

Original Article

Lessons from a population-based bladder cancer registry: exploring why survival is not improving

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Objective

To explore the causes of the decrease in bladder cancer survival that has occurred over the past four decades.

Methods

We extracted data from the South Australian Cancer Registry. Data from the period 1 January 1977 to 31 December 2020 were extracted to explore changes in incidence and survival among a total of 8356 patients diagnosed with \geq pT1 disease. Invasive bladder cancer was defined as \geq pT1 in this study.

Results

Invasive bladder cancer age-standardized incidence decreased from 7.20 cases per 100 000 people in 1977 to 5.85 cases per 100 000 in 2020. The mean age at diagnosis increased from 68 years to 76 years. The crude incidence for patients aged 80 years and over increased by 3.3% per year (95% confidence interval [CI] 2.1 to 4.6). Overall survival decreased over the study period (hazard ratio [HR] 1.22 [95% CI 1.09 to 1.35]), however, survival increased after adjusting for age at diagnosis (HR 0.80 [95% CI 0.76 to 0.94]). Despite a decrease in non-bladder cancer-specific deaths in older people, there was no change in the bladder cancer-specific death rate in older people (HR 0.94 [95% CI 0.70 to 1.26]). Male sex was associated with higher survival (HR 0.87 [95% CI 0.83 to 0.92]), whereas socioeconomic advantage was not.

Conclusions

Invasive bladder cancer survival has decreased over the past 40 years, with the age structure of the population being a significant contributing factor.

Patient summary

We looked at why bladder cancer survival is decreasing using a large cancer registry with information from 1977 to 2020. We found that people are now more likely to be diagnosed at an older age. Older people often live for a shorter time with bladder cancer compared to younger people. Bladder cancer survival has decreased because there are more older people with the disease than previously.

Keywords

bladder cancer, elderly, older people, survival, urology

Introduction

Australia, like many more economically developed countries, has seen an increase in cancer survival generally [1,2].

Bladder cancer appears to be an outlier in this trend, with evidence of decreasing survival in Australia [2,3]. The fall in survival appears counterintuitive given that there has been a

reduction in age-standardized mortality for bladder cancer in the region [4]. A lack of survival improvement has been reported elsewhere in Australia, and in Northern Europe [2,5].

Globally, the incidence of bladder cancer is decreasing to a greater extent in patients aged <75 years than in patients

aged ≥ 75 years [4]. Similarly, bladder cancer mortality has reduced more in younger patients than in older patients. Given that age is the most important risk factor for bladder cancer development and survival, and there is a worldwide trend towards aging populations, it is concerning that older people may not have ready access to bladder cancer treatments [6–9].

In this paper, we explore the changing demographics in South Australia and analyse why bladder cancer survival has been decreasing.

Methods

Data Source

In January 2023, data were extracted from the South Australian Cancer Registry (SACR), a state-wide registry that has collected data since 1977. The registry covers the state of South Australia, which has an estimated population of 1.8 million, with notification of cancer diagnoses to the registry mandated by law [10]. The SACR stores diagnosis data, age at diagnosis, sex, place of residence, date of death, and cause of death. The SACR is linked with South Australia's Births, Deaths and Marriages registry and periodically to the National Death Index.

Statistical Analysis

Data Tabulation

The International Classification of Diseases for Oncology, third edition (ICD-O-3) criteria were used to classify cancer site, morphology, stage and grade at diagnosis [11]. In this study, 'invasion' was based on the translation of ICD-O-3 to TNM staging and therefore we will use 'non-invasive' to describe both carcinoma *in situ* and pTa tumours and 'invasive' for tumours of stage \geq pT1. Data from all bladder cancer diagnoses between 1977 and 2020 were extracted from the registry and tabulated by invasive and non-invasive status with categories for age, histology, socioeconomic disadvantage using Socio-Economic Indexes for Areas (SEIFA) quintiles, sex and survival, reported as *n* (%). The SEIFA system was developed by the Australian Bureau of Statistics to score areas according to relative socioeconomic advantage and disadvantage [12].

Data were collected at the tumour level, therefore, patients were duplicated if they had recurrent bladder tumours or upstaging from non-invasive to invasive cancer. For the demographic and incidence analysis, duplicates were removed. Non-invasive cancer data in the early years of the registry were not collected in full and therefore incidence trends were not analysed for non-invasive bladder cancers. For analysis of survival, the time from diagnosis to death

from the first non-invasive tumour for each patient was used. Due to the incomplete collection of non-invasive tumours in the registry's early years, the time of diagnosis of patients' first invasive tumour was used when patients had both non-invasive and invasive tumours recorded.

Incidence

To assess the incidence of bladder cancer over time we first calculated crude incidence using the number of diagnosed cases and the reported South Australian population. To calculate the age-standardized incidence we used the direct method and the 2001 Australian Standard Population [10,13]. Annual percent change with 95% CIs was calculated and joinpoint modelling was used to assess changes in incidence [14]. Loess smoothing was applied to trend lines.

To further explore if changes in incidence were related to changes in the population age structure, we plotted the annual crude incidence for each age category by the total population for each year in each age category.

Survival

Survival was measured from the recorded date of diagnosis to the first of either date of death or a censor date of 31 December 2020. Seven patients had missing cause-of-death data and were excluded from analysis of cause of death.

To assess bladder cancer survival over time, we used Cox proportional hazards modelling. We adjusted for confounding factors that may affect survival estimates, including age at diagnosis, sex, year of diagnosis, histopathological type, and SEIFA category. To assess bladder cancer-specific causes of death we performed competing risk regression with Fine-Grey modelling and cumulative incidence plots.

All statistical analysis was performed using the R statistical program by two authors (J.T. and M.O.C.) [15].

Ethics Approval

Ethics approval was granted after review by the Southern Adelaide Clinical Human Research Ethics Committee (Project HRE00882).

Results

Cohort Demographics

Over the study period, 15 820 patients were diagnosed with bladder cancer, 8356 of whom had invasive bladder cancer. Patients aged ≥ 70 years made up 65.8% of invasive bladder cancer diagnoses (Table 1). Urothelial carcinoma made up 90.4% of pT1 and above tumours and 99.4% of carcinoma *in situ* and pTa tumours. The median time between diagnosis of

Table 1 Cohort demographics, South Australia, 1977–2020.

	Invasive (N = 8356)	Non-invasive (N = 7464)
Age at diagnosis, n (%)		
<40 years	56 (0.7)	164 (2.2)
40–59 years	182 (2.2)	331 (4.4)
50–59 years	775 (9.3)	884 (11.8)
60–69 years	1845 (22.1)	1876 (25.1)
70–79 years	2821 (33.8)	2526 (33.8)
80–89 years	2168 (25.9)	1490 (20.0)
90–99 years	501 (6.0)	190 (2.5)
100 years and over	8 (0.1)	3 (0.0)
Histology type, n (%)		
Urothelial carcinoma	7554 (90.4)	7419 (99.4)
Squamous cell carcinoma	198 (2.4)	2 (0.0)
Carcinosarcoma	16 (0.2)	0 (0)
Sarcoma	37 (0.4)	0 (0)
Adenocarcinoma	109 (1.3)	2 (0.0)
Neuroendocrine carcinoma	12 (0.1)	0 (0)
Lymphoma	8 (0.1)	0 (0)
Neoplasm (unspecified)	399 (4.8)	41 (0.5)
Missing	23 (0.3)	0 (0)
Socioeconomic disadvantage (SEIFA), n (%)		
First quintile (most disadvantaged)	1727 (20.7)	1689 (22.6)
Second quintile	1557 (18.6)	1374 (18.4)
Third quintile	1715 (20.5)	1518 (20.3)
Fourth quintile	1783 (21.3)	1654 (22.2)
Fifth quintile (least disadvantaged)	1567 (18.8)	1228 (16.5)
Missing	7 (0.1)	1 (0.0)
Grade, n (%)		
Poorly differentiated	3268 (39.1)	78 (1.0)
Moderately differentiated	733 (8.8)	545 (7.3)
Well differentiated	168 (2.0)	606 (8.1)
Anaplastic	58 (0.7)	0 (0)
Missing	4129 (49.4)	6235 (83.5)
Survival		
Mean (SD) years	5.83 (7.46)	9.27 (7.80)
Median [min., max.] years	2.75 [0, 44.9]	7.10 [0, 39.7]
Missing, n (%)	12 (0.1)	1 (0.0)
Sex, n (%)		
Female	2116 (25.3)	1717 (23.0)
Male	6240 (74.7)	5747 (77.0)

Abbreviation: SEIFA, Socio-Economic Indexes for Areas.

invasive cancer and death was 2.8 years, compared to 7.1 years for non-invasive tumours ($P < 0.001$). Men were more commonly diagnosed with bladder cancer than women, with a 3:1 ratio.

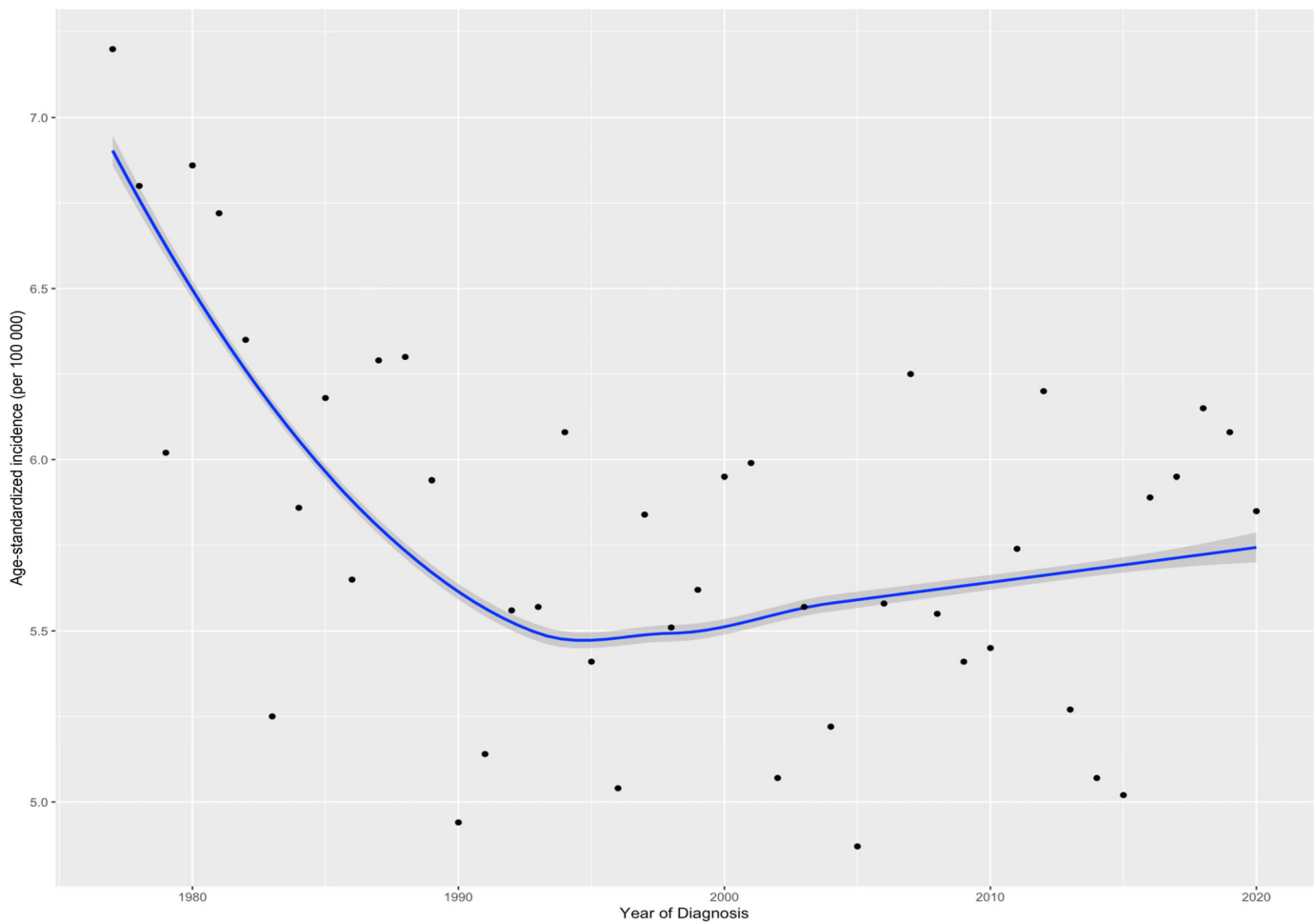
Incidence

In 2020, 275 diagnoses of invasive bladder cancer were made in South Australia, an increase from 159 in 1977. The age-standardized incidence of invasive bladder cancer decreased from 7.20 cases per 100 000 people in 1977 to 5.85 cases per 100 000 in 2020, with a nadir of 4.87 in 2004 (Fig. 1). Annual percentage change analysis describes a breakpoint at the year 1990 for change of incidence trajectory, with a change between 1977 and 1990 of -9.5% (95% CI -14.5 to -4.3) and $+1.0\%$ (95% CI -0.8 to 2.8) between 1990 and 2020.

Change in Survival over Time

Five-year overall survival for invasive bladder cancer decreased from 56% to 43% over the study period (Fig. 2). Cox proportional hazards modelling showed that the hazard ratio [HR] for death for patients with an invasive bladder cancer diagnosis made between 2010 and 2019 was 1.22 (95% CI 1.09 to 1.35) compared to diagnoses made between 1977 and 1979 ($P < 0.001$; Table S1). For non-invasive bladder cancer, 5-year survival was 75% in 1982 and 76% in 2015 with no change in the HR based on decade of diagnosis according to Cox proportional hazards modelling (Table S2).

Kaplan–Meier and Cox proportional hazards modelling showed that invasive bladder cancer survival decreased with age (Fig. 3 and Table 2). Overall survival was negatively correlated with increasing age with an HR for death of 4.90 for patients aged 70–79 years compared to those aged

Fig. 1 Age-standardized incidence for invasive bladder cancer in South Australia (1977–2020).

<50 years (95% CI 4.04 to 5.94; $P < 0.001$). Patients aged >80 years had an HR for death of 9.07 (95% CI 7.46 to 11.0; $P < 0.001$). Cox proportional hazards modelling for invasive bladder cancer showed that, after adjusting for the increasing age at diagnosis across the decades of diagnosis, overall survival improved, with an HR of 0.85 (95% CI 0.76 to 0.94) for those diagnosed after 2010 compared to those diagnosed in the period 1977–1979.

Age at Diagnosis

Between 1977 and 1980 the mean age at time of invasive bladder cancer diagnosis was 68.1 years and this increased to 75.5 years between 2015 and 2020 (Fig. S1). Between 1980 and 1984 the mean age at diagnosis for non-invasive bladder tumours was 64.3 years and this increased to 72.3 years between 2015 and 2020.

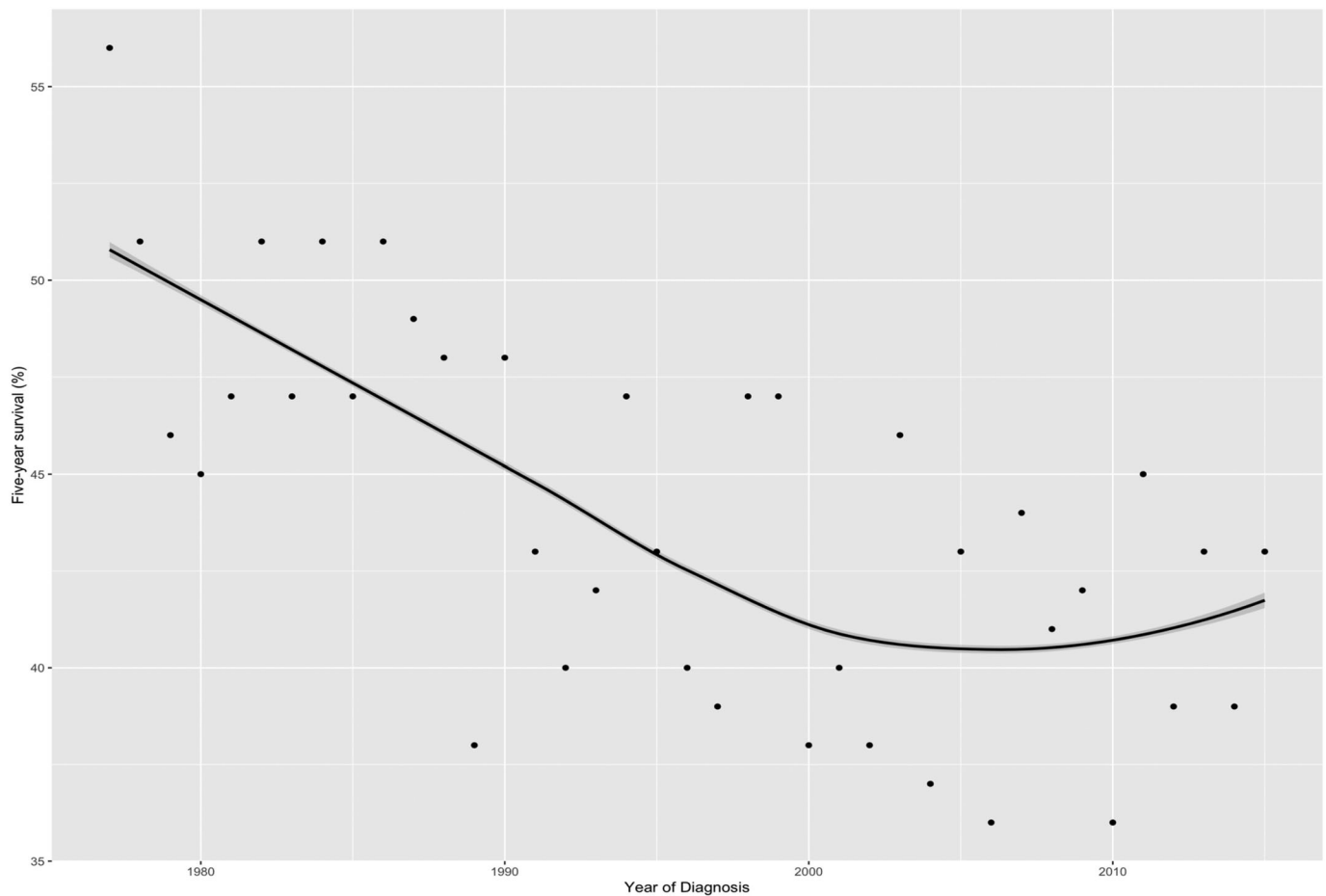
The incidence of invasive bladder cancer in patients aged >80 years saw an annual percentage change of 3.3% (95% CI

2.1 to 4.6), from 1.3 cases per 100 000 in 1977 to 6.0 per 100 000 in 2020 (Fig. S2). There was no statistically significant change in annual percentage change in crude incidence for other age groups (Table S3 and Fig. S3).

There was no statistically significant change in incidence in any age group after adjusting for the state population structure, as determined by overlapping 95% CIs using Annual Percentage Change (APC) calculations (Fig. S3 and Table S4).

Change in Survival over Time by Age Group

Overall survival for invasive bladder cancer only improved for patients in the age category 70–79 years, as demonstrated by Cox proportional hazards modelling (Table S5). The overall survival trend for invasive bladder cancer was found to be increasing for patients aged 60–69 years and those >80 years, however, this was not statistically significant. The overall survival trend for patients aged 50–59 years was found to be decreasing, however, this trend was not statistically significant.

Fig. 2 Change in invasive bladder cancer 5-year survival over time.

Causes of Death

Patients diagnosed with invasive bladder at the age of >80 years had a bladder cancer-specific death rate of 45.0% 5 years after diagnosis, whilst 28.8% died from non-bladder cancer causes (Figs S4 and S5). Among patients aged 70–79 years with invasive bladder cancer, bladder cancer-specific death was observed in 33.2% at 5 years, while in those aged 60–69 years this figure was 26.7% and for those aged 50–59 years it was 24.8%.

Competing risk regression modelling showed that there was no change in bladder cancer-specific deaths over time (Table S6), however, after adjusting for the increasing age at diagnosis, a decrease in bladder cancer-specific deaths was observed (Table S7). The risk of a bladder cancer-specific death from invasive cancer was higher with increasing age, with a sub-HR of 2.40 (95% CI 1.33 to 2.15) for patients aged ≥ 80 years compared to patients aged <50 years (Table S7).

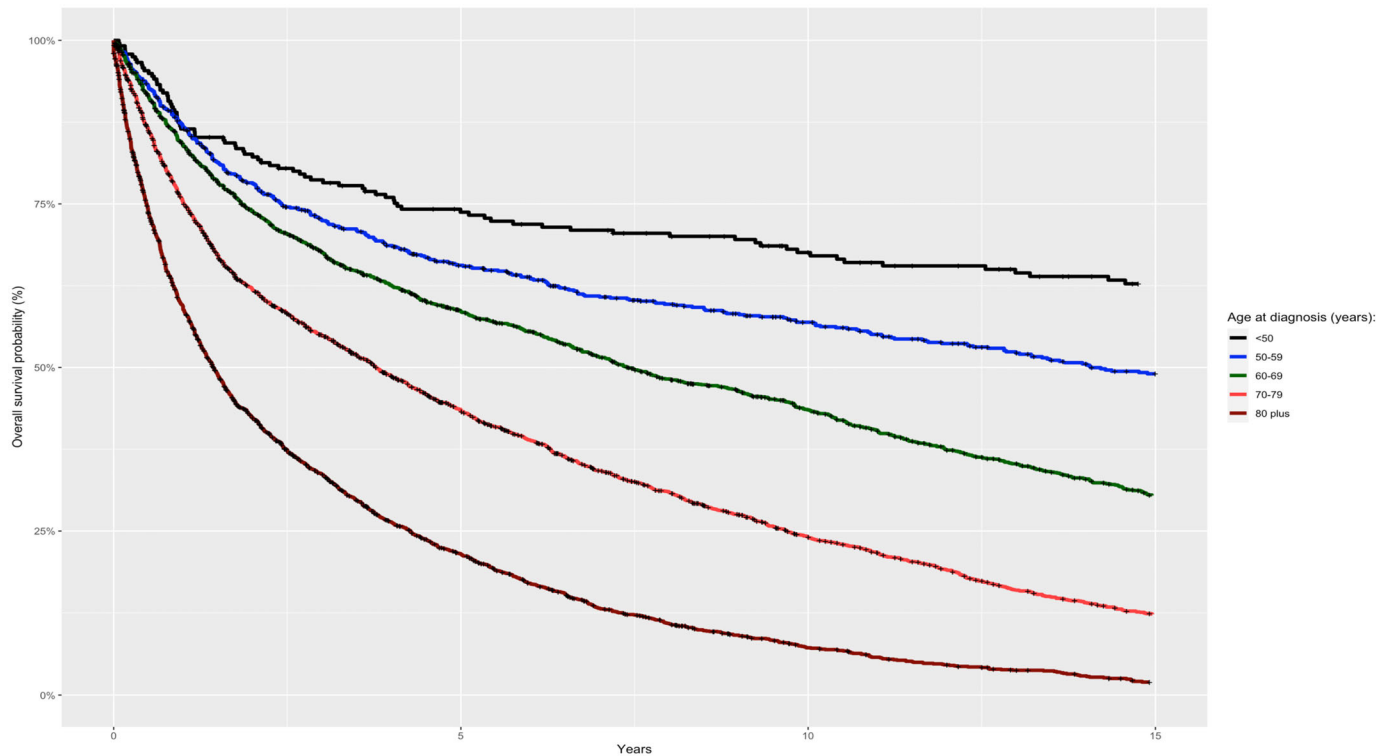
The risk of non-bladder cancer-specific death decreased throughout the study period for those diagnosed with

invasive cancer, with a sub-HR of 0.50 (95% CI 0.43 to 0.58) for those diagnosed in 2010–2019 compared to the period 1977–1979 (Table S8). Older people were more likely to die from a non-bladder cancer cause than younger patients.

Competing risk regression modelling showed that no age category was associated with a statistically significant change in bladder cancer-specific death after diagnosis with invasive bladder cancer; however, there was a trend towards improvement in survival in age groups aged >60 years (Table S9).

Other Factors for Changes in Survival

Confounding factors were tested with Cox proportional hazards modelling, including change in sex distribution, change in histological type and change in distribution of socioeconomic disadvantage over the study period (Table S10). Female sex was associated with lower survival as determined by Cox proportional hazard modelling. Despite histology type and sex being important factors in survival outcomes, Cox modelling showed that they did not contribute

Fig. 3 Kaplan–Meier plot of invasive bladder cancer survival by age at diagnosis.**Table 2** Cox proportional hazard modelling for invasive bladder cancer over time, adjusted for age of diagnosis.

Characteristic	HR	95% CI
Year of diagnosis	—	—
1977–1979	1.00	0.90, 1.11
1980–1989	0.93	0.84, 1.04
2000–2009	0.92	0.83, 1.02
2010–2019	0.85*	0.76, 0.94
Age at diagnosis	—	—
<50 years	1.86**	1.52, 2.28
50–59 years	2.95**	2.43, 3.58
60–69 years	4.90**	4.04, 5.94
70–79 years	9.07**	7.46, 11.0

Abbreviation: HR, hazard ratio. * $P < 0.05$. ** $P < 0.001$.

to the change in 5-year survival rates for invasive bladder cancer reported over the study period.

Discussion

The crude number of invasive bladder cancer cases in South Australia has increased since 1977, but age-standardized incidence has decreased due to an aging population. Overall survival from invasive bladder cancer decreased over the study period, during which non-invasive bladder cancer survival remained stable. We have demonstrated that the

decreasing invasive bladder cancer survival resulted from an increase in mean age at diagnosis, from 68 years between 1977 and 1980 to 76 years between 2015 and 2020.

Incidence

The age-standardized incidence of invasive bladder cancer has decreased since 1977. The decreasing age-standardized incidence possibly reflects a reduction in smoking in Australia from 35% in the 1980s to 11% in 2019 [16,17]. Occupational exposure to bladder cancer carcinogens in Australia has likely decreased over the past 55 years as the workforce has shifted to tertiary industries from primary and secondary industries, in which carcinogen exposure is higher [18].

Figure 1 shows a decrease in age-standardized incidence between 1977 and 1991 and then a gradual increase until 2020. Further statistical analysis of incidence changes using the state population structure over time, instead of the 2001 Australian standard population, shows that, in each age group, there was no statistically significant change in crude incidence. Instead, the increase in age-standardized incidence from 1991 to 2020 was probably attributable to the increase in the number of older people living in the state, to a greater extent than factored in for the 2001 Australian population. It is also possible that the decrease in age-standardized incidence between 1977 and 1991 may have resulted from a

change in coding practice, with more tumours being described as 'invasive' in the earlier years of the registry.

Increasing Age at Diagnosis of Bladder Cancer

Patients diagnosed with bladder cancer aged >80 years were the only age group with a statistically significant increase in crude incidence over the study period, with an average yearly increase of 3.3%. South Australia's population aged >80 years increased from 22 181 in 1977 to 87 370 in 2019. After adjusting for the change in state population for each age group, there was no increase in invasive bladder cancer incidence for any age group over the study period. Therefore, older people are no more likely to develop bladder cancer now than they were 40 years ago; instead, the overall increase in crude incidence is a result of an aging population. The increasing age at diagnosis across the study period had the greatest effect on bladder cancer survival. The incidence of bladder cancer relative to each age category's population remained static in all age groups.

Survival

Invasive bladder cancer 5-year survival decreased over the study period, however, from 2004 to 2020 there was a small increase. Cox proportional hazard modelling shows that overall survival improved in patients aged >60 years, although this did not reach statistical significance in all age groups. Competing risk regression modelling showed a reduction in both bladder cancer-specific deaths and non-bladder cancer-specific deaths for older patients between 2010 and 2019, suggesting improvement in both overall health in older people and bladder cancer treatment in older people. Bladder cancer survival decreases with age. Overall survival for invasive bladder cancer has improved for patients aged 70–79 years since 1977, a trend seen in patients aged 60–69 years and in patients aged >80 years, without reaching statistical significance. However, once non-bladder cancer deaths were excluded, there was no statistically significant change in survival for these patients. These findings suggest that patients aged >60 years may be surviving longer following a diagnosis of invasive bladder cancer due to being healthier overall, and benefiting from improvements in prevention and treatment for other comorbidities, therefore, they are less likely to die from a non-cancer-related issue. Given that such a large proportion of invasive bladder cancer diagnoses are in patients aged >70 years (65% in this study), and that there was no improvement in bladder cancer-specific survival for patients in this age group, optimizing treatment for these patients is of great importance.

Possible changes in coding practices between 1977 and 1991, which might have resulted in some non-invasive lesions being miscoded as invasive, would have resulted in the 'invasive' group being diluted with non-invasive lesions with better

prognoses. If this assumption is correct, survival rates might appear higher in the earlier years of the study. Unfortunately, we can only speculate about this and we do not know if these early results could be affected by changes in coding practice or the potential extent to which they may have been affected.

Sex

Men with a diagnosis of invasive bladder cancer had an HR of 0.87 for death compared to women ($P < 0.001$). It is well reported in the literature that women have worse early bladder cancer survival, with suggested reasons including delayed diagnosis, hormone response, anatomical differences and poorer response to treatment [19].

Bladder Cancer Survival in Older People

Older people are diagnosed with higher stage and grade disease, possibly due to later diagnosis, the symptoms of bladder cancer perhaps being overlooked or misdiagnosed as benign conditions or impaired biochemical response to neoplasms [20].

With older age, mutation recognition and DNA repair becomes less effective as immune and inflammatory responses become increasingly dysregulated [21]. Cancer cell recognition and destruction early in mutation development is reduced and neoplastic progression becomes more likely [21]. Frailty in older people reduces the likelihood of satisfactory response from curative treatments and enduring treatment without intolerable side effects [21]. There is evidence of under-treatment of both non-invasive and invasive bladder cancer in older people, which may result from hesitancy in order to avoid harm, given that older people are more susceptible to complications [6–9].

Mortality vs Survival

Analysis of WHO data determined that bladder cancer mortality had decreased for men in Oceania by 0.57% annually between 1967 and 2016 [4]. Table S11 shows the worldwide changes in male patient bladder cancer mortality between 2002 and 2012, demonstrating that mortality is decreasing generally across the world. These mortality trends do not necessarily correlate with survival as mortality is affected by change in incidence whereas survival is not [22]. The reporting of survival in nationwide databases is sparse in the contemporary literature given that survival analysis requires registries reporting the date of diagnosis in addition to date of death [4]. Consequently, studies focusing on survival are rare and have the benefit of assessing change in bladder cancer care without change in incidence impacting the results. The SACR only records cancer diagnoses made after 1976 and therefore it is not possible to perform a mortality analysis of the SACR data compared to the

mortality trend of the wider region as diagnoses made prior to 1977 would not be included in the analysis. Given our findings of decreasing bladder cancer survival in South Australia it is likely that the reason for Australia's improving bladder cancer mortality results from the decrease in bladder cancer incidence.

Implications of this Study

These findings, based on data from South Australia, are likely to be typical of trends across Australia and more economically developed countries where there is an aging population. South Australia matches national averages for the surgical treatment of carcinoma invading bladder muscle [23]. Certainly, there is a trend towards aging populations in more economically developed countries and this, in combination with age as a strong risk factor for bladder cancer development and poor survival, results in the need for clinicians to optimize treatment and diagnosis of bladder cancer in older people. In particular, further research is warranted to better determine the risk to benefit ratio of bladder cancer treatments and the reason for under-treatment of bladder cancer in older people so that the largest age group receiving bladder cancer diagnoses is optimally managed.

Although smoking rates are decreasing in Australia, urologists should continue to consider the seriousness of smoking as a risk factor in bladder cancer. Urologists should discuss smoking cessation with all patients who smoke given that the number needed to treat for smoking cessation from simple advice provided by a doctor is between 50 and 120, however, the number needed to treat may be lower in patients who are due to undergo surgery or with risk factors for bladder cancer [24].

Compared to prostate cancer, there is lower awareness of bladder cancer and it receives less research funding [25,26]. The general population may be less aware of bladder cancer symptoms and their seriousness and therefore present later. Urological societies, urologists and charities may be in a suitable position to raise the profile of bladder cancer in communities to educate about symptoms, advise about the harms of smoking beyond cardiovascular disease and encourage earlier presentation and referrals.

Urologists should consider how to make best use of the evolving technology available to them to improve bladder cancer care. Despite video-endoscopy being used throughout Australia at all stages of bladder cancer care, and the clear benefits of clinical images that are correctly obtained [27], there is evidence that video-urology could be used more efficiently as only 18.6% of urologists routinely record cystoscopic photographs [28]. The under-utilization of electronic medical records (EMR) for research purposes has

recently been highlighted [29]. EMR have the potential for drawing together huge quantities of data; however, due to their design strategy targeting billing rather than ease of clinician data entry or extraction, EMR may not be fully utilized for large database studies until they are compatible across multiple sites and are integrated with larger research databases [29]. In general, we should consider how existing and emerging technologies can best be used for improving detection and treatment of bladder cancer.

Limitations

Important risk factors for bladder cancer development, including smoking and occupational exposure, are not recorded by the SACR and therefore we could not adjust for their effect as confounders. The reduction in smoking and occupational carcinogen exposure reported elsewhere may explain the increasing age of onset of bladder cancer development seen in this study [16–18]. Staging beyond $<pT1$ and $\geq pT1$, treatment and comorbidity data are not recorded in the SACR and therefore changes in these factors over time were not analysed.

Conclusion

Invasive bladder cancer survival decreased in South Australia over the study period 1977–2020, which appears to be the result of an aging population. Age at diagnosis increased from 68 to 76 years over the study period, perhaps due to reduced exposure to carcinogens. Age was inversely correlated to bladder cancer survival, and Cox proportional hazard modelling showed that the largest impact on decreasing survival over the study period was increasing age at diagnosis. Bladder cancer-specific survival did not improve for any age category over the study period and new treatments to address this are needed.

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Disclosure of Interests

None declared.

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Abbreviations: EMR, electronic medical records; ICD-O-3, International Classification of Diseases for Oncology, third edition; SACR, South Australian Cancer Registry; SEIFA, Socio-Economic Indexes for Areas.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Fig. S1. Mean age at diagnosis for bladder cancers in South Australia (1977–2020).

Fig. S2. Invasive bladder cancer crude incidence (per 100 000 total population) by age at diagnosis.

Fig. S3. Invasive bladder cancer incidence by age category (total diagnoses/population in each age category).

Fig. S4. Cumulative incidence of non-bladder cancer specific deaths by age groups (invasive).

Fig. S5. Cumulative incidence of bladder cancer specific deaths by age groups (invasive).

Table S1. Cox proportional hazard modelling for invasive bladder cancer over time.

Table S2. Cox proportional hazard modelling for non-invasive bladder cancer over time.

Table S3. Estimated annual percentage change for invasive bladder cancer crude incidence by age category.

Table S4. Estimated annual percentage change for invasive bladder cancer incidence by age category (total diagnoses/population in each age category).

Table S5. Separate Cox proportional hazards models demonstrating change of overall survival over the study period.

Table S6. Competing risk regression modelling for bladder cancer specific death by year of diagnosis.

Table S7. Competing risk regression modelling for bladder cancer specific death by year of diagnosis adjusted for age at diagnosis.

Table S8. Competing risk regression modelling for non-bladder cancer specific death by year of diagnosis and age at diagnosis.

Table S9. Competing risk regression modelling for bladder cancer specific death by year of diagnosis and age at diagnosis.

Table S10. Cox Proportional Hazard modelling adjusting for survival confounders.

Table S11. Average annual percentage change in the male mortality of bladder cancer between 2002 and 2012.