Poster 203

Extended Presentation

Modelling the burden of non-muscle-invasive bladder cancer in Europe

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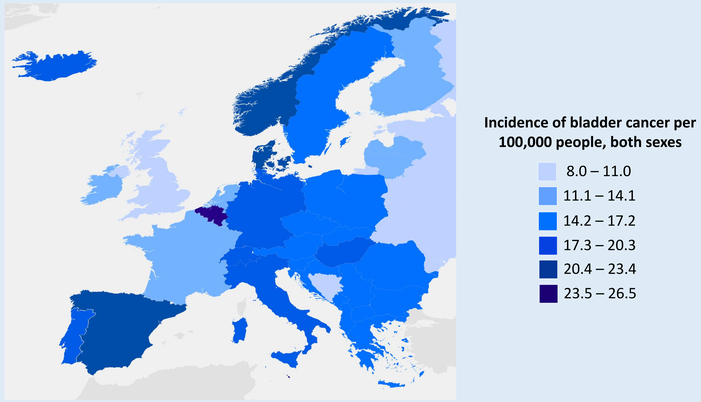
BACKGROUND + AIMS

- Bladder cancer is relatively common – the average age-standardised annual incidence rates for men and women per 100,000 in the EU-27 are 26.9 and 5.3, respectively (1), and reported incidence varies widely **(Figure 1)**.
- Mortality of 4.7 per 100,000 individuals annually across the European Union.
- Most cases are non-muscle-invasive bladder cancer (NMIBC), classified into risk groups based on their chance of progression, which determines the frequency and duration of monitoring after treatment.
- Few data about the relative prevalence of disease by risk group and burden of monitoring are available.

Figure 1: Annual incidence of bladder cancer per 100,000 people in Europe



We aimed to:

- Create a flexible tool to estimate the burden of NMIBC cases in eleven European countries.
- Estimate the number of monitoring cystoscopies by risk group based on national or regional guidelines.

METHODS

- Searched the literature on bladder cancer diagnosis, treatment and monitoring in the UK and Europe.
- Created a conceptual framework for understanding patients' progression through disease stages.
- Built a pathway framework in Excel, with an embedded Markov model which stratifies NMIBC patients by risk group after diagnosis, and follows them for 10 years to estimate disease burden (**Figure 2**).
  - Estimated the number of NMIBC cases annually per risk group that recur, progress, recover, and die.
  - Number of cystoscopies = (annual number of cases)x(specified number of monitoring cystoscopies
  - Parameter values were extracted from published data (2-6). Estimates for progression and recurrence were only available for years 1 to 5 of follow up; we estimated these for years 6 to 10.
- As 'prevalence' is a problematic term in cancer research, we have defined it thus:

prevalence = (people diagnosed in the past 10 years who are now in a given risk category) – (mortality) – (progression to muscle invasive bladder cancer)

Tool assumptions

- *Only one state change (i.e. progression) occurs annually.*
- *Progression implies a state change to the next higher risk category.*
- *Only one recurrence is allowed per person in the 10-year period.*
- *Incidence of bladder cancer in England, Scotland, Northern Ireland and Wales is assumed to be the same as that reported by IARC for the entire UK.*
- *The maximum follow-up period is 10 years.*
- *Background mortality unrelated to bladder cancer is excluded.*
- *Current guidelines are being followed perfectly!*

RESULTS I

The pathway framework developed is presented in **Figure 2**, and has default data for England, using the EAU monitoring guidelines. In this tool, users can select one of eleven pre-programmed countries' data, or override defaults with data from their country or region.

Figure 2: Tool, populated with English data, under EAU NMIBC monitoring guidelines

Select country	UK: England*	
Population	54,316,618	
Number of new cases per year	7,317	IARC, 2012
Incidence +	9.1	IARC, 2012
Prevalence (5 year) +	52.8	IARC, 2012

Number of new diagnoses of bladder cancer annually (1 year incidence): 7,317

Annual incidence of low risk NMIBC	Annual incidence of intermediate risk NMIBC	Annual incidence of high risk NMIBC	Annual incidence of MIBC
1,610	1,610	2,305	1,800

Total 10-year progressions to MIBC: 488

Estimated 10-year prevalence of NMIBC *: 49,187

33%	32%	36%
10-year prevalence of low risk NMIBC: 16,097	10-year prevalence of intermediate risk NMIBC: 15,622	10-year prevalence of high risk NMIBC: 17,468

Baseline value for calculating the number of cystocopies: 10-year prevalence

Guidelines to estimate the number of cystoscopies annually: EAU guidelines

	Low risk NMIBC	Intermediate risk NMIBC	High risk NMIBC
Year 1	2	2	4
Year 2	1	2	4
Year 3	1	2	2
Year 4	1	2	2
Year 5	1	2	2
Year 6	0	1	1
Year 7	0	1	1
Year 8	0	1	1
Year 9	0	1	1
Year 10	0	1	1
Number of years of monitoring	5	10	10
Total number of tests per person	6	15	19

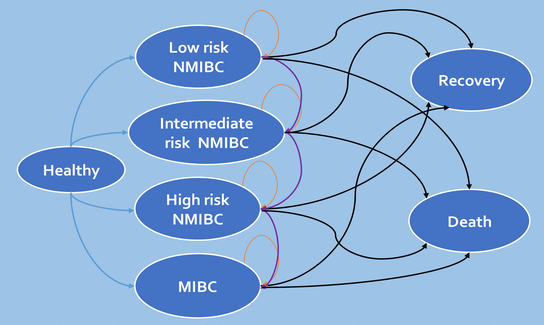
Population under monitoring for low risk NMIBC	Population under monitoring for intermediate risk NMIBC	Population under monitoring for high risk NMIBC
9,906	15,679	18,222
Number of cystoscopies for monitoring low-risk NMIBC annually: 12,258	Number of cystoscopies for monitoring intermediate risk NMIBC annually: 24,959	Number of cystoscopies for monitoring high risk NMIBC annually: 41,256

Total 10- year prevalence of NMIBC	Total number of cystoscopies for monitoring annually	Total 10-year recurrent cases
49,187	78,472	2,693

RESULTS II

- A schematic for the annual progression of patients through the Markov model is given in **Figure 3**.

Figure 3: Conceptual framework for tracking patients through risk groups over 10 years



- Our model, populated with English data and following EAU guidelines, estimates that there will be 78,472 monitoring cystoscopies in England annually, a total 10-year prevalence of NMIBC of 49,187, and a total of 2,693 recurrent cases. Following the NICE guidelines yields a reduction to 55,843 monitoring cystoscopies.
- The split of patients into the NMIBC risk groups at diagnosis is: 29% low risk, 29% intermediate risk, and 42% high risk. However, due to the differing recurrence, progression, and mortality rates in each category, the 10-year prevalence proportions change and the split of risk categories is: 33% low risk, 32% intermediate risk, and 36% high risk.

Table 1: Model outputs, by risk classification and guidance

Risk Category	Population under monitoring		Monitoring cystoscopies	
	EAU	NICE	EAU	NICE
Low	9,906	2,352	12,258	4,704
Intermediate	15,679	9,280	24,959	11,647
High	18,222	18,222	41,251	39,492

A note about 'prevalence':

NMIBC prevalence has been reported as 10x higher than incidence (7). In the UK, prevalence was 46,500 at the end of 2006 (NCIN, 2010) and was the number of people alive 10 years after diagnosis, which is only 5x incidence. In this case, 'prevalence' depends only on incidence and mortality. We wanted to know how many people are actively being monitored (those receiving monitoring cystoscopies).

DISCUSSION/FURTHER STEPS

- More data are needed on the breakdown of risk group at diagnosis!
- Our model captures the fact that once a patient recurs or progresses, he begins their monitoring regimen at year 1 again. This is important to understand the true burden of monitoring, as progression and recurrence occur, and are not usually accounted for in estimates.
- Results inform the epidemiology and burden of NMIBC and its ongoing monitoring in Europe. There is a large burden of monitoring cystoscopies after treatment, with which some patients and clinics may find it challenging to comply. Health systems across Europe could explore alternative approaches to monitoring.
- Changes in guidelines affect the burden of cystoscopies, and any differences in national or local guidelines could mean result in a different burden to healthcare systems for monitoring.
- Even if published guidelines are recommended in a given country, they may not always be followed. We have estimated the expected burden given the guidelines are followed perfectly, and would require better access to clinical data to determine the monitoring picture in Europe to validate our estimated numbers.

REFERENCES

1. Ferlay et al. Cancer incidence and mortality patterns in Europe: Estimates for 40 countries in 2012. European Journal of Cancer (2013) 49, 1374-1403.
2. Millan Rodrigues et al. Primary superficial bladder cancer risk groups according to progression, mortality and recurrence. Journal of Urology (2000) 164, 680-4.
3. Babjuk et al. Guidelines on non-muscle-invasive Bladder Cancer (Ta, T1, and CIS). European Association of Urology (2015).
4. NICE. Bladder Cancer: diagnosis and Management. NICE (2015).
5. Boustead GB et al. Stage, grade and pathological characteristics of bladder cancer in the UK: British Association of Urological Surgeons (BAUS) urological tumour registry. BJU International (2014) 113, 924-30.
6. Aldousari et al. Update on the management of non-muscle invasive bladder cancer. Canadian Urological Association Journal (2010) 4, 56-64.
7. Botteman et al. The Health Economics of Bladder Cancer. PharmacoEconomics (2003) 18, 1315-1330.

The information presented here is based on the authors' independent views.

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