.71 [0.67, 0.75]	0.68 [0.67, 0.72]	0.66 [0.62, 0.71]
	65					0.61 [0.58, 0.64]	0.56 [0.52, 0.61]	0.52 [0.51, 0.58]	0.48 [0.42, 0.53]
	80					0.43 [0.40, 0.47]	0.34 [0.27, 0.40]	0.35 [0.33, 0.42]	0.20 [0.11, 0.28]
Uterine	50					0.92 [0.91, 0.93]	0.90 [0.88, 0.91]	0.89 [0.87, 0.92]	0.87 [0.85, 0.89]
	65					0.88 [0.87, 0.89]	0.87 [0.85, 0.88]	0.88 [0.85, 0.88]	0.81 [0.79, 0.83]
	80					0.76 [0.74, 0.78]	0.61 [0.58, 0.64]	0.74 [0.72, 0.77]	0.41 [0.36, 0.45]
Prostate	50	1.00 [1.00, 1.00]	0.98 [0.98, 0.98]	0.99 [0.99, 1.00]	0.95 [0.95, 0.96]				
	65	1.00 [1.00, 1.00]	0.94 [0.94, 0.94]	0.99 [0.99, 1.00]	0.86 [0.85, 0.87]				
	80	0.96 [0.95, 0.96]	0.72 [0.72, 0.72]	0.94 [0.92, 0.95]	0.42 [0.41, 0.43]				
Kidney	50	0.85 [0.83, 0.87]	0.84 [0.81, 0.86]	0.82 [0.79, 0.85]	0.79 [0.76, 0.82]	0.90 [0.88, 0.92]	0.89 [0.87, 0.91]	0.88 [0.85, 0.91]	0.86 [0.83, 0.89]
	65	0.82 [0.80, 0.84]	0.78 [0.76, 0.80]	0.79 [0.76, 0.81]	0.68 [0.66, 0.71]	0.84 [0.82, 0.87]	0.81 [0.79, 0.84]	0.81 [0.77, 0.84]	0.74 [0.70, 0.78]
	80	0.72 [0.68, 0.75]	0.52 [0.48, 0.56]	0.69 [0.65, 0.73]	0.30 [0.25, 0.35]	0.68 [0.63, 0.72]	0.55 [0.50, 0.60]	0.64 [0.58, 0.69]	0.35 [0.28, 0.42]
NHL	50	0.90 [0.89, 0.91]	0.89 [0.87, 0.90]	0.87 [0.85, 0.89]	0.84 [0.82, 0.86]	0.94 [0.92, 0.95]	0.93 [0.91, 0.94]	0.91 [0.90, 0.93]	0.89 [0.88, 0.91]
	65	0.84 [0.83, 0.86]	0.80 [0.78, 0.81]	0.79 [0.77, 0.81]	0.69 [0.67, 0.71]	0.91 [0.90, 0.92]	0.88 [0.86, 0.89]	0.88 [0.86, 0.89]	0.80 [0.79, 0.82]
	80	0.67 [0.64, 0.69]	0.49 [0.46, 0.51]	0.60 [0.57, 0.64]	0.27 [0.23, 0.30]	0.65 [0.63, 0.68]	0.53 [0.50, 0.56]	0.57 [0.54, 0.61]	0.32 [0.27, 0.36]
Leukaemia	50	0.86 [0.85, 0.88]	0.85 [0.83, 0.87]	0.84 [0.82, 0.86]	0.81 [0.79, 0.83]	0.79 [0.77, 0.82]	0.79 [0.76, 0.81]	0.77 [0.74, 0.80]	0.76 [0.73, 0.79]
	65	0.74 [0.72, 0.76]	0.70 [0.68, 0.73]	0.68 [0.65, 0.71]	0.60 [0.56, 0.63]	0.76 [0.73, 0.78]	0.73 [0.70, 0.76]	0.72 [0.68, 0.75]	0.66 [0.62, 0.70]
	80	0.50 [0.47, 0.53]	0.37 [0.33, 0.41]	0.41 [0.37, 0.46]	0.19 [0.14, 0.25]	0.47 [0.43, 0.51]	0.39 [0.35, 0.43]	0.40 [0.35, 0.45]	0.24 [0.17, 0.29]
Head and neck	50	0.85 [0.83, 0.86]	0.83 [0.82, 0.85]	0.83 [0.81, 0.85]	0.81[0.78, 0.81]	0.86 [0.83, 0.88]	0.85 [0.82, 0.87]	0.85 [0.82, 0.88]	0.84 [0.80, 0.86]
	65	0.74 [0.72, 0.76]	0.70 [0.68, 0.71]	0.69 [0.67, 0.72]	0.60 [0.58, 0.63]	0.79 [0.76, 0.82]	0.76 [0.73, 0.79]	0.77 [0.73, 0.81]	0.70 [0.66, 0.74]
	80	0.70 [0.67, 0.73]	0.51 [0.48, 0.54]	0.66 [0.62, 0.70]	0.29 [0.24, 0.33]	0.74 [0.70, 0.78]	0.60 [0.56, 0.64]	0.71 [0.66, 0.77]	0.39 [0.33, 0.45]
All cancers	50	0.81 [0.81, 0.81]	0.80 [0.80, 0.81]	0.81 [0.80, 0.81]	0.78 [0.77, 0.78]	0.85 [0.85, 0.85]	0.85 [0.84, 0.85]	0.82 [0.81, 0.82]	0.81 [0.80, 0.81]
	65	0.77 [0.77, 0.78]	0.76 [0.76, 0.77]	0.80 [0.76, 0.82]	0.70 [0.69, 0.70]	0.75 [0.74, 0.75]	0.74 [0.74, 0.74]	0.74 [0.71, 0.72]	0.67 [0.67, 0.68]
	80	0.69 [0.69, 0.69]	0.45 [0.45, 0.46]	0.61 [0.59, 0.67]	0.27 [0.26, 0.28]	0.61 [0.61, 0.62]	0.47 [0.46, 0.48]	0.55 [0.52, 0.59]	0.31 [0.30, 0.32]

NHL Non-Hodgkin lymphoma.
1. Values for 2013 predicted from the flexible parametric relative survival models adjusted for age and year at diagnosis (both as continuous variables), interactions between age and year, and case mix for head and neck or all cancers. Models stratified by sex (where relevant). Refer to text for further details.

screening prevalence is typically higher among affluent Australians [32], who are also probably healthier [35], thereby adding these healthier people to the cancer cohort, hence reducing the crude probability of competing deaths [2,4]. While not conclusive, there is some suggestion this has occurred for melanoma, breast and prostate cancers. That the pattern is also evident for cervical cancer is surprising, as cervical screening enables detection of pre-cancerous lesions rather than early cancers [32].

Despite the problems discussed above, it should be emphasised that at least some of the improved survival for melanoma, breast and prostate cancer likely reflect real survival benefits through early detection of tumours before they progressed to advanced disease [29] and treatment advances [23,36] including targeted breast cancer therapies [21,37].

In contrast to trends for most sites, prognosis for lung and pancreas cancers, which are typically diagnosed at an advanced stage [38,39] remained poor over the entire study period. In the current absence of effective treatment strategies, prevention efforts designed to further reduce the prevalence of known risk factors are crucial. Moreover, concerted efforts to improve detection and treatments for pancreatic cancers [40] and promote earlier lung cancer diagnosis [41] are critical to improve outcomes.

The very high predicted 10-year net survival estimates for prostate cancer cases diagnosed from 2009 onwards, regardless of age, were consistent with reports from the United States, where 5-year net survival also approaches 100% [2]. However, focusing on net survival estimates increases the possibility that they will be incorrectly interpreted as 100% of prostate cancer patients will be alive in five years. Reporting both net and crude probabilities of death in combination provides a more complete picture of the cancer burden, especially for older patients. For example, while both measures tended to be similar for a 50-year-old man diagnosed with prostate cancer in 2013, the net and crude probabilities for an 80-year old were 0.01 versus 0.58.

Our estimates suggest that temporal improvements in cancer survival now mean if an 80-year-old diagnosed with cancer (except lung, pancreas or stomach), dies within the next ten-years, the cause of death is more likely to be competing causes. This is a very different situation to previous years, for example until 2004, when the crude probabilities of cancer deaths were generally higher. Not only does this provide quantitative evidence of the increasing success of cancer treatments, it highlights the importance of clinicians using the cancer diagnosis as an opportunity to promote healthy lifestyles among cancer survivors, to further reduce the risks of competing mortality [23,42].

Differences in health systems can limit the generalizability of international findings to the Australian context. However, a few European studies found that the difference between estimated net and crude probability of death in the relative survival framework increased with age for prostate [3,4] and female breast cancer [8]. Moreover, Charvat et al. [7] reported changes in crude probability of cancer deaths for five sites in France as an average over all ages combined rather than for individual ages; hence limiting the comparability of their findings to ours.

Study strengths include the use of national [9] high-quality [40,43] population-based cancer registration and mortality data [16] including published projections from 2018 onwards [17]. Survival analyses in a relative survival framework allowed estimation of three informative outcome measures at the individual-level from the same flexible parametric models [3,14,18] without requiring cause-of death information, an advantage when using population-based data where the specific cause of death can be uncertain [4].

The lack of data on potential confounders notably stage at diagnosis [6], treatment [23], comorbidities [44] and lifestyle factors [45], all of which can impact survival, limits insights into reasons for observed patterns. Relative survival assumes that mortality from cancers and other causes are independent and comparable between the general population and the cancer cohort [3,8,46]. Although these assumptions are generally considered reasonable [8,46], they may be less valid for certain sites due to shared risk factors like smoking for both cancer and competing mortality causes [2,46].

For more recently diagnosed patients, our estimates were based on extrapolated information, hence some caution is required as it is possible that they will not reflect the observed results 10 years after diagnosis. However, flexible parametric models have been shown to allow robust extrapolation [47], especially when at least part of the cohort had complete follow-up, as is the case for this study.

5. Conclusions

By providing two additional cancer survival measures using an Australian population-based cohort, we have highlighted the changing contribution that cancer and competing mortality causes have on the prognosis of Australians diagnosed with the most common cancers by age and time period. While the observed reductions in probabilities of death over three decades are promising, our study also highlights the ongoing mortality burden of a cancer diagnosis, and so should motivate continuing efforts to improve prevention, diagnosis and treatment for these cancers. Further understanding of the reasons for the temporal trends will require more information about additional patient and clinical factors, particularly stage at diagnosis.

Contributors

PDB conceived the study. PD performed the analysis. PD and PDB drafted the manuscript. All authors contributed to, read and approved the final manuscript.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.canep.2019.101568.

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