Bladder cancer is the tenth commonest cancer in Australia, accounting for approximately 2 per cent of all new cancers. In 2010 it had an age-standardised incidence of 10.1 per 100 000 population, which had reduced from a figure of 17.9 in 1982. In keeping with most other countries, the incidence of bladder cancer in Australia is more than three times higher in men than in women.

While mortality has reduced from 5.4 to 4.1 deaths per 100 000 population between 1982 and 2010, this reflects its decreasing incidence as opposed to improving survival; the mortality-incidence ratio has increased from 0.30 to 0.41 over this period. Unfortunately, bladder cancer is the only cancer in Australia in which survival is worsening; five-year survival has fallen from 68 to 58 per cent in the past 30 years. Of additional concern is the significantly lower five-year survival for women, which is 50 per cent, as compared with 60 per cent in men. Interestingly, these figures and trends are extremely similar to those in the UK (Table 1).

DO CODING CHANGES ACCOUNT FOR DETERIORATING SURVIVAL?
Could the apparent deterioration in five-year survival from bladder cancer in Australia over the past 30 years be explained by changes in coding practices over that period? This is certainly a possibility given that, while state cancer registries record all cases of bladder cancer, non-invasive cancers (Ta and CIS) are excluded from published statistics; a similar approach is adopted by UK cancer registries. This means that if there has been an improvement in the accuracy of coding over time, older data may contain disproportionately more non-invasive cancer that has been miscoded as invasive. Five-year survival would therefore be expected to be erroneously high for earlier cohorts as a result of the inclusion of this lower-risk disease.

This theory is supported by the dramatic decrease in the incidence of bladder cancer in Australia over the past 30 years. It has almost halved over this period, and this seems too large a reduction to be attributed to a reduction in risk factors or improved early detection. Additionally, a study of histopathology reports over the past 30 years in Western Australia revealed that the percentage of tumours coded as invasive that were actually non-invasive...
It is the strong opinion of the authors that all patients with bladder cancer, including those with non-invasive disease, should be included in registry data. This is particularly pertinent for bladder cancer in view of the relatively high rates of recurrence and progression associated with non-invasive disease.

It has been hypothesised that an ageing population may explain the reduction in survival from bladder cancer in Australia over the past 30 years, but is there any evidence to support this? Certainly the ageing population is resulting in an increased age at diagnosis of bladder cancer; national data demonstrate that the percentage of patients diagnosed with bladder cancer who are aged 80 years or older has increased from 15.6 to 36.2 per cent over the past 30 years. Given that older patients are less likely to be candidates for radical treatments such as cystectomy or chemoradiation, it seems reasonable to consider that this advanced age at diagnosis may be contributing to a deteriorating survival trend.

Evidence to support this was provided by a South Australian study, which found that patients over the age of 80 had much poorer survival from bladder cancer than younger patients. Interestingly, this study also found that when non-invasive disease (Ta and CIS) was included in overall five-year survival analysis, there was actually a significant improvement in survival over time (72.9 per cent in 1980–84 versus 80.2 per cent in 1995–2004).

ARE DELAYS IN DIAGNOSIS CONTRIBUTING TO DECLINING SURVIVAL?
While it is theoretically possible that longer delays in diagnosis are responsible for the deteriorating survival trend for bladder cancer in Australia, the available data suggest that early diagnosis has actually improved over time. Some evidence for this is provided by the aforementioned South Australian study; 53.5 per cent of tumours diagnosed between 2000 and 2004 were non-invasive (Ta or CIS) compared to 23.7 per cent of those diagnosed between 1980 and 1984.

Dedicated haematuria clinics are an efficient way to manage haematuria referrals; however, they are not widely utilised in Australia. This is possibly a result of health service configuration issues that provide barriers to the development of ‘one-stop’ rapid-access diagnostic services. Nonetheless they are more prevalent now than they were 30 years ago and appear to be gaining in popularity. One such clinic in Western Australia has assessed more than 1000 patients since its introduction in 2008, and has been successful in reducing the mean wait time for cystoscopy by 22 per cent.

Finally, new technologies in the detection and treatment of bladder cancer are more prevalent in Australia today than they were 30 years ago; these may result in improvements in early diagnosis of bladder cancer. Narrow-band imaging is widely available and, while photodynamic diagnosis is licensed, uptake has been minimal.

Table 1. Comparison of Australian and UK bladder cancer data and trends

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<tbody>
<tr>
<td>Overall age-standardised incidence (per 100 000 population)</td>
<td>17.9</td>
<td>10.1</td>
<td>16.0 (1982)</td>
<td>11.0</td>
</tr>
<tr>
<td>Male age-standardised incidence (per 100 000 population)</td>
<td>30.8</td>
<td>17.0</td>
<td>28.0 (1982)</td>
<td>18.0</td>
</tr>
<tr>
<td>Female age-standardised incidence (per 100 000 population)</td>
<td>8.6</td>
<td>4.6</td>
<td>7.7 (1982)</td>
<td>5.5</td>
</tr>
<tr>
<td>Age-standardised mortality rate (per 100 000 population)</td>
<td>5.4</td>
<td>4.1</td>
<td>6.6 (1982)</td>
<td>4.8</td>
</tr>
<tr>
<td>Mortality/incidence ratio</td>
<td>0.30</td>
<td>0.41</td>
<td>0.41 (1982)</td>
<td>0.44</td>
</tr>
<tr>
<td>Overall 5-year survival</td>
<td>68%</td>
<td>58%</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Male 5-year survival</td>
<td>–</td>
<td>60%</td>
<td>64% (1995)</td>
<td>58%</td>
</tr>
<tr>
<td>Female 5-year survival</td>
<td>–</td>
<td>50%</td>
<td>59% (1995)</td>
<td>50%</td>
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Table 1. Comparison of Australian and UK bladder cancer data and trends

COULD SURVIVAL BE DETERIORATING BECAUSE THE DISEASE IS CHANGING?
While deteriorating survival from bladder cancer could conceivably be because bladder cancer is evolving to become more aggressive, the authors are unaware of any evidence to support this. Although smoking rates and other risk factors for bladder cancer have reduced over the past 30 years, bladder cancer occurring in the absence of risk factors is not known to be more aggressive. Additionally, there does not appear to be any evidence that the proportion of high-grade disease, non-uromithelial tumours, or cancers with divergent differentiation is increasing in Australia.

COULD WORSENING TREATMENT BE THE CAUSE OF POORER SURVIVAL?
While worsening treatment could potentially explain worsening survival, the authors believe that the treatment of bladder cancer in Australia has improved considerably over the past 30 years. Before examining this, though, two unique aspects of practising urology in Australia must be understood.

First, Australia has a population density approximately 160 times smaller than the...
UK (three people/km² compared with 480 people/km² in the UK). While most Australians live in major cities, 29 per cent reside outside major cities, with 8 per cent of these people living in remote or very remote areas.6 Providing acceptable access, treatment and surveillance to people living in these areas can be quite challenging – visiting the nearest urological centre can require a flight or several days of travel by car.

Second, the majority of elective surgery in Australia is performed in the private sector. While this may relieve some of the burden on the public system, it also provides barriers to the centralisation of bladder cancer services. This may impact negatively on many aspects of bladder cancer care such as a multidisciplinary care team-based approach, intravesical therapy administration and centralisation of cystectomy.

Below we will examine individual aspects of bladder cancer management likely to impact on overall outcomes, with reference to Australian data where available.

NON-MUSCLE-INVASIVE BLADDER CANCER
Quality of initial resection
Data are lacking on the quality of resection of bladder tumours in Australia. A retrospective study was conducted of more than 1000 transurethral resection of bladder tumour (TURBT) specimens collected over a five-year period in Sydney.7 Of some concern was the fact that muscularis propria was identified in the resected specimen of less than 40 per cent of high-risk tumours (high-grade Ta or T1), with 19 per cent of those without muscularis propria on initial resection being subsequently upstaged on re-resection.7

Postoperative and adjuvant intravesical therapy
Following initial resection of a bladder tumour, a single dose of postoperative intravesical chemotherapy is recommended, as it has been shown to reduce the risk of recurrence.8 Additionally high-risk non-muscle-invasive bladder cancer (NMIBC), if managed with a bladder-preserving approach, is best treated with adjuvant intravesical BCG with maintenance.9 A South Australian study of patients presenting over a five-year period found that 59 per cent of patients undergoing TURBT were given a postoperative dose of intravesical chemotherapy; only 24 per cent of those not receiving treatment had a clear contraindication on review of their operative records.9 Use of BCG in T1 and CIS disease was 54 per cent overall but improved over time (34.5 per cent in 2005–07 versus 63.6 per cent in 2008–09).9

A study of nearly 700 patients with NMIBC in Victoria between 1990 and 1995 found that, although 38 per cent of tumours were T1 or CIS, only 8.5 per cent of patients received adjuvant intravesical treatment.10 Additionally, only 44 per cent of those who developed recurrences proceeded to intravesical or radical treatment, even though 57 per cent of recurrences had occurred by three months.10

Surveillance
While data are lacking on surveillance, in the previously mentioned South Australian study, 55 per cent of patients with low-risk NMIBC appeared to undergo excessive cystoscopic surveillance regimens and 43 per cent of higher-risk NMIBC was subject to under-surveillance.11 Additionally, use of cytology (3 per cent) and upper-tract imaging (30 per cent) in higher-risk NMIBC was poor.9

MUSCLE-INVASIVE BLADDER CANCER
Radical cystectomy
Radical cystectomy is the predominant treatment modality for muscle-invasive bladder cancer (MIBC) in Australia; primary chemoradiation is less commonly offered. However, establishing high-volume
centres is made difficult by the population distribution, large private sector, and the genuine need for Australian urologists to have a more generalised training. These reasons also likely explain the limited uptake of robotic cystectomy in Australia.

A retrospective study of more than 200 cystectomy specimens collected in New South Wales between 1998 and 2008 revealed relatively high rates of positive margins (15 per cent main tissue margin, 11.5 per cent ureteric margin, 7.5 per cent urethral margin). Additionally there were relatively low rates of lymphadenectomy (70 per cent), and low lymph node yields in those who did undergo this (75 per cent had fewer than 10 nodes identified). However, improvements in positive margin rates and lymph node dissections were observed over time.

A retrospective analysis of lymphadenectomy practice was performed for 87 patients who underwent radical cystectomy at a large Melbourne centre between 2004 and 2011. Although only 66 per cent of patients underwent a lymph node dissection overall, the proportion of patients undergoing lymphadenectomy (3/7 in 2004 versus 10/10 in 2011) and the median lymph node harvest (5 in 2004 versus 18 in 2011) both showed a significant increase over time.

Neoadjuvant and adjuvant chemotherapy
The same Melbourne centre also reported on a reassuring trend on use of perioperative chemotherapy in patients undergoing radical cystectomy. Although only 17 per cent of patients with MIBC received neoadjuvant chemotherapy overall, there was a significant increase in its use over time (0/25 in 2004–06 versus 11/38 in 2007–11); this increase appeared to coincide with the introduction of a regular multidisciplinary meeting. Additionally, 46 per cent of patients with T3, T4 or nodal disease received adjuvant chemotherapy, with the majority of patients not receiving it doing so for clear clinical reasons. The chemotherapy delivered appeared to be both effective (0.41 relative risk of recurrence after controlling for age, T-stage and N-stage, p<0.05) and well tolerated (percentage completing their planned number of cycles: 85 per cent [neoadjuvant], 67 per cent [adjuvant]).

There are several trials relating to bladder cancer that are in their early stages, which have been developed through the Australian and New Zealand Urogenital and Prostate (ANZUP) Cancer Trials Group. ANZUP is a cancer co-operative clinical trials group that was established in 2008 to improve multidisciplinary collaboration regarding clinical trial research into the management of bladder cancer.

KEY POINTS

- Analysis of Australian bladder cancer trends is complicated by non-reporting of non-invasive disease, as well as changes in coding practices
- Nonetheless, the incidence of invasive bladder cancer is reducing, while it appears as though survival is worsening; this is in keeping with UK data
- Changes in coding practices, increased age at diagnosis and improved detection of bladder cancer while still at a non-invasive stage appear to best explain these trends
- While some of the data discussed demonstrate significant potential for improvement in bladder cancer management in Australia, treatment trends appear to be moving in a positive direction
- The utilisation of multidisciplinary meetings, rapid-access diagnostic clinics and clinical guidelines and pathways seems to be increasing
- In collaboration with ANZUP, bladder cancer research in Australia is gaining momentum; results from clinical trials are to be expected with increasing regularity over the coming years
management of urologic cancers; its bladder cancer subcommittee now has more than 175 members.

One ANZUP study is the BCGMMC trial, which is a currently recruiting national randomised phase 3 trial of combined BCG and mitomycin versus BCG alone in the treatment of high-risk NMIBC. Other collaborations include radiotherapy trials with the Trans Tasman Radiation Oncology Group (BOLART) and UK researchers (Raider-B). Other concepts at an advanced stage of development include studies relating to chemotherapy regimens in different settings (peri-cystectomy, renal impairment, second-line therapy).

Declaration of interests: none declared.

REFERENCES