





Care of bladder cancer patients diagnosed in Northern Ireland 2010 & 2011

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FOREWORD

This report describes the characteristics of patients with bladder cancer and their care in 2010 and 2011. Survival of women with bladder cancer is lower than men, and in N. Ireland was lower in published international survival data. This audit allowed this to be explored further. Unfortunately late diagnosis is a recurring theme in the cancer arena and we must work hard with the public and professionals to reduce delay. I am pleased to read that overall services are provided by well functioning teams. We need to improve access to specialist diagnostic and support services and reduce delays in investigation and treatment.

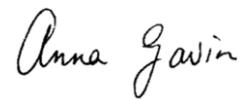
This report provides valuable information which is essential in helping us to track progress and identify those areas where change is needed. This report highlights the importance of the collaborative work between the Cancer Registry, Guidelines and Audit Implementation Network (GAIN) and clinicians in providing a leading role in monitoring cancer care within Northern Ireland and Commissioners and providers of service.



Dr. Michael McBride
Chief Medical Officer
January 2014

ACKNOWLEDGEMENTS

This report has been compiled in collaboration with the Northern Ireland Cancer Network (NICaN) Urology Regional Cancer Group. I am grateful to the clinicians who helped with determining the data items to collect, their interpretation and final presentation. The N. Ireland Cancer Registry (NICR) is funded by the Public Health Agency (PHA) and this work was facilitated by funding from the Guideline and Audit Implementation Network (GAIN). The quality of data in this project is the result of the work of the Registry Tumour Verification Officers, Bernadette Anderson, Julie McConnell, and Jackie Kelly who meticulously extracted detailed information from clinical records for analysis and presentation in this report. Data abstraction was facilitated by Colin Fox of the Registry's IT group. The analysis of data and report writing was undertaken by Dr Finian Bannon with clinical guidance from Dr Lisa Ranaghan. A special word of gratitude goes to the Medical Records staff of all the hospitals in N. Ireland, who have facilitated the Registry in this work. I wish also to record my thanks to the Steering Group and Council of the Registry who guide that work and the Public Health Agency which funds the N. Ireland Cancer Registry.



Anna Gavin
Director, NICR
January 2014

INTRODUCTION

Aims

1. To detail the care pathway of bladder cancer patients in N. Ireland and assess compliance with recommended guidelines for investigation and treatment.
2. To explore reasons for differences in bladder cancer survival in women compared to men.
3. To serve as a benchmark for further audits.
4. To make recommendations for service improvement if necessary.

Background

This report, the 10th in the current audit series undertaken by the N. Ireland Cancer Registry, describes the characteristics of patients with bladder cancer and their care pathway in 2010 and 2011. It was requested by the clinicians, who treat bladder cancer, and who were concerned about the reported poor survival in EUROCARE-4¹ of women with bladder cancer in N. Ireland when compared internationally.

Changes in cancer service provision have been driven by recommendations and guidance developed by several working groups and public bodies over the past 15 years.

Documents providing guidance for better service provision of bladder cancer patients are:

- *Cancer Services: Investing for the Future* (1996)², or more commonly known as *The Campbell Report*, was a landmark report arising from the work of clinicians, service planners and patients who worked together with the aim of improving cancer services in N. Ireland.
- *Cancer Services: Investing for the Future. Cancer Working Group Sub-group reports*³, documents recommendations, arising from the *Campbell Report*, for bladder cancer services in N. Ireland.
- *A Cancer Control Programme for Northern Ireland*⁴ (2008) was developed by the Department of Health, Social Services and Public Safety to set out clear standards for the quality of cancer care in Northern Ireland over the next ten years.
- The *Service Framework for Cancer Prevention Treatment and Care*⁵ (2008) prioritised the recommendations coming out of the *A Cancer Control Programme for Northern Ireland*⁴. Overarching Standard Number 45 directly relates to bladder cancer: "Radical surgery for prostate and bladder cancer should be provided by teams carrying out a total of at least 50 such operations per annum and should take place on a single site, which offers appropriate post-operative care".
- The National Institute for Clinical Excellence (NICE) produced guidelines which dealt with bladder cancer: *Improving outcomes in urological cancers* (2002)⁶.
- Scottish Intercollegiate Guidelines Network (SIGN) produced *Management of transitional cell carcinoma of the bladder- a national clinical guideline*⁷ in 2005.
- The British Association of Urological Surgeons (BAUS) and the British Uro-oncology Group (BUG) have jointly developed guidance *Multi-disciplinary Team Guidance for Managing Bladder Cancer*⁸ in 2013.

INTRODUCTION

- The European Association of Urology issued *Guidelines on Non-muscle-invasive bladder cancer (TaT1 and CIS)*⁹ and *Guidelines on bladder cancer muscle-invasive and metastatic*¹⁰ in 2013.
- The National Comprehensive Cancer Network (NCCN) issued guidelines *Bladder Cancer*¹¹ in 2013.
- Appendix A presents a summary of bladder cancer aetiology and treatment with recommendations, that largely reflects the guidance listed above. In addition, standards and waiting time targets as laid down by the Department of Health, Social Services and Public Safety Northern Ireland (DHSSPSNI)^{2,3,5} are included where relevant.

Areas for Audit

This report includes the following areas of audit which were considered important in delivering care according to the recommendations laid out in *Appendix A*.

Areas of Audit include:

1. Referral and presentation.
2. Patient factors – lifestyle, family history, comorbidities, and symptoms.
3. Investigations, in particular cystoscopy and tumour stage.
4. Stage-specific treatments received, i.e. oncology, surgery, or palliative supportive care.
5. Patient survival.
6. Number of Trusts with haematuria clinic services that perform a range of diagnostic services in the one appointment (sometimes referred to as ‘one-stop clinic’) for patients with haematuria (blood in the urine).
7. Number of hospitals in N. Ireland providing cystoscopy and transurethral resection of the bladder (TURB).
8. Multidisciplinary team meetings.
9. Timelines from referral to presentation, investigations, staging and treatment.
10. Surgeon case volumes for major procedures, such as cystectomy/cystoprostatectomy, and the proportion of these carried out by specialist uro-oncology surgeons.
11. Additional care services e.g. physiotherapy, palliative care, social worker.
12. Patient information.
13. Communication with primary care.

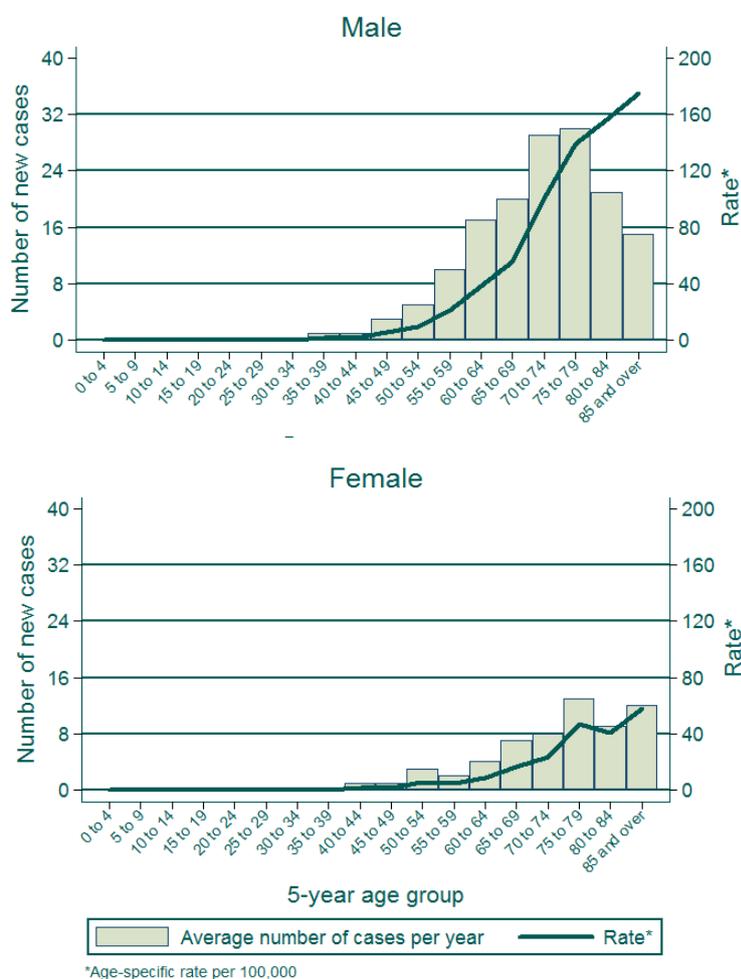
Note: Data sources for the audit were clinical notes (where available), electronic patient records and pathology reports.

OVERVIEW OF BLADDER CANCER IN N. IRELAND

Incidence 2007-2011

Transitional cell carcinoma (TCC) of the bladder was the 8th most common cancer in men and 16th in women accounting for 2.6% of all cancers (excluding non-melanoma skin cancer), with an average 154 men and 60 women being diagnosed annually. The higher incidence in men 2.6:1 is likely largely related to lifestyle/occupational risk factors (Appendix A, Risk factors). The European age-standardised rate was 16/100,000 for men and 5/100,000 for women. The cumulative risk of getting the disease (from age 0 to 74) was 1.2% (1 in 86) in men and 0.3% (1 in 323) in women. Age-specific rates in both men and women increase with age, though the age-decade in which most patients are diagnosed is the 70s (Fig. 1). The median age at diagnosis is 74. There is evidence that bladder cancer rates (2002-2011) are associated with socio-economic deprivation in N. Ireland being higher in more deprived areas; this may be due to higher prevalence of smoking in deprived areas.

Figure 1: Age distribution of patients diagnosed with bladder cancer in N. Ireland 2007-2011 by sex, with age-specific rates

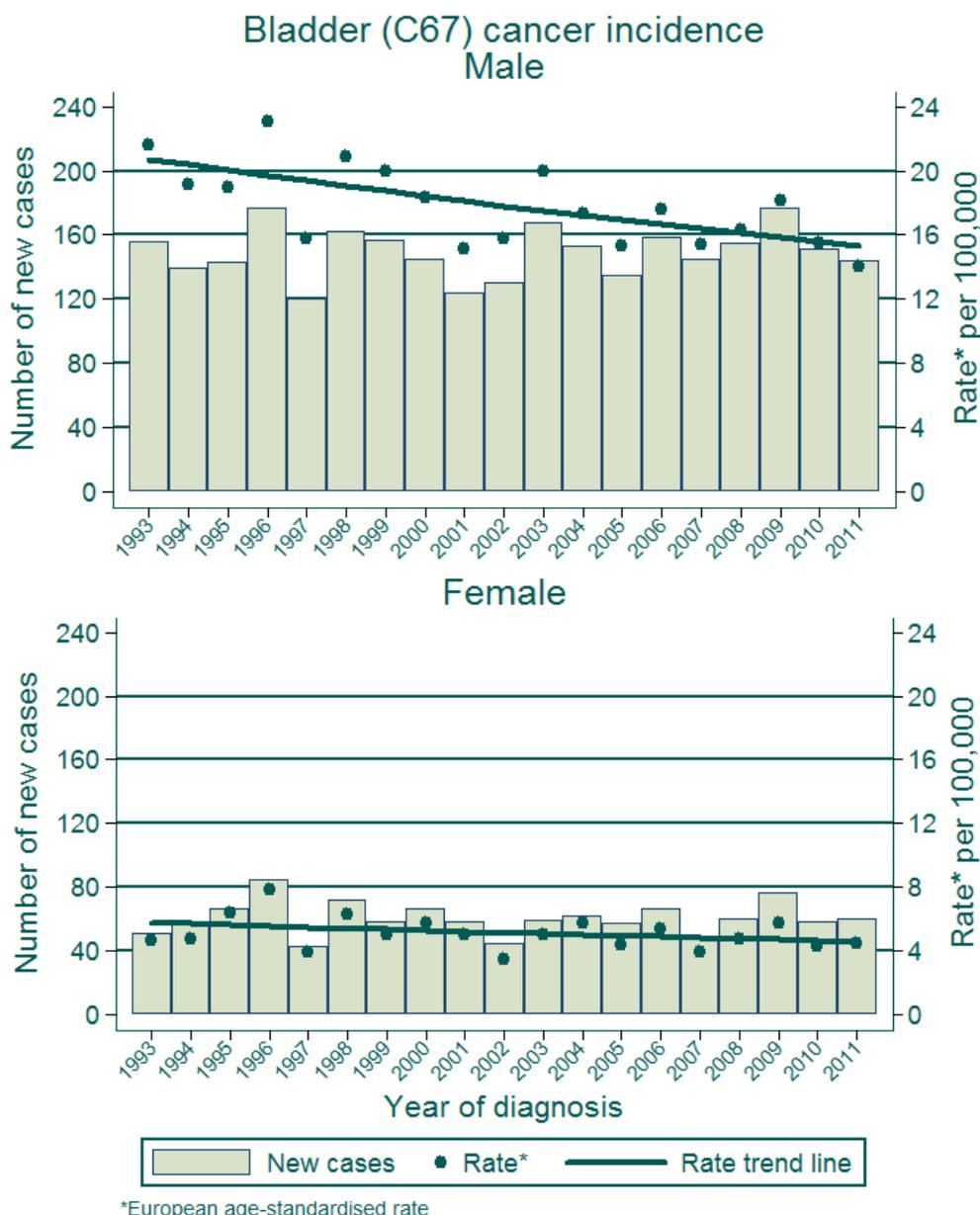


OVERVIEW OF BLADDER CANCER IN N. IRELAND

Incidence trends 1993-2011

Although, the numbers of people diagnosed has remained relatively constant from 1993 to 2011, age-standardised rates (Fig. 2) have been falling by 1.7% ($P<0.01$) per year in men, and 1.3% ($P=0.13$) in women. This fall in age-standardised rates while total numbers remains stable reflect the ageing of the population. The faster-falling standardised-incidence rates in men possibly reflect changes in smoking-habits between the sexes.

Figure 2: Number of new cases of bladder cancer in N. Ireland from 1993 to 2011 by sex, with European age-standardised incidence rate



Deaths 2007-2011

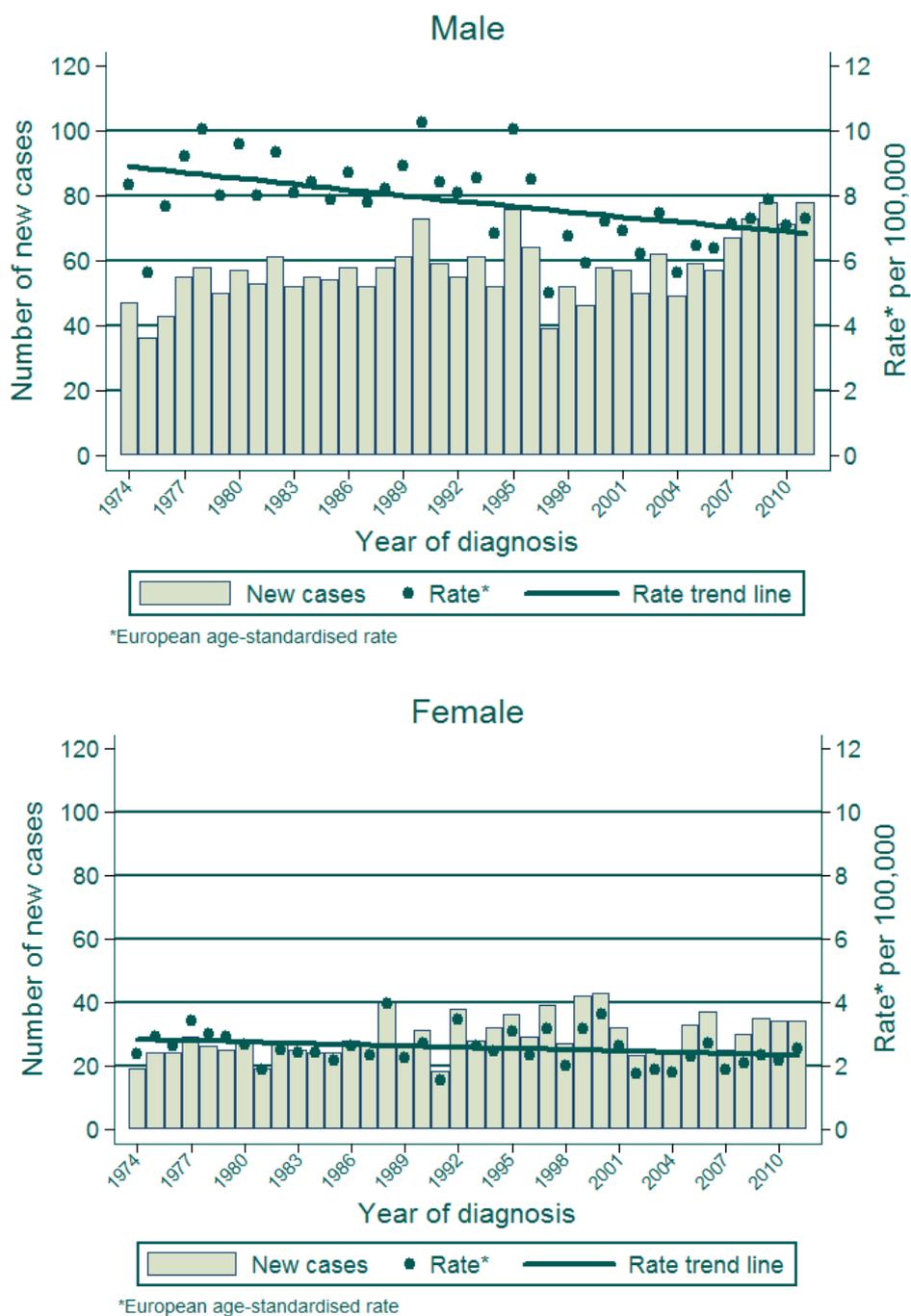
Bladder cancer was the 7th most common cause of cancer death in men and 15th in women. It accounted for 2.7% of all cancer deaths, with an average of 73 men and 32 women dying annually. The age-standardised mortality rate was 7.4/100,000 and 2.2/100,000 for men and women, respectively. The cumulative risk of dying from the disease (from age 0 to 74) was 0.4% (1 in 955) in men and 0.1% (1 in 247) in women. The median age at death was 78 years.

OVERVIEW OF BLADDER CANCER IN N. IRELAND

Trends in mortality 1974-2011

Age-standardised mortality rates (Fig. 3) have been falling by 0.7% ($P < 0.01$) per year in men, and 0.5% ($P = 0.10$) in women.

Figure 3: Numbers of deaths from bladder cancer in N. Ireland from 1974 to 2011 by sex, plus European age-standardised mortality rate



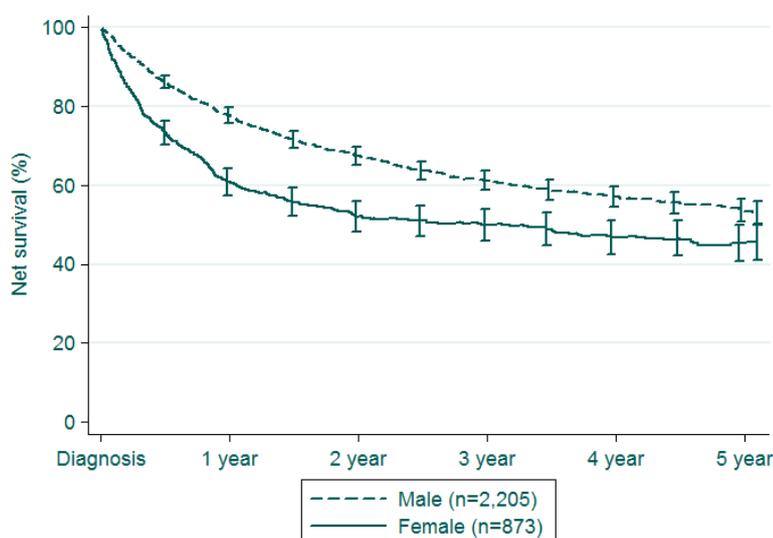
OVERVIEW OF BLADDER CANCER IN N. IRELAND

Net survival in N. Ireland 1997-2006

Net survival is the cancer survival in the absence of other causes of death. It is achieved by adjusting for and removing the effect of population background mortality rates. It is considered a better estimate of survival than 'relative survival' which gives undue weight to younger patients when estimating survival.

The 5-year net survival from bladder cancer for patients diagnosed from 1997-2006 in N. Ireland was 58.7%. However, for patients diagnosed over 10-year period (1997-2006) and followed-up to 2011, there is a significantly lower survival for women than men, by a magnitude of 10% (Fig. 4a).

Figure 4a: Net survival of patients diagnosed with bladder cancer from 1997 to 2006 followed-up till 2011, by sex



Over time since 1993 5 year net survival from bladder cancer has remained steady at approximately 60% for men and 40% for Women (Fig. 4b).

Figure 4b: N. Ireland survival at 5 years for males and females over time



OVERVIEW OF BLADDER CANCER IN N. IRELAND

International comparisons

Incidence: 1998-2007

Incidence rates of bladder cancer in N. Ireland (male 11.8/100,000, female 3.2/100,000 [world age-standardised rate]) during 1998-2002 were among the lowest in the Western World being significantly lower than most European countries, including the rest of the UK¹². By 2003-2007 rates in N. Ireland had increased to 18.3/100,000 and 5.5/100,000 for males and females respectively, both of which were similar to the rates in England although they were still lower than those in Scotland and Denmark among others. (Fig. 5)

Relative survival: 1995-2007

The five-year (age-standardised) relative survival for bladder cancer patients diagnosed in 1995-1999 in N. Ireland was poor in comparison to the European average and England & Wales. The rate in men (65.0%) was comparable to Scotland, Slovenia, Poland, and France, but for women N. Ireland (54.6%) had the lowest survival rate among the EURO CARE-4¹ countries (Fig. 6). The EURO CARE-5¹³ data for patients diagnosed in 2000-2007 indicates that survival in N. Ireland was better than the European average for men and was similar to the average for women. However N. Ireland has a small number of female bladder cancers diagnosed each year, with the result that survival estimates fluctuate from year to year.

Impact of coding standards

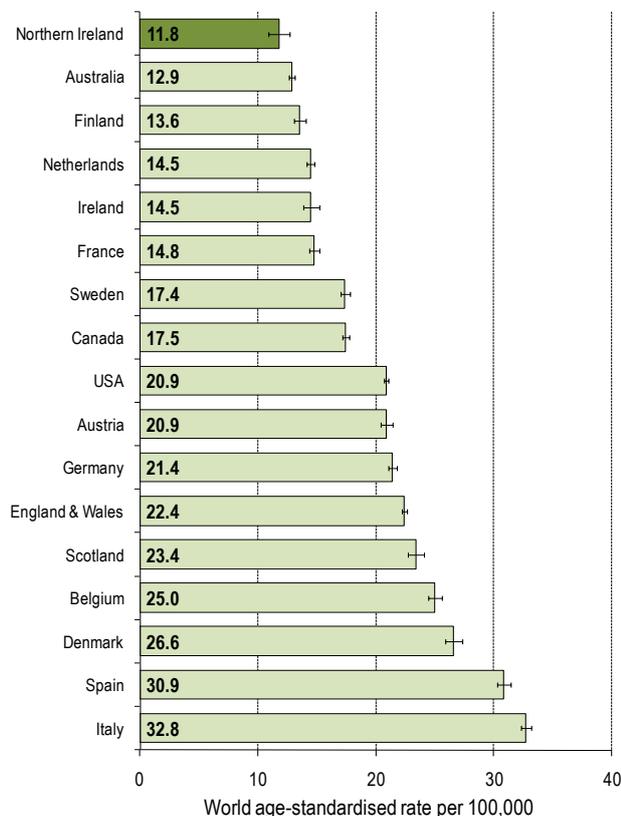
International comparisons of bladder cancer are difficult due to the different coding classification in different countries with many registries assigning malignant status to non-invasive (pTa/CIS) diagnoses. Typically international comparisons include non-invasive bladder cancer as malignant. The N. Ireland Cancer Registry does not report tumours with morphology codes, 8120/2 (flat carcinoma in situ of urothelium) 8130/1 & 8130/2, as bladder cancer, whereas they are included as bladder transitional cell carcinoma in Cancer Incidence in Five Continents¹².

OVERVIEW OF BLADDER CANCER IN N. IRELAND

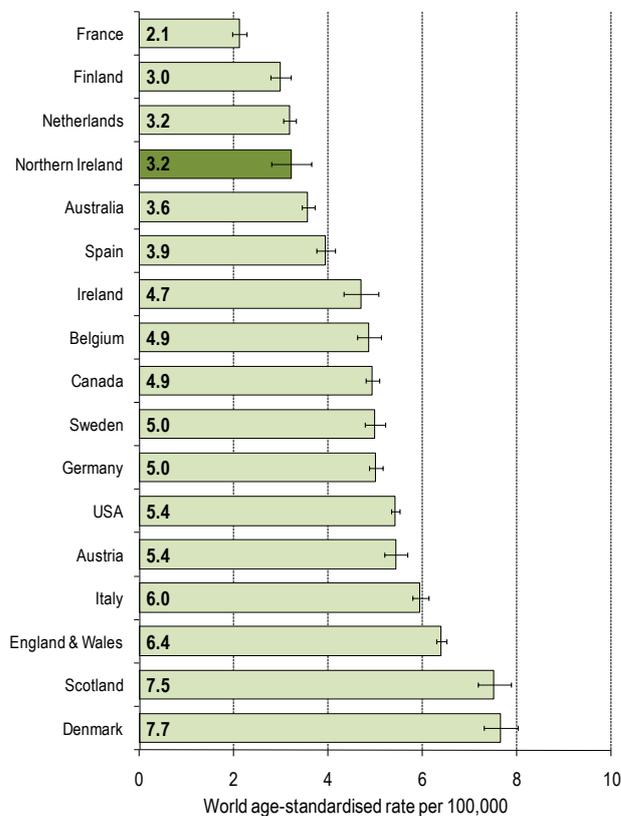
Figure 5: International comparison of world age-standardised incidence rates for men and women diagnosed between 1998 and 2007 (Source: Cancer Incidence in Five Continents (CIV)¹²)

Males

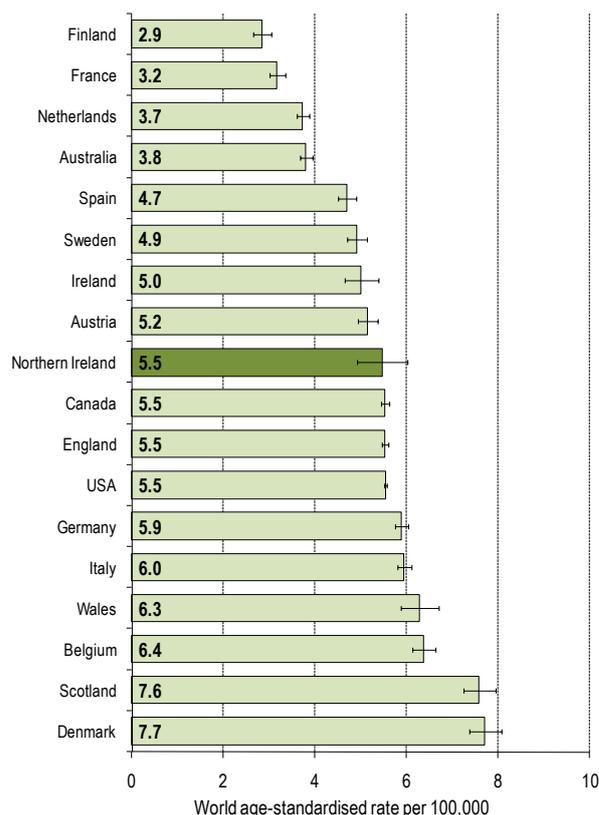
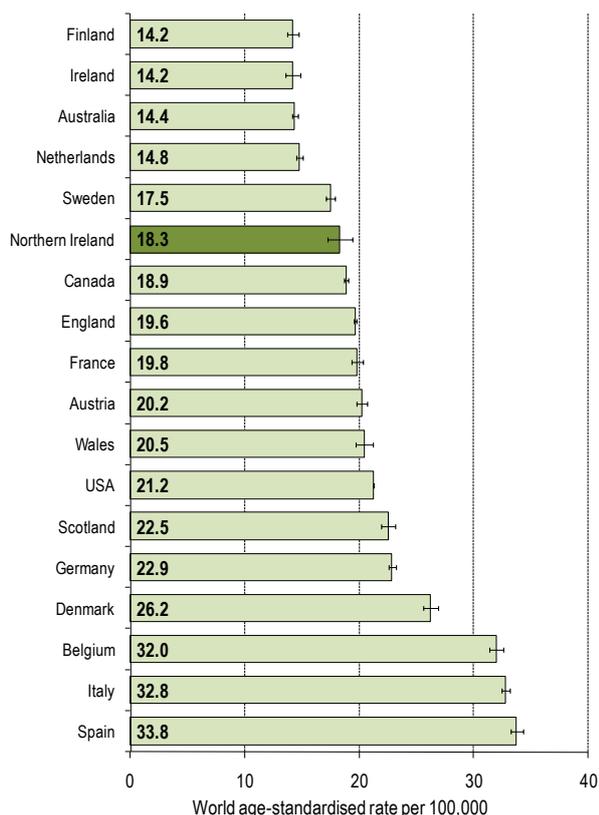
Diagnosed 1998-2002 (CIV – Volume IX)



Females



Diagnosed 2003-2007 (CIV – Volume X)

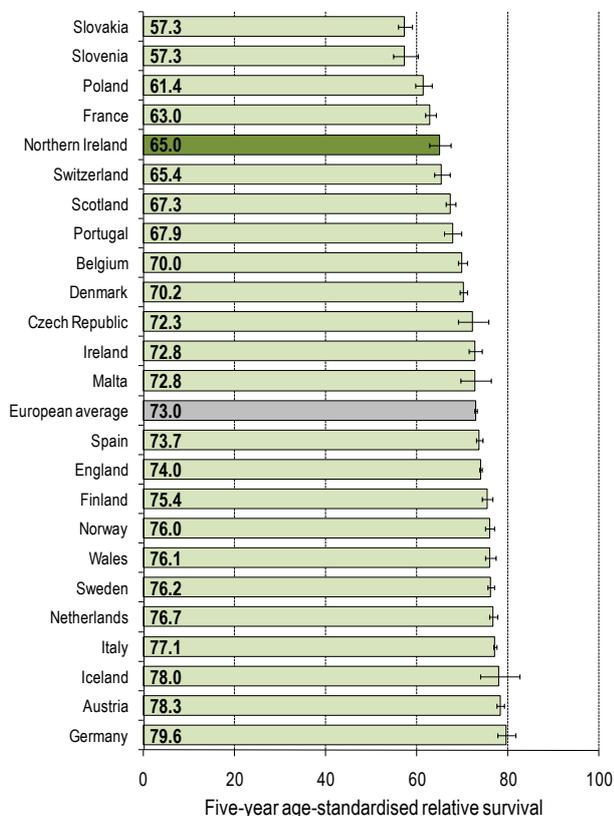


OVERVIEW OF BLADDER CANCER IN N. IRELAND

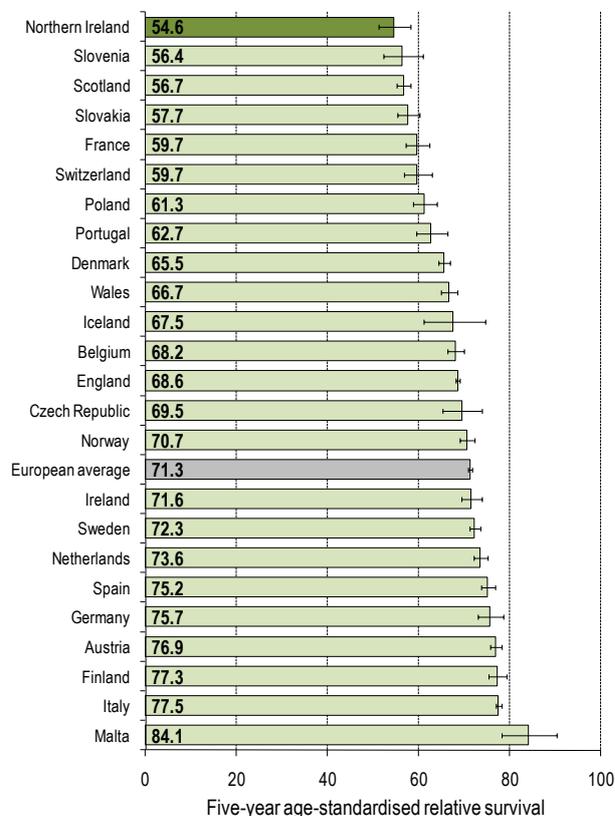
Figure 6: International comparison of age-standardised relative survival rates for men and women diagnosed between 1998 and 2007. (Source: EUROCARE-4 & 5^{1,13})

Males

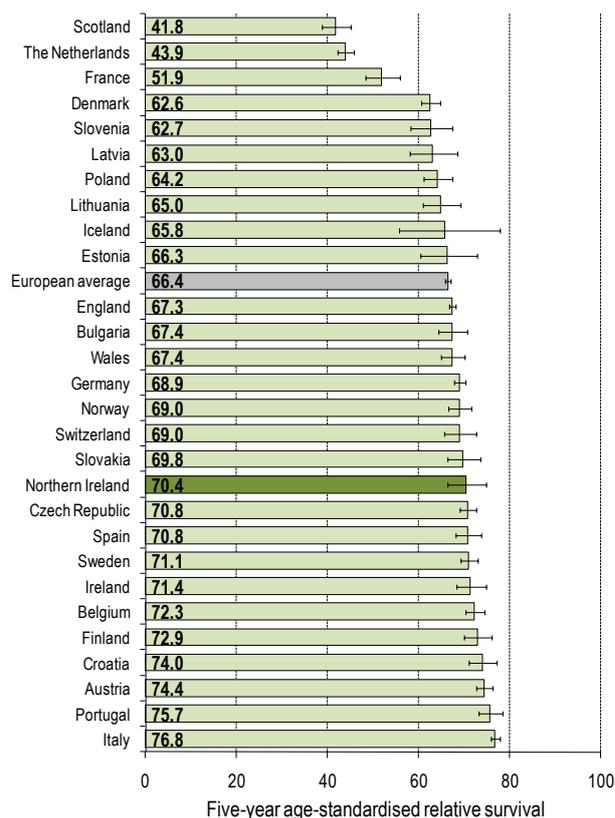
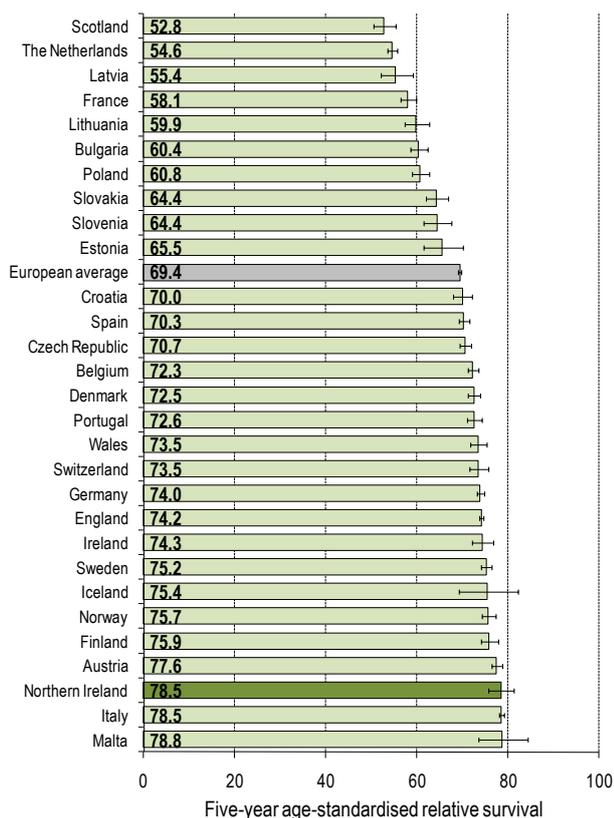
Diagnosed 1995-1999 (EUROCARE-4)



Females



Diagnosed 2000-2007 (EUROCARE-5)



METHODOLOGY

Bladder cancer was identified using the ICD10¹⁴ code 'C67'; this selection excludes non-invasive pTa/pTis tumours.

Audit data collection

The data items collected in the audit were agreed following consultation with urology clinicians. An electronic proforma, developed in Microsoft Access, was used to collect the audit information. It was populated electronically with patient details extracted from the NICR database in 2012. However, as not all items required for the audit were available on the NICR database, data from the Cancer Patient Pathway System (CaPPS) and the Clinical Oncology Information System (COIS) was extracted by the Registry Tumour Verification Officers (TVOs), who also examined the clinical notes when available. Inconsistencies between the four different datasets were then resolved, and after validation checks were complete, a detailed dataset was imported to the Stata statistical software for analysis. Data collection was completed in May 2013, with final data cleaning finished in October 2013.

In order to provide geographic and socio-economic information, the 2011 central postcode directory was used to assign patients to a census output area (COA) based upon their postcode of usual residence. The COA was then used to assign a Health and Social Care Trust of residence and a deprivation quintile from the income domain of the 2010 multiple deprivation measure¹⁵ with the latter used to provide an approximate socio-economic classification for each patient.

Limitations

While every effort has been made to obtain all the required information on each patient, there were several limitations imposed upon the collection of data:

- Outpatient records of private patients (n=26) were sometimes unavailable resulting in some missing information on presentation dates and follow up.
- The Multidisciplinary Team Meeting data download from CaPPS was not complete for all patients at the time of data extraction.
- Discharge letters from the Belfast City Hospital (where most surgery was performed) were not always available in the patient notes held in other hospitals. In each of the above scenarios alternative sources of information were explored.

Exclusions

Patients were excluded from the audit if their records lacked sufficient information (n=6) or if information was available only from a death certificate (DCO) (n=2).

Private patients

In this study, we have defined private patients as those patients who presented via the private sector. Although, these patients may enter the NHS later for investigations and treatment, they are not included in the timeline analysis, but are included for any care in the NHS.

METHODOLOGY

Data analysis

The majority of results are presented in tables in which patients are classified in various categories (such as 'mode of presentation' or 'hospital of presentation') yielding numbers and proportions. Caution must be exercised when comparing such proportions as apparent differences might well be explained by random chance; a valid statistical test is required to demonstrate significance. In addition, in large tables the probability is greater still of concluding a difference when none, in fact, exists; special statistical tests are required where this danger, arising from 'multiple comparisons', exists. The chi-square test is used to test for differences in the distribution of a categorical variable between two groups (e.g. males vs females) of another categorical variable. For continuous variables, a t-test is employed to compare groups. In all tests a 95% confidence level is applied. A non-parametric test, the log-rank test, is used to compare timeline duration distribution between groups of patients (e.g. men versus women).

In this report, net survival has been estimated to describe the survival of patients; net survival can be considered as the theoretical survival of cancer patients if they could not die from other causes. It is appropriate for comparing the survival experience of cancer patients from different territories or calendar periods where background population mortality rates are different. It is used here to refine the analysis of the survival data of bladder cancer patients, so that differences between men and women can be explored.

All patients were followed-up to ascertain if alive until the end of May 2013, giving a minimum follow-up of 1.4 years for all patients, at least 2 years follow-up for two thirds (242/362) of all patients. Assuming that follow-up length is independent of dying from cancer, net survival estimates at 2 years can be estimated. Net survival analysis was implemented using the user-led *stns*¹⁶ command in Stata.

RESULTS

Study Population

Table 1: Study patients

Total patients	Year diagnosed 2010 & 2011
Invasive bladder cancer	370
Death certificate only cases excluded	2
Exclusion – Insufficient information	6
Total reported on (% of bladder cancer patients)	362 (98.4%)
% Male	72.9%

- In the 2-year audit period 2010 to 2011, 370 patients were diagnosed with invasive bladder cancer in N. Ireland. As only 8 patients were excluded from the audit, case ascertainment was very good (98.4%).

Table 2: Age at diagnosis

Age at diagnosis	2010 & 2011 (n=362)		
	Male (n=264)	Female (n=98)	Total
Under 65	68 (25.8%)	19 (19.4%)	87 (24.0%)
65 to 74	87 (33.0%)	22 (22.4%)	109 (30.1%)
75 to 79	44 (16.7%)	25 (25.5%)	69 (19.1%)
80 and over	65 (24.6%)	32 (32.7%)	97 (26.8%)
Mean age	72.1	74.1	72.7
Median age	73.2	76.3	74.0

- The median age at diagnosis was 74 years. Invasive bladder cancer was much more common in men with a ratio of (2.7: 1). A significantly higher proportion of women than men were age 75 years or over (58% vs 41%, P<0.05).

RESULTS

Lifestyle

- Just under three quarters (72%) of all patients were current or ex-smokers with men being significantly more likely to be current or ex-smokers compared to women 75.8% vs 61.2% ($P < 0.01$) (Table 3). Women were more likely to live alone, most likely due to the lower life-expectancy of men.

Table 3: Patient lifestyle factors

Lifestyle factors	2010 & 2011		
	Male (n=264)	Female (n=98)	Total (n=362)
Lives with spouse/partner/relative	76.1%	52.0%	69.6%
Lives alone	14.8%	37.8%	21.0%
Lives in residential setting*	4.6%	6.1%	4.9%
Current smoker	27.3%	30.6%	28.2%
Ex-smoker	48.5%	30.6%	43.7%
Never or non-smoker	20.8%	33.7%	24.3%
Recorded history of alcohol abuse	5.3%	2.0%	4.4%

*Hostel, nursing home, residential home, sheltered dwelling/fold

Comorbidities

- The majority (78%) of patients with bladder cancer had at least one comorbidity. Hypertension (48.3%), cardiovascular disease (31.2%), obesity (21.3%) and chronic obstructive pulmonary disease (19.6%), were the most common comorbidities recorded (Table 4).
- The percentage of patients with each comorbidity did not differ significantly ($P > 0.10$) between men and women (not shown).

Table 4: Comorbidities

Comorbidity	Patients (% of Total)
Chronic obstructive pulmonary disease	71 (19.6%)
Cardiovascular disease	113 (31.2%)
Cerebrovascular disease	44 (12.2%)
Diabetes	61 (16.9%)
Hypertension	175 (48.3%)
Dementia	20 (5.5%)
Psychiatric disorder	30 (8.3%)
Cancer other than bladder	28 (7.7%)
Renal disease	58 (16.0%)
Obesity	77 (21.3%)

Note: patients may have more than one comorbidity

RESULTS

Charlson Comorbidity Score

The Charlson comorbidity score¹⁷ is a summary statistic of both the age and level of comorbidity a patient has that is related to their life expectancy or risk of mortality. It is used here to describe and compare groups of patients (e.g. men and women). Appendix B gives more detail on how it is calculated for each patient.

Table 5: Charlson comorbidity score (see Appendix B for components)

Charlson score	Number (% of total)		
	Male (n=264)	Female (n=98)	Total (n=362)
1 to 4 (low)	37 (14.0%)	13 (13.3%)	50 (13.8%)
5 to 6*	99 (37.5%)	33 (33.7%)	132 (36.5%)
7 to 9	104 (39.4%)	41 (41.8%)	145 (40.1%)
10 to 16 (high)	24 (9.1%)	11 (11.2%)	35 (9.7%)

* A Charlson score of 6 predicts a 10-year-survival probability $\leq 2\%$ ¹⁷

- Half of bladder cancer patients had a Charlson comorbidity score of 7 or greater. There was no difference in the distribution of Charlson scores between the men and women (P=0.86).

Family History of Cancer

Table 6: Family history* of cancer

Family history	2010 & 2011 (n=362)		
	Male (n=264)	Female (n=98)	Total (n=362)
Yes	58 (22.0%)	27 (27.6%)	85 (23.5%)
No	111 (42.0%)	36 (36.7%)	147 (40.6%)
Not recorded	95 (36.0%)	35 (35.7%)	130 (35.9%)

* a first or second degree relative

- A positive family history of cancer was recorded in 23.5% of patients.

RESULTS

Bladder Cancer Pathway: Referral and Presentation

Table 7: Referral source

Referral source	2010&2011		
	Male (n=264)	Female (n=98)	Total (n=362)
GP referral to outpatients (Total)	131 (49.6%)	38 (38.8%)	169 (46.7%)
GP - Red flag to outpatients	55 (20.8%)	11 (11.2%)	66 (18.2%)
GP - Urgent/Semi-urgent	19 (7.2%)	6 (6.1%)	25 (6.9%)
GP - Routine	11 (4.2%)	2 (2.0%)	13 (3.6%)
GP - Consultant upgrade	37 (14.0%)	16 (16.3%)	53 (14.6%)
GP - Not known/specified	9 (3.4%)	3 (3.1%)	12 (3.3%)
A&E Total	49 (18.6%)	26 (26.5%)	75 (20.7%)
Self-referral	21 (8.0%)	8 (8.2%)	29 (8.0%)
GP	22 (8.3%)	16 (16.3%)	38 (10.5%)
Non-specified	6 (2.3%)	2 (2.0%)	8 (2.2%)
Other consultant	24 (9.1%)	17 (17.3%)	41 (11.3%)
Under regular outpatient review	33 (12.5%)	10 (10.2%)	43 (11.9%)
Private sector	17 (6.4%)	2 (2.0%)	19 (5.2%)
Other	9 (3.4%)	4 (4.1%)	13 (3.6%)
Not known	1 (0.4%)	1 (1.0%)	2 (0.6%)

- In the 2 year audit period over half (57%) of all patients were referred by their GPs (to outpatients or A&E).
- Overall 18% of patients were referred to outpatients by GPs as red flag suspect cancers and a further 14.6% were upgraded by consultants to a red flag pathway. GP referrals to A&E accounted for 10.5% while 11% were GP routine/urgent/semi-urgent/ referrals to outpatients.
- 12% of patients were under regular outpatient review at the time of diagnosis.
- 21% of patients presented via A&E. Although a higher percentage of women presented at A&E compared to men, this was not significant (P=0.10).

Bladder Cancer Detected During Urological Surveillance

- 33 patients diagnosed with invasive bladder cancer in 2010/2011 were under urological surveillance following previous TURB where either non-invasive pTa (n=19) and/or carcinoma in situ (n=4) was found.

RESULTS

Trust and Hospital First Presentation

Table 8: Trust and Hospital of first presentation (this table excludes patients that were under regular hospital review when bladder cancer was diagnosed [n=43])

Trust & hospital of first presentation	2010 & 2011
	Total (n=319)
Belfast City Hospital	65 (20.4%)
Royal Victoria Hospital	6 (1.9%)
Mater Infirmorum Hospital	13 (4.1%)
Belfast HSCT	84 (26.3%)
Antrim Area Hospital	8 (2.5%)
Causeway Hospital	41 (12.9%)
Mid-Ulster Hospital	1 (0.3%)
Whiteabbey Hospital	1 (0.3%)
Northern HSCT	51 (16.0%)
Ulster Hospital	24 (7.5%)
Lagan Valley Hospital	27 (8.5%)
Downe Hospital	6 (1.9%)
Ards Hospital	6 (1.9%)
Bangor Hospital	2 (0.6%)
South-Eastern HSCT	65 (20.4%)
Craigavon Area Hospital	44 (13.8%)
Daisy Hill Hospital	16 (5.0%)
Southern HSCT	60 (18.8%)
Altnagelvin Hospital	34 (10.7%)
Erne Hospital	3 (0.9%)
Tyrone County Hospital	2 (0.6%)
Western HSCT	39 (12.2%)
Ulster Independent Clinic	18 (5.6%)
Hillsborough Private Clinic	1 (0.3%)
Private Sector	19 (6.0%)
Unknown	1 (0.3%)

- Over a quarter of patients first-presented to the Belfast Trust.
- 6% of patients presented via the private sector.

RESULTS

Location of First Seen

Table 9: Location of first presentation (this table excludes patients that were under regular hospital review when bladder cancer was diagnosed [n=43])

Location first seen	2010 & 2011		
	Male (n=231)	Female (n=88)	Total (n=319)
Outpatients	144 (54.5%)	43 (43.9%)	187 (51.7%)
Haematuria clinic	40 (15.2%)	16 (16.3%)	56 (15.5%)
A&E, followed by admission	32 (12.1%)	19 (19.4%)	51 (14.1%)
A&E, other	17 (6.4%)	7 (7.1%)	24 (6.6%)
Private sector	17 (6.4%)	2 (2.0%)	19 (5.2%)
Inpatients	11 (4.2%)	9 (9.2%)	20 (5.5%)
Not known	3 (1.1%)	2 (2.0%)	5 (1.4%)

- 52% of patients were first seen in outpatient clinics, with a further 16% being first seen at a designated haematuria clinic.
- 21% of patients presented at A&E.
- Although there were a higher proportion of women first seen at A&E, the proportion of patients first seen in any of the locations above did not differ significantly ($P>0.05$) between men and women.

Speciality First Seen

Table 10: Speciality first seen (patients under-review at time of diagnosis [n=43] are excluded)

Speciality first seen	2010 & 2011		
	Male (n=231)	Female (n=88)	Total (n=319)
Urology	209 (90.5%)	64 (72.7%)	273 (85.6%)
General/Geriatric Medicine	7 (3.0%)	9 (10.2%)	16 (5.0%)
General Surgery	7 (3.0%)	7 (8.0%)	14 (4.4%)
Gynaecology	0 (0%)	3 (3.4%)	3 (0.9%)
Other	8 (3.5%)	5 (5.7%)	13 (4.1%)

- 86% of patients were first seen by urology.
- A significantly higher proportion of men than women (90% vs 73%) were first seen by urology $P<0.01$.
- 22% of women were initially on a non-urology pathway.

RESULTS

Symptoms at Presentation

Table 11: Symptoms at presentation

Symptoms*	2010 & 2011		
	Male (n=264)	Female (n=98)	Total (n=362)
Macroscopic haematuria (visible blood in urine)	216 (81.8%)	75 (76.5%)	291 (80.4%)
Urinary frequency	83 (31.4%)	25 (25.5%)	108 (29.8%)
Dysuria (pain on passing urine)	50 (18.9%)	18 (18.4%)	68 (18.8%)
Urinary urgency	38 (14.4%)	13 (13.3%)	51 (14.1%)
Lower abdominal/back pain	46 (17.4%)	33 (33.7%)	79 (21.8%)
Weight-loss	31 (11.7%)	18 (18.4%)	49 (13.5%)
Lethargy	7 (2.7%)	18 (18.4%)	25 (6.9%)

*Patients may have multiple symptoms and be counted more than once

- Macroscopic haematuria (visible blood in urine) was the most common presenting symptom (80%).
- Women were more likely than men to present with abdominal pain ($P<0.01$), lethargy ($P<0.01$), and weight loss ($P=0.10$), suggesting more advanced stage at presentation.

Symptom Duration

- Duration of macroscopic haematuria was recorded for 77% of patients presenting with haematuria (Table 12).
- 58% of patients with duration recorded, reported haematuria for more than 4 weeks before presentation, 12% more than 6 months.
- Although the proportion of patients reporting haematuria for less than 4 weeks was greater for men (44.3%) than women (33.9%), this was not significant ($p=0.17$).

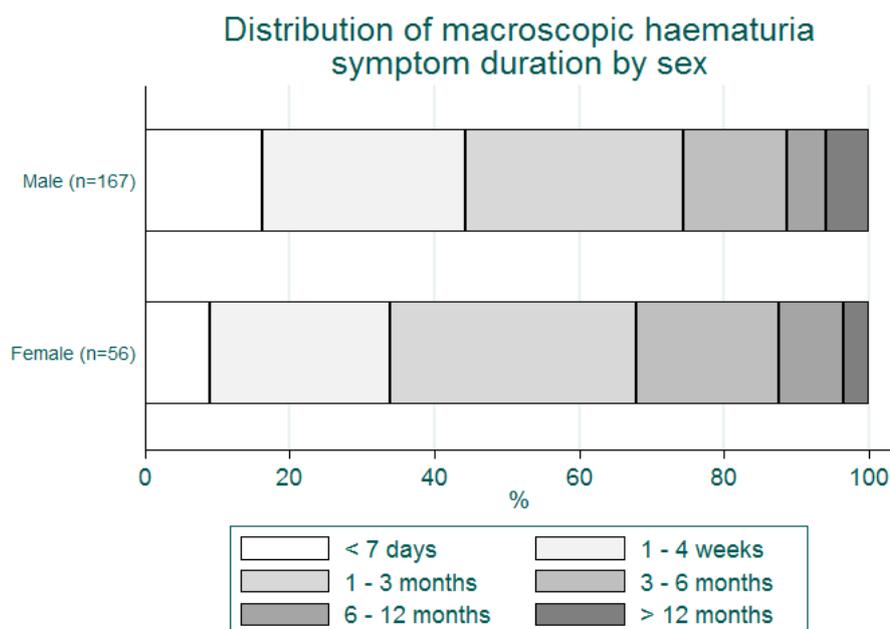
Table 12: Duration of macroscopic haematuria (obvious blood in the urine)

Duration	Patients with macroscopic haematuria (% of those with recorded duration)		
	Male (n=167)	Female (n=56)	Total (n=223)
Under 7 days	27 (16.2%)	5 (8.9%)	32 (14.3%)
1 - 4 weeks	47 (28.1%)	14 (25.0%)	61 (27.4%)
1 - 3 months	50 (29.9%)	19 (33.9%)	69 (30.9%)
3 - 6 months	24 (14.4%)	11 (19.6%)	35 (15.7%)
6 - 12 months	9 (5.4%)	5 (8.9%)	14 (6.3%)
> 12 months	10 (6.0%)	2 (3.6%)	12 (5.4%)
	Male (n=216)	Female (n=75)	Total (n=291)
Duration not recorded (% of patients with haematuria)	49 (22.7%)	19 (25.3%)	68 (23.4%)

RESULTS

- There was no significant difference in the distribution of macroscopic haematuria symptom duration between men and women ($P>0.05$) (Fig. 7).
- When vague symptoms (lethargy, lower abdominal/back pain, weight loss) were grouped together, there was no significant difference in symptom duration (not shown) between men and women.

Figure 7: Distribution of recorded macroscopic haematuria duration



Diagnosis: Investigations

Table 13: Diagnostic and staging investigations

Investigation	2010 & 2011*		
	Male	Female	Total
Cystoscopy	257/262 (98.1%)	96/98 (98.0%)	353/360 (98.1%)
TURB**	252/264 (95.5%)	93/98 (94.9%)	345/362 (95.3%)
CT Scan	192/261 (73.6%)	84/98 (85.7%)	276/359 (76.9%)
Ultrasound Scan	150/264 (56.8%)	59/97 (60.8%)	209/361 (57.9%)
MRI Scan	38/263 (14.4%)	16/98 (16.3%)	54/361 (15.0%)
PET Scan	3/263 (1.1%)	2/98 (2.0%)	5/361 (1.4%)
Chest X-ray	85/264 (32.2%)	40/98 (40.8%)	125/362 (34.5%)
Bone Scan	51/263 (19.4%)	26/98 (26.5%)	77/361 (21.3%)
Urogram	57/263 (21.7%)	13/98 (13.3%)	70/361 (19.4%)
At least one scan	264/264 (100.0%)	98/98 (100.0%)	362/362 (100.0%)

* The denominator is the total number of patients adjusted for patients that had a record in their notes stating that they either 1) did not attend, 2) were too unfit, or 3) refused

** Transurethral resection of bladder

RESULTS

- 98% of patients had a cystoscopy; of these patients 98% (345/353) had a TURB, while 76% (267/353) of cystoscopy patients had a CT scan.
- 96% of patients with muscle invasive bladder cancer (TNM stage 2, 3 or 4) had either a CT or an MRI scan (not shown).

Basis of Diagnosis

Table 14: Basis of diagnosis

Method of diagnosis	2010 & 2011
	Total (n=362)
Histologically verified	352 (97.2%)
Clinical investigation alone	10 (2.8%)

- The majority (97.2%) of patients were histologically verified.

Histological Type

Table 15: Histological type

Histological type	2010 & 2011		
	Male (n=264)	Female (n=98)	Total (n=362)
Transitional Cell Carcinoma	233 (88.3%)	78 (79.6%)	311 (85.9%)
Squamous Cell Carcinoma	8 (3.0%)	7 (7.1%)	15 (4.1%)
Other*	23 (8.7%)	13 (13.3%)	36 (9.9%)

*Other includes the following: Neoplasm NOS (12), Carcinoma NOS (6), Carcinoma, anaplastic (1), Pseudosarcomatous carcinoma (3), Small cell carcinoma (5), Adenocarcinoma, NOS (2), Mucinous adenocarcinoma (2), Signet ring cell carcinoma (2), Carcinosarcoma, NOS (3)

- Transitional cell carcinoma was the most common histological type (86%).
- There was a higher proportion ($P < 0.05$) of transitional cell carcinoma among men (88%) than women (80%).

RESULTS

TNM Stage

The UICC overall integrated stage is shown in Table 16 which is determined on the basis of clinical, imaging and pathology data following the first surgical treatment ie. this is the integration of the pathological and clinical stage.

Table 16: Integrated TNM Stage (Either recorded in the notes or derived by Registry staff from data in the records)

Stages	2010 & 2011		
	Male (n=264)	Female (n=98)	Total (n=362)
Stage 1: Non-muscle invasive (T1 N0 M0)	126 (47.7%)	35 (35.7%)	161 (44.5%)
Stage 2 & 3: Muscle invasive (T2/T3/T4a, NX, N0, M0)	69 (26.1%)	31 (31.6%)	100 (27.6%)
Stage 4: Locally advanced/metastatic (T4b, N0, M0; Any T, N1-3, M0; Any T, Any N, M1)	68 (25.8%)	26 (26.5%)	94 (26.0%)
Stage unknown	1 (0.4%)	6 (6.1%)	7 (1.9%)

* Patients who were unstaged were either too unfit for investigation/treatment due to comorbidity/patient decision

- It was possible to assign a TNM stage in 98.1% of patients from the clinical notes and electronic patient information systems.
- 44.5% of patients were diagnosed with Stage 1 non-muscle invasive disease.
- A higher proportion of women were unstaged ($P < 0.01$).
- There was no difference in the overall distribution of disease stage at diagnosis between men and women (excluding the unstaged patients) ($P < 0.23$); although men had a higher proportion of Stage 1 non-invasive disease than women this was not significantly ($P = 0.10$) different.

TNM Stage by Age

Table 17: Integrated TNM Stage by age group (age groups are defined by tertiles of patient population)

Stages	Age group			
	0-69 (n=128)	70-77 (n=117)	78+ (n=117)	All ages (n=362)
Stage 1	62 (48.4%)	53 (45.3%)	46 (39.3%)	161 (44.5%)
Stage 2 & 3	22 (17.2%)	37 (31.6%)	41 (35.0%)	100 (27.6%)
Stage 4	44 (34.4%)	27 (23.1%)	23 (19.7%)	94 (26.0%)
Stage unknown	0 (0%)	0 (0%)	7 (6.0%)	7 (1.9%)

* Patients who were unstaged were either too unfit due to comorbidity for further investigation or treatment

- Stage distribution differed ($P < 0.01$) between age groups, with patients aged 70 years or more having a higher proportion of Stage 2&3 disease ($P < 0.01$).
- Younger patients (aged 0-69) had the highest proportion of both Stage 1 and Stage 4 disease.

RESULTS

- In the younger age group, although 50% of women (n=13/26) had Stage 4 disease, compared with 30% in men (n=31/102), this did not reach significance (P=0.06).
- All unstaged patients were aged 78 years or older.

Multidisciplinary Team Meetings

Table 18: Multidisciplinary Team meetings (MDM)

Trust/location of presentation	Discussed at MDM: number/total (%)
Belfast HSCT	93/99 (93.9%)
Northern HSCT	52/59 (88.1%)
South-Eastern HSCT	61/70 (87.1%)
Southern HSCT	63/69 (91.3%)
Western HSCT	43/45 (95.6%)
Private sector	11/19 (57.9%)
Total	324/362 (89.5%)

**One patient's 'Trust of presentation' was unknown*

- Just under 90% of patients were discussed at an MDM.
- Patients presenting via the private sector were less likely (P<0.01) to have their case discussed at an MDM (58%).
- 38 patients (10.5%) were not discussed at an MDM. Eight of these patients (21.0%) were first seen in the private sector. The remaining patients were from the Belfast Trust (6), Northern Trust (7), South Eastern Trust (9), Southern trust (6) and Western trust (2). Ten patients (26%) presented via A&E and 16% were under regular outpatient urology review. 12/38 (32%) of patients who did not have an MDM recorded died within 3 months of their diagnosis.

RESULTS

Treatment Modality by TNM Stage

Table 19: Treatment modalities by stage (Modality here refers to main treatment for cancer)

Treatment modalities	TNM Stage				
	Stage 1 Non-muscle invasive (n=161)	Stage 2&3 Muscle invasive (n=100)*	Stage 4 Locally advanced/metastatic (n=94)	Stage unknown (n=7)	Total (n=362)
TURB & intravesical chemotherapy ± intravesical Bacillus Calmette-Guérin (BCG)	99 (61.5%)	2 (2.0%) [§]	0 (0%)	0 (0%)	101 (27.9%)
TURB alone	37 (23.0%)	24 (24.0%) [§]	1 (1.1%)	0 (0%)	62 (17.1%)
Neoadjuvant chemotherapy & radical cystectomy	2 (1.2%)	2 (2.0%)	6 (6.4%)	0 (0%)	10 (2.8%)
**Cystectomy alone	15 (9.3%)	30 (30.0%)	10 (10.6%)	0 (0%)	55 (15.2%)
**Cystectomy with palliative oncological therapy	1 (0.6%)	4 (4.0%)	12 (12.8%)	0 (0%)	17 (4.7%)
Radical radiotherapy	2 (1.2%)	17 (17.0%)	0 (0%)	1 (14.3%)	20 (5.5%)
Palliative radiotherapy alone	2 (1.2%)	15 (15.0%)	23 (24.5%)	0 (0%)	40 (11.0%)
Chemotherapy and radiotherapy (curative intent, concurrent/sequential)	1 (0.6%)	3* (3.0%)	0 (0%)	0 (0%)	4 (1.1%)
Palliative chemotherapy alone or with radiotherapy	2 (1.2%)	1 (1.0%)	18 (19.1%)	0 (0%)	21 (5.8%)
***No active treatment	0 (0%)	2 (2.0%) [§]	24 (25.5%)	6 (85.7%)	32 (8.8%)

*One patient had a salvage cystoprostatectomy following radical chemotherapy and radiotherapy. **Cystectomy category includes cystoprostatectomy & anterior exenteration. Two of the cystectomies reported above were partial. ***17 patients were not fit for curative treatment due to advanced age and comorbidity, 7 patients died within a few months of TURB

Stage 1 (Non-muscle invasive disease, n=161, Table 19)

- The majority of patients with Stage 1 (non-muscle invasive disease), 139/161 (86%) had organ-conserving treatment (i.e. TURB, or radical oncology). Just under two thirds (62%) received courses of intravesical chemotherapy and/or intravesical Bacillus Calmette-Guérin (BCG) therapy. Just under a quarter (23%) had local tumour resection (TURB) alone with repeat cystoscopy/biopsy to ensure disease eradication.
- 11% of Stage 1 patients underwent radical cystectomy.

Stage 2 & 3 (Muscle invasive disease, n=100)

- A third (36%) of patients with muscle invasive disease (Stage 2&3) had major surgical resection while 20% of patients had organ-conserving curative intent oncological therapy. A further 16% had palliative oncological treatment.

RESULTS

- In total 27% of patients with muscle invasive disease (Stage 2&3) had localised therapy only (TURB). After MDM discussion (23/27 patients) and oncology assessment (10 patients) significant co-morbidities and/or poor performance status deemed patients unsuitable for active treatment. (Median age 83 years with 70% aged 80+ years). Three of the four patients not discussed at MDM died soon after diagnosis.

Stage 4 (Locally advanced/metastatic, n=94)

- Just under one third (n=28) of patients with locally advanced/metastatic disease (Stage 4) had radical cystectomy with 6 patients having pre-operative chemotherapy and 12 patients requiring adjuvant palliative radiotherapy for residual/progressive disease following cystectomy. One quarter (n=23) of patients were treated with palliative radiotherapy, while 26% of patients received supportive palliative care alone.

Surgical Procedures

Table 20: Surgical procedures performed

Procedures	2010 & 2011		
	Male (n=264)	Female (n=98)	Total (n=362)
TURB	252 (95.5%)	93 (94.9%)	345 (95.3%)
Cystoprostatectomy	52 (19.7%)	—	52 (14.4%)
Cystectomy	10 (3.8%)	6 (6.1%)	16 (4.4%)
Anterior exenteration of pelvis	1 (0.4%)	14 (14.3%)	15 (4.1%)

- 95% of patients had a TURB.
- 83 surgical resections were performed: cystoprostatectomy (52), cystectomy (16), and anterior exenteration of pelvis (15).
- There was no significant difference in the major resection rate between men and women, even when adjusted for age and stage of disease.

RESULTS

TURB

Table 21: Trust/Hospital/Location of TURB (One procedure is reported per patient)

Trust/ Hospital/Location	TURB
Belfast City Hospital	100 (29.0%)
Mater Infirmorum Hospital	16 (4.6%)
Belfast HSCT	116 (33.6%)
Causeway Hospital	48 (13.9%)
Mid-Ulster Hospital	1 (0.3%)
Whiteabbey Hospital	1 (0.3%)
Northern HSCT	50 (14.5%)
Ulster Hospital	56 (16.2%)
South-Eastern HSCT	56 (16.2%)
Craigavon Area Hospital	53 (15.4%)
Daisy Hill Hospital	15 (4.3%)
Southern HSCT	68 (19.7%)
Altnagelvin Hospital	40 (11.6%)
Western HSCT	40 (11.6%)
Ulster Independent Clinic	15 (4.3%)
Private Sector	15 (4.3%)
Total	345

- A third of all TURB's were performed in the Belfast Trust.

Major Surgery

Table 22: Trust/Hospital/Location of Major Surgery*

Trust /Hospital/Location	Major surgery*
Belfast City Hospital	77 (92.8%)
Belfast HSCT	77 (92.8%)
Craigavon Area Hospital	4 (4.8%)
Southern HSCT	4 (4.8%)
Altnagelvin Hospital	1 (1.2%)
Western HSCT	1 (1.2%)
Ulster Independent Clinic	1 (1.2%)
Private Sector	1 (1.2%)
Total	83

*Major surgery is defined as cystoprostatectomy, cystectomy, or anterior exenteration

RESULTS

- The majority (93%, 77/83) of radical cystectomies were performed in the Regional Urology Centre at Belfast City Hospital with 4 being performed in the Southern Trust, 1 in the Western Trust, and 1 in the private sector.

Urinary Diversion

Table 23: Urinary diversions performed

Urinary diversions	Number of patients (% of total patients)			
	Invasive procedures			
	Anterior exenteration of pelvis	Cysto-prostatectomy	Cystectomy	Total patients
Ileal conduit	13 (86.7%)	47 (90.4%)	10 (62.5%)	70 (84.3%)
Orthotopic (neobladder)	0 (0.0%)	3 (5.8%)	1 (6.3%)	4 (4.8%)
No recorded urinary diversion	2 (13.3%)	2 (3.8%)	5 (31.3%)	9 (10.8%)
Total patients	15	52	16	83

- 89% (74/83) of patients undergoing major resection had a urinary diversion procedure performed.
- 95% (70/74) of the urinary diversions were ileal conduit, the remainder were orthotopic (neobladder).
- All (100%) orthotopic (neobladder) and 93% of ileal conduit urinary diversion procedures took place in Belfast City Hospital.

Table 24: Surgeon case volumes – number of procedures

Number of procedures	Number of surgeons (% of total procedures)
	Major surgery* (n=83)
21-35	2 (66.3%)
11-20	1 (22.9%)
2-5	4 (9.6%)
1	1 (1.2%)
Total surgeons	8

*Includes anterior exenteration of pelvis, cystoprostatectomy, cystectomy

- 89% of major surgical resections were performed by a uro-oncology surgeon with a case-load volume of 11 or more major procedures during the audit period.
- 11% were performed by urologists who performed 5 or fewer major procedures during the audit period.
- 8 patients who presented via the private sector had their surgery performed by a uro-oncology surgeon who performed ≥ 19 such operations in 2010 & 2011.

RESULTS

Lymph Node Resection

Table 25: Lymph node resection

Invasive procedure	Number of patients with lymph node dissection	
	Number (% of total)	Total patients
Anterior exenteration	12 (80.0%)	15
Cystoprostatectomy	47 (90.4%)	52
Cystectomy	10 (62.5%)	16
Total patients undergoing major surgery*	69 (83.1%)	83

*Major surgery is defined as having received one of the following procedures: cystoprostatectomy, cystectomy, or anterior exenteration

- 83% of patients undergoing major surgery had lymph node resection performed. The median number of lymph nodes examined was 15 (range, 1-35) and the median number of positive nodes was 0 (range, 0-18).

Incidental Prostate Cancer

- Incidental prostate cancer was detected in 17/54 (32%) of men who had a cystoprostatectomy or an anterior exenteration. Gleason scores were as follows: 3+3 (8), 3+4 (4), 4+3 (2), 4+4 (2), 4+5 (1). T-stage profile was PT2a (5), pT 2b (2) pT2c (9); one patient had pT3a disease.

RESULTS

Communication with Primary Care

Table 26: Information in the GP letter

Information in the GP letter	2010 & 2011 (n=362)
Diagnosis	348 (96.1%)
Management plan	347 (95.9%)
Diagnosis discussed with patient	242 (66.9%)
Diagnosis discussed with family	125 (34.5%)
Palliative care	111 (30.7%)

- Over 95% of patients had their diagnosis and management plan recorded in their GP letter.
- Two thirds of GP letters mentioned that diagnosis was discussed with the patient, and a third of letters that diagnosis had been discussed with their family.
- In 31% of the letters, palliative care was mentioned.

Patient Information

Table 27: Information provided to patient as recorded in the notes

Information recorded in notes	2010 & 2011 (n=362)
Diagnosis discussed with patient	304 (84.0%)
Diagnosis discussed with relatives	211 (58.3%)
Treatment plan discussed with patient	290 (80.1%)
Written information given	139 (38.4%)
Clinical Nurse Specialist services	134 (37%)
Clinical trial discussed with patient	2 (0.6%)
Clinical trial recorded in notes	0 (0%)

- Discussion of diagnosis and treatment plan was recorded in the clinical notes/CaPPS in just over 80% of patients.
- Two patients had a clinical trial discussed with them, but neither was enrolled.

RESULTS

Clinical Nurse Specialist

Table 28: Record of Clinical Nurse Specialist during diagnosis/treatment

Seen by a specialist care nurse	2010 & 2011		
	Male (n=264)	Female (n=98)	Total (n=362)
Yes	106 (40.2%)	28 (28.6%)	134 (37%)
No/Not recorded	158 (59.8%)	70 (71.4%)	228 (63%)

- 37% of patients were recorded as having been seen by a Urology Clinical Nurse Specialist. This figure may be an underestimate as this data may not have been consistently available in the clinical notes or CaPPS.

Onward Referrals to other Health Professionals

Table 29: Referral for specialist care

Referral for specialist care*	2010 & 2011 (n=362)
Physiotherapist	119 (32.9%)
Occupational therapist	78 (21.5%)
Social worker	109 (30.1%)
Psychologist referral	10 (2.8%)
Palliative care team	92 (25.4%)
Palliative care consultant	69 (19.1%)
Marie Curie nurse	9 (2.5%)
Macmillan nurse	59 (16.3%)
Information on support groups	4 (1.1%)
Hospice	43 (11.9%)
Community nurse	97 (26.8%)
No onward referral recorded	140 (39.0%)

*Patients may have multiple referrals and be counted more than once

- Physiotherapist (33%), social worker (30%), community nurse (27%), and palliative care team (25%) were among the most frequent forms of specialist care for onward patient referral.
- A third of patients (33%) had a referral to palliative/hospice care, i.e. at least one of the following: palliative care team, palliative care specialist, Marie Curie nurse, Macmillan nurse, or hospice.

RESULTS

Bladder Cancer Pathway: Timelines

Timelines monitor the investigation and treatment-delivery timeliness in the patient care pathway which is important when early diagnosis improves outcome. N. Ireland has the following waiting time targets for cancer patients (The Northern Ireland Cancer Access Standards¹⁸).

1. 95% of patients urgently referred by GPs as a suspected cancer should begin their first definitive treatment within a maximum of 62 days.
2. 98% of patients diagnosed with cancer (decision to treat) should begin their treatment within a maximum of 31 days from the date the decision to treat is made between the patient and the responsible consultant.

First definitive treatment

The TURB counts as the first definitive treatment when carried out with the intention of tumour debulking. For cancer access targets TURB remains the first definitive treatment even for patients who require further treatment such as cystectomy or oncological therapy.

Table 30: Time from referral to TURB, by referral type* (private patients, patients under-review at time of diagnosis, or patients who did not receive a TURB, are excluded)

Days	Primary referral type		
	Route to diagnosis		
	Red flag pathway*	GP other	A&E
1-14	1 (<1%)	2 (3.8%)	29 (44.6%)
15-28	15 (12.6%)	2 (3.8%)	10 (15.4%)
29-42	22 (18.5%)	1 (1.9%)	4 (6.2%)
43 or more	81 (68.0%)	48 (90.5%)	22 (33.8%)
Total	119	53	65
Mean (days)	77	88.3	40.3
Median (days)	63	76	16

*Includes GP red flag referrals (n=66) and consultant upgrades (n=53)

- Patients who were referred to A&E (GP/self-referral) had the shortest duration from time of referral to TURB (P<0.05).
- For patients on a red flag pathway the median time to TURB was 63 days. 13% had TURB within 4 weeks of referral, 32% within 6 weeks, while over two thirds waited more than 6 weeks.
- Patients referred by GPs as routine, urgent/semi-urgent had the longest time from referral to TURB (P<0.05).
- There was no difference in this timelines between men and women (not shown) (P=0.91).

RESULTS

Referral to First Seen by Urologist

Table 31: Timeline from referral to first seen by urologist by Trust of presentation (private patients [n=19], or patients under-review at time of diagnosis [n=43], are excluded)

Days	Trust of presentation					
	Belfast	Northern	South-Eastern	Southern	Western	Total
1-14	25 (29.8%)	12 (24.5%)	32 (50.0%)	30 (50.0%)	16 (41.0%)	115 (38.9%)
15-28	13 (15.5%)	11 (22.4%)	12 (18.8%)	8 (13.3%)	14 (35.9%)	58 (19.6%)
29-42	9 (10.7%)	13 (26.5%)	8 (12.5%)	8 (13.3%)	5 (12.8%)	43 (14.5%)
43 or more	37 (44.0%)	13 (26.5%)	12 (18.8%)	14 (23.3%)	4 (10.3%)	80 (27.0%)
Total	84	49	64	60	39	296
Mean (days)	43.0	32.2	24.5	31.7	29.5	33.2
Median (days)	33.5	32	14.5	15	19	23

- Overall 59% of patients were seen by a urologist within 4 weeks of referral while 27% waited over 6 weeks.
- The overall duration from referral received to first seen by urologist was longer for patients presenting in the Belfast Trust ($P < 0.05$).
- A lower proportion of patients presenting in the Belfast and Northern Trusts were seen by a urologist within 4 weeks ($P < 0.01$), 45% and 47% respectively, compared to 69%, 63% and 77% in the South Eastern, Southern and Western Trusts respectively.
- There was no difference between men and women in duration from referral received to first seen by urologist ($p = 0.93$).

Table 32: Timeline from referral to TURB by Trust of first presentation (private patients, patients under-review at time of diagnosis, or patients who did not receive a TURB, are excluded)

Days	Trust of presentation					
	Belfast	Northern	South-Eastern	Southern	Western	Total
1-14	9 (11.3%)	6 (12.5%)	13 (21.0%)	15 (26.3%)	7 (18.9%)	50 (17.6%)
15-28	7 (8.8%)	4 (8.3%)	7 (11.3%)	10 (17.5%)	2 (5.4%)	30 (10.6%)
29-42	7 (8.8%)	5 (10.4%)	9 (14.5%)	3 (5.3%)	6 (16.2%)	30 (10.6%)
43 +	57 (71.3%)	33 (68.8%)	33 (53.2%)	29 (50.9%)	22 (59.5%)	174 (61.3%)
Total	80	48	62	57	37	284
Mean	95.9	65.4	53.8	56.9	77.3	71.3
Median	88.5	63.5	46.5	45	51	60

- Overall 28% of patients had their cancer diagnosed within 4 weeks of referral, while 61% waited 6 weeks or more.

RESULTS

- A significantly ($P<0.01$) higher proportion of patients in the Southern Trust (44%) had a TURB within 4 weeks of referral compared to the other 4 Trusts (24%).
- The overall duration from referral received to TURB was longer (median 88 days) for patients presenting in the Belfast Trust ($P<0.01$).

TURB to First MDM Discussion by Trust/Location of Presentation

Table 33: Time from TURB to MDM by Trust/location of presentation (excludes patients whose MDM pre-dates TURB)

Days	Trust of presentation						Total
	Belfast	Northern	South-Eastern	Southern	Western	Private sector	
1-14	15 (17.0%)	21 (44.7%)	16 (27.6%)	26 (52.0%)	30 (81.1%)	1 (9.1%)	109 (37.5%)
15-28	51 (58.0%)	13 (27.7%)	24 (41.4%)	14 (28.0%)	3 (8.1%)	6 (54.5%)	111 (38.1%)
29-42	16 (18.2%)	4 (8.5%)	8 (13.8%)	3 (6.0%)	0 (0%)	2 (18.2%)	33 (11.3%)
43 +	6 (6.8%)	9 (19.1%)	10 (17.2%)	7 (14.0%)	4 (10.8%)	2 (18.2%)	38 (13.1%)
Total	88	47	58	50	37	11	291
Mean	24.2	26.4	26.5	23	20.6	31.3	24.6
Median	20.5	15	21	13	10	22	17

- 38% of patients had a MDM discussion within 2 weeks of diagnosis, while one quarter were discussed 4 weeks or more after diagnosis.

RESULTS

Referral to Treatment Modality

Non-muscle invasive bladder cancer (NMIBC)

For patients with non-muscle invasive Stage T1 bladder cancer TURB is considered first line therapy.

Table 34: Referral to Treatment for Stage 1 NMIBC (private patients, or patients under-review at time of diagnosis are excluded)

Days	Non-muscle invasive Stage T1 bladder cancer
1-14	8 (6.3%)
15-28	12 (9.5%)
29-42	11 (8.7%)
43-62	21 (16.7%)
>62	74 (58.7%)
Total	126
Median	69
Mean	81.8

- For patients with non-muscle invasive bladder cancer median time to treatment (TURB) was 69 days with 41% of patients having first treatment within 62 days.

Muscle invasive bladder cancer (MIBC) Stage T2 disease or higher

Radical cystectomy is the standard treatment for localized MIBC. The use of pre-operative cisplatin-containing chemotherapy improves overall survival and is recommended in suitable patients with localized disease who have good performance status and adequate renal function¹⁰. Recurrence-free and overall survival have been shown to be better in patients undergoing surgery within 90 days of diagnosis¹⁹.

Time from referral to first line treatment modality is shown in table 35.

Table 35: Referral to start of first line treatment modality for muscle invasive disease (T2 or higher)

(private patients, or patients under-review at time of diagnosis are excluded)

Days	Treatment modality	
	Major surgery*/ Pre-operative chemotherapy	Curative-intent oncological therapy (radiotherapy or chemoradiotherapy)
1-14	0 (0%)	0 (0%)
15-31	1 (2.0%)	0 (0%)
32-62	4 (8.3%)	1 (5.9%)
>62	43 (89.6%)	16 (94.1%)
Total	48	17
Mean	128	172.3
Median	118	171

*For patients undergoing neoadjuvant chemotherapy the start date of chemotherapy was taken, not the start date of surgery

RESULTS

- 10.3% of patients with muscle invasive disease had their major surgery or commenced pre-operative chemotherapy within 62 days of first referral to secondary care.
- Median time from referral was 118 days for major surgery and 171 days for curative-intent oncology.

Diagnostic TURB to Treatment Modality

Table 36: TURB to first line treatment modality for muscle invasive disease (T2 or higher), private patients excluded

Days	Treatment modality	
	Major surgery*/ Pre-operative chemotherapy	Curative-intent oncological therapy (radiotherapy or chemoradiotherapy)
From TURB		
1-14	1 (1.8%)	0 (0%)
15-31	5 (8.8%)	0 (0%)
32-62	18 (31.6%)	5 (25%)
63-90	20 (35.0%)	6 (30%)
>90	13 (22.8%)	9 (45%)
Total	57	20
Mean	71	93.8
Median	65	84

*For patients undergoing neoadjuvant chemotherapy the start date of chemotherapy was taken, not the start date of surgery

- 42% of patients with muscle invasive disease had their major surgery within 62 days of their TURB.
- Time to major surgery was greater than 90 days in almost one quarter of patients.
- Median time from TURB to treatment was 65 days for surgery, 84 days for curative-intent oncology.
- 26% of patients with muscle invasive disease had their curative-intent oncological therapy within 62 days of their TURB.

RESULTS

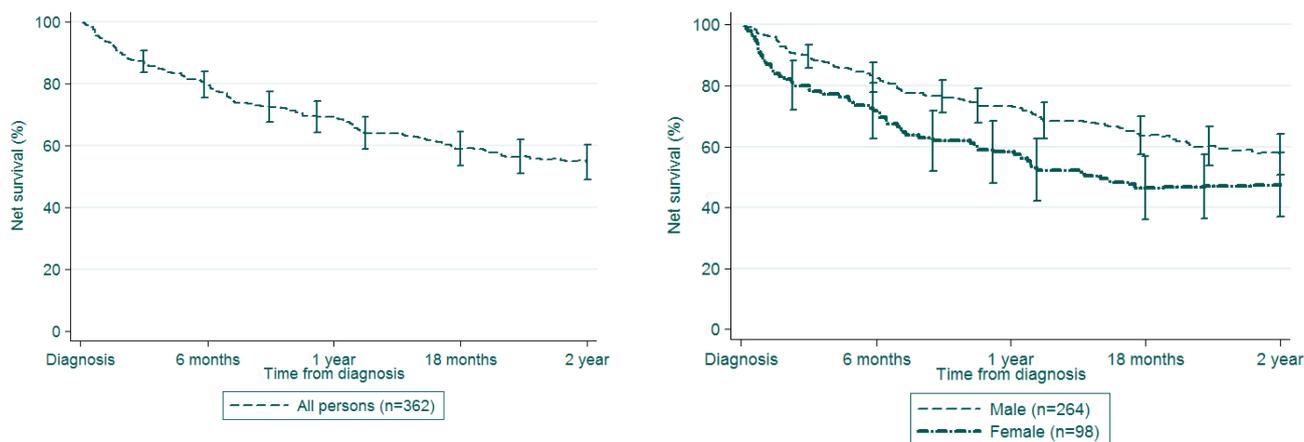
Survival

International comparisons of bladder cancer survival identify consistently lower survival in women compared to men. In the EUROCare-4 comparison of cancer survival for patients diagnosed 1995 to 1999, N. Ireland had amongst the lowest survival in Europe for women with bladder cancer.

This combined with low incidence of bladder cancer in N. Ireland compared to other European countries likely reflects as artefact of data collection as at that time Bladder Cancer figures for N. Ireland reported only invasive disease and did not count borderline pTa, pTis level bladder tumours as cancers. Many other registries included these non-invasive tumours in their figures inflating cancer incidence and raising survival due to the inclusion of tumours with very good survival. This has since changed and now like most registries NICR includes borderline pTa, pTis tumours. With this anomaly corrected the survival for bladder cancers in N. Ireland is recorded as among the highest in Europe in EUROCare-5. However we have small numbers of bladder cancers in women and year to year variation is large. The poorer survival of women with bladder cancer is internationally recognised. In a retrospective study of patients who had undergone radical cystectomy, it was found that women were more likely to be diagnosed with primary muscle invasive disease than men (85% vs 51%)²⁰. It has been suggested that women are more likely to be older than men when diagnosed, with a direct effect on their survival. In addition, delayed diagnosis is more likely in women after haematuria is observed, as the differential diagnosis in women includes diseases that are more prevalent than bladder cancer²¹.

The following graphs and tables present results of estimating and comparing net survival groups (sex, age, stage) using a non-modelling approach, which is like a Kaplan-Meier but using weights to correct for background mortality. These estimates give the true unadjusted estimates of net survival of these groups. The confidence intervals are set at 95%. The observed survival is included in the tables for comparison.

Figure 8: Net survival of all bladder cancer patients in N. Ireland by sex (2010 & 2011 combined)



RESULTS

Table 37: Observed and net survival

Time from diagnosis	Survival 2010 & 2011 (n=362)		
	Male (n=264)	Female (n=98)	Total (n=362)
	Observed Survival (with 95% confidence intervals)		
6 months	81.4% (76.2%, 85.6%)	70.4% (60.3%, 78.4%)	78.5% (73.9%, 82.3%)
1 year	71.2% (65.3%, 76.3%)	56.1% (45.7%, 65.3%)	67.1% (62.0%, 71.7%)
18 months	60.5% (54.4%, 66.1%)	43.9% (33.9%, 53.4%)	56.0% (50.7%, 61.0%)
2 years	54.2% (47.9%, 60.1%)	43.9% (33.9%, 53.4%)	51.4% (46.0%, 56.5%)
	Net Survival		
6 months	82.8% (78.0%, 87.5%)	71.7% (62.5%, 80.8%)	79.8% (75.5%, 84.1%)
1 year	73.4% (67.7%, 79.0%)	58.2% (48.1%, 68.3%)	69.4% (64.4%, 74.3%)
18 months	63.6% (57.4%, 69.9%)	46.5% (36.1%, 56.9%)	59.0% (53.6%, 64.4%)
2 years	58.2% (51.5%, 64.8%)	46.5% (36.1%, 56.9%)	55.3% (49.6%, 60.9%)

- At 2-years after diagnosis, men had 58% net survival while women had 47%. Although, the confidence intervals of these net survival estimates are over-lapping, a multivariate analysis, which corrects for age at diagnosis, demonstrates that there is a significant difference ($P < 0.05$) in the net survival experience of men to women (excess hazard risk of 1.5:1, or 50% higher). However, when stage of disease was added to the model, this showed a decline to 1.3:1, or 30% higher risk of cancer death in women ($P = 0.12$, which is not significant). A different distribution of stage at diagnosis between the sexes may be responsible for the difference in survival between men and women; however, we would need a bigger study to demonstrate this.

RESULTS

Figure 9: Net survival of bladder cancer patients in N. Ireland by stage (2010 & 2011 combined)

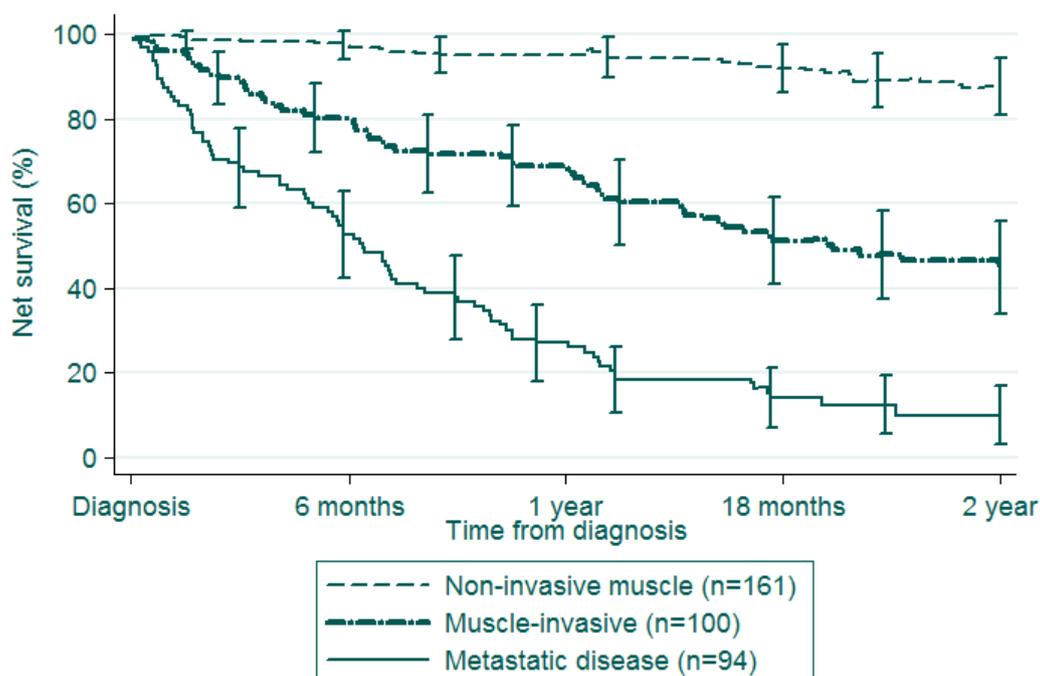


Table 38: Observed and net survival by stage group at diagnosis

Time from diagnosis	Survival 2010 & 2011 (n=355*)		
	Non-invasive muscle (n=161)	Muscle invasive (n=100)	Locally advanced/metastatic (n=94)
	Observed Survival (95% confidence intervals)		
6 months	95.7% (91.1%, 97.9%)	79.0% (69.6%, 85.8%)	52.1% (41.6%, 61.6%)
1 year	92.6% (87.3%, 95.7%)	67.0% (56.9%, 75.3%)	26.6% (18.2%, 35.8%)
18 months	86.9% (80.6%, 91.3%)	49.0% (38.9%, 58.3%)	13.7% (7.6%, 21.5%)
2 years	81.1% (73.9%, 86.5%)	44.3% (34.2%, 53.8%)	9.7% (4.2%, 18.0%)
	Net Survival		
6 months	97.4% (94.2%, 100.0%)	80.2% (72.1%, 88.3%)	52.7% (42.6%, 62.8%)
1 year	95.0% (90.9%, 99.2%)	69.0% (59.5%, 78.5%)	27.1% (18.1%, 36.1%)
18 months	92.0% (86.3%, 97.6%)	51.3% (41.0%, 61.6%)	14.1% (7.1%, 21.1%)
2 years	87.8% (80.9%, 94.6%)	46.9% (36.2%, 57.5%)	10.1% (3.4%, 16.9%)

*7 patients were unstaged

- Large differences ($P < 0.05$) in net survival at 2 years were present between the 3 stage groups: non-muscle invasive (88%), muscle invasive (47%), and metastatic (10%).

RESULTS

Figure 10: Net survival of patients in N. Ireland by age (2010 & 2011 combined)

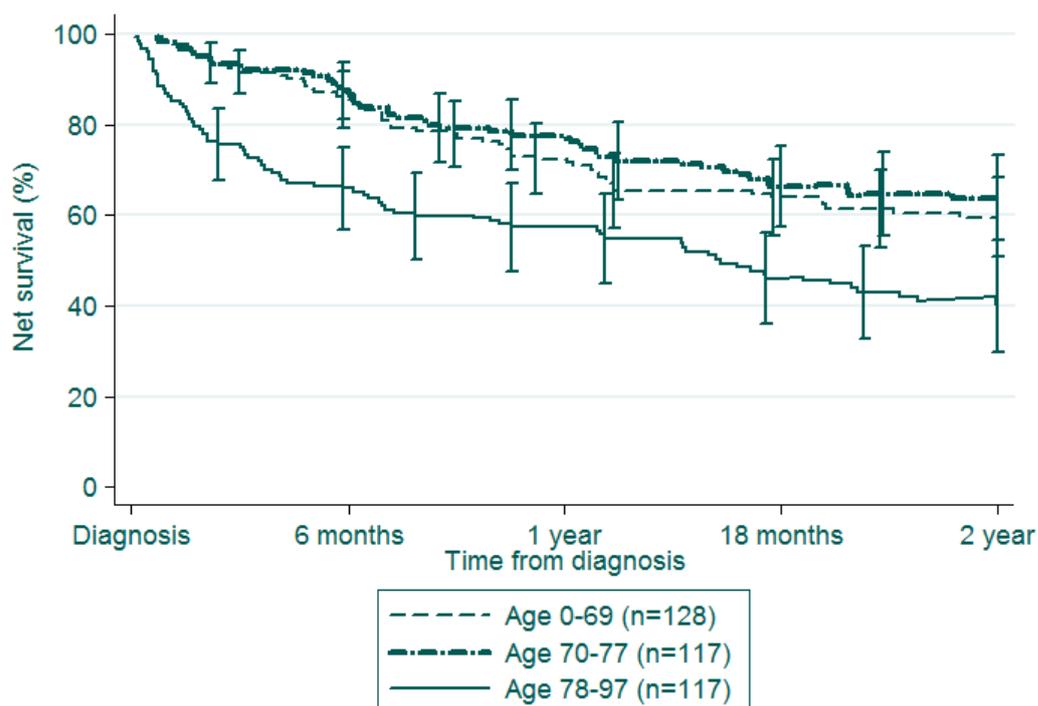


Table 39: Observed and net survival by age group

Time from diagnosis	Survival 2010 & 2011 (n=362)		
	Age 0-69 (n=128)	Age 70-77 (n=117)	Age 78-97 (n=117)
	Observed Survival (95% confidence intervals)		
6 months	85.2% (77.7%, 90.3%)	86.3% (78.7%, 91.4%)	63.3% (53.8%, 71.3%)
1 year	71.9% (63.2%, 78.8%)	76.1% (67.3%, 82.8%)	53.0% (43.6%, 61.6%)
18 months	63.3% (54.3%, 71%)	64.0% (54.5%, 71.9%)	40.2% (31.3%, 48.9%)
2 years	58.7% (49.5%, 66.8%)	60.7% (51.0%, 69.0%)	34.4% (25.9%, 43.1%)
	Net Survival		
6 months	85.5% (79.3%, 91.6%)	87.3% (81.1%, 93.6%)	65.9% (56.9%, 75.0%)
1 year	72.4% (64.6%, 80.2%)	77.7% (69.9%, 85.6%)	57.3% (47.6%, 67.0%)
18 months	64.0% (55.6%, 72.4%)	66.5% (57.5%, 75.5%)	46.1% (36.0%, 56.2%)
2 years	59.6% (50.8%, 68.3%)	64.0% (54.6%, 73.4%)	42.0% (31.5%, 52.5%)

- At 2 years after diagnosis the older age group (age 78 to 97 years) at diagnosis had significantly poorer net survival (42%) ($P < 0.05$) than the younger age groups: 60% and 64% for age groups 0 to 69 and 70 to 77 respectively (note: net survival takes background mortality into account).
- The net survival decreased with age which means that older patients are more likely to die from their bladder cancer than younger patients even when stage is accounted for.

SUMMARY

Presentation, Diagnosis and Staging

- 98% of bladder cancer patients diagnosed 2010 and 2011 were included in the audit (n=362 patients).
- Half of patients were over 74 years and 73% were men.
- 72% were current or ex-smokers.
- Macroscopic haematuria was the most common presenting symptom (80%).
- 58% of patients with symptom duration recorded had haematuria for at least 1 month and 12% over 6 months.
- Women were more likely than men to present with abdominal pain, lethargy and weight loss, possibly reflecting later stage of disease at presentation.
- 57% of all patients were referred by their GPs (outpatients and A&E).
- Overall 18% of patients were referred to outpatients by GPs as red flag suspect cancers and a further 14.6% were upgraded by consultants to a red flag pathway. GP referrals to A&E accounted for 10.5% while 11% were GP routine/urgent/semi-urgent/ referrals to outpatients.
- 31% of patients referred to outpatients by GPs were upgraded to 'red flag' by consultants.
- 21% of patients presented via A&E.
- Over a quarter of patients first presented to the Belfast Trust.
- 52% of patients first presented in outpatient clinics, with a further 16% first seen at a designated haematuria clinic.
- 86% of patients were first seen by urology.
- 73% of patients had seen a urologist within 42 days of referral, 39% within 2 weeks.
- The duration from referral received to first seen by urologist was longer among patients who presented in the Belfast Trust.
- 90% of patients were discussed at MDM – Private patients were less likely to be discussed.
- 98% of patients had a cystoscopy; of these patients 98% had a TURB and 77% had a CT scan.
- 96% of patients with muscle invasive bladder cancer had an CT/MRI scan.
- 97% were histologically verified with 86% having transitional cell carcinoma.
- 98% of patients were staged, 45% Stage 1 and 26% Stage 4 at diagnosis.

Treatment

- 95% of patients had a Trans Urethral Resection of Bladder -TURB.
- A third of all TURBs were carried out in the Belfast Trust.
- Stage 1 (Non-muscle invasive disease, n=161) treatment modality
 - The majority of patients with non-muscle invasive disease, or Stage 1, (86%, 139/161) had organ-conserving treatment with 11% (18/161) having radical cystectomy. Just under two thirds (62%) received courses of intravesical chemotherapy and/or BCG therapy. Just under a quarter had local tumour resection (TURB) with repeat cystoscopy to ensure disease eradication.

SUMMARY

- Stage 2 & 3 (Muscle invasive disease, n=100) treatment modality
 - A third (36%) of patients with muscle invasive disease (Stage 2&3) had major surgical resection while 20% of patients had organ-conserving curative intent oncological therapy. A further 16% had palliative oncological treatment.
 - In total 28% of patients with muscle invasive disease (Stage 2&3) had localised therapy only (TURB+/- intravesical therapy). Sixteen of these 28 patients were deemed unfit due to advanced age and/or comorbidity, and a further 7 patients (25%) died within 3 months of diagnosis.
- Stage 4 (Advanced metastatic, n=94)
 - Just under one third (n=28) of patients with locally advanced/metastatic disease (Stage 4) had radical cystectomy with 6 patients having pre-operative chemotherapy and 12 patients requiring adjuvant palliative radiotherapy for residual/progressive disease following cystectomy. One quarter (n=23) of patients were treated with palliative radiotherapy, while 26% of patients received supportive palliative care alone.
- 83 major surgical resections were performed: cystoprostatectomy (52), cystectomy (16), and anterior exenteration of pelvis (15).
- The majority (93%) of radical cystectomies were performed in the Belfast City Hospital with 4 being performed in the Southern Trust, 1 in the Western Trust and 1 in the private sector.
- 89% of major surgical resections were performed by a uro-oncology surgeon with a case-load volume of 11 or more major procedures during the audit period.
- 11% were performed by urologists who performed 5 or fewer major procedures during the audit period.
- 83% of patients undergoing major surgery had lymph node resection performed. The median number of lymph nodes examined was 15 (range, 1-35) and the median number of positive nodes was 0 (range, 0-18).
- 37% of patients were recorded as having been seen by a Urology Clinical Nurse Specialist. This figure may be an underestimate as this data may not have been consistently available in the clinical notes or CaPPS.
- Incidental prostate cancer was detected in 17/54 (32%) of men who had major surgical resection.

Timelines: Referral to diagnosis and treatment

Referral to First Seen by Urologist and TURB

- 59% of patients were seen by a urologist within 4 weeks of referral while 27% waited over 6 weeks.
- The overall duration from referral received to first seen by urologist was longer for patients presenting in the Belfast Trust ($P<0.05$).
- A lower proportion of patients presenting in the Belfast and Northern Trusts were seen by a urologist within 4 weeks ($P<0.01$), 45% and 47% respectively, compared to 69%, 63% and 77% in the South Eastern, Southern and Western Trusts respectively.
- Overall 28% of patients had their cancer diagnosed by TURB within 4 weeks of referral, while 61% waited 6 weeks or more.

SUMMARY

- A significantly ($P<0.01$) higher proportion of patients in the Southern Trust (44%) had a cancer diagnosis within 4 weeks of referral compared to the other 4 Trusts (24%).
- Patients who were referred to A&E (GP/self-referral) had the shortest duration from time of referral to TURB ($P<0.05$).
- For patients on a red flag pathway the median time to TURB was 63 days. 13% had TURB within 4 weeks of referral, 32% within 6 weeks, while over two thirds waited more than 6 weeks.
- Patients referred by GPs as routine, urgent/semi-urgent had the longest time from referral to TURB ($P<0.05$).

Referral to Treatment

- For patients with non-muscle invasive bladder cancer median time from first referral to secondary care to treatment (TURB) was 69 days with 41% of patients having first treatment within 62 days.
- For patients with muscle invasive disease (T2 or higher) median time from first referral to secondary care to major surgery was 118 days and median time to curative-intent oncology was 171 days.

Diagnosis to Treatment

- 42% of patients with muscle invasive disease had their major surgery within 62 days of diagnostic TURB.
- Time to major surgery from TURB was greater than 90 days in one quarter of patients.
- Median time from diagnostic TURB to treatment was 65 days for major surgery and 84 days for curative-intent oncology.

Communication with Primary Care and Patient Information

- Over 95% of patients had their diagnosis and management plan recorded in their GP letter.
- Two thirds of GP letters mentioned that diagnosis was discussed with the patient, and a third of letters that diagnosis had been discussed with their family.
- In 31% of the letters, palliative care was mentioned.
- Discussion of diagnosis and treatment plan was recorded in the clinical notes/CaPPS in just over 80% of patients.

Survival

- Risk of death from bladder cancer was higher for women 1.5:1. However, when stage of disease was taken into account, this reduced to 1.3:1, or 30% higher in women. This however was no longer statistically significant.
- The net survival decreased with age which means that older patients are more likely to die from their bladder cancer than younger patients, even when stage is taken into account.
- 2 years after diagnosis, men had 57% net survival while women had 47%.
- Large differences in net survival at 2 years were present between the 3 stage groups: non-muscle invasive (88%), muscle invasive (47%), and locally advanced/metastatic disease (10%).
- Those over 78 years at diagnosis had significantly poorer net survival (42%), than the younger age groups: 60% and 64% for age groups 0 to 69 and 70 to 77, respectively.

CONCLUSIONS AND RECOMMENDATIONS

This work assessed the care pathway of bladder cancer patients in N. Ireland and compliance with recommended guidelines for investigation and treatment. It found that patients are managed by well-functioning multidisciplinary teams that record diagnosis and treatment plans and communicate well with primary care. The majority of major bladder cancer surgery in 2010 & 2011 was performed by speciality uro-oncology surgeons in the Belfast City Hospital reflecting centralisation of surgery in keeping with clinical management guidelines.

We explored reasons for bladder cancer survival differences in women compared to men and confirmed a 10% lower survival for women with some, but not all, of this due to later stage of disease at diagnosis. This audit did not find any differences in the treatment of men and women.

However as with any service, improvements may be made.

- A considerable proportion (21%) of bladder cancer patients had an emergency admission via A&E and 34% of younger patients (aged 0-69) presented with Stage 4 disease (50% in women) which is in keeping with late presentation.
- 41% of patients waited over 4 weeks to see a urologist and 61% (almost two thirds) waited at least 6 weeks from referral to diagnosis.
- Median time from referral to treatment was 118 days for major surgery and 171 days for curative-intent oncology.
- The proportion of patients recorded as having received assistance from a Clinical Nurse Specialist was low at 37%.

Recommendations

1. The public need to be educated about haematuria as an alarm symptom for cancer.
2. Reasons for late and delayed presentation should be investigated.
3. Access to urology services should be assessed regionally.
4. The pathways for bladder cancer investigation and treatment should be explored to speed up this process.
5. Clinical Nurse Specialists should be available for all patients.
6. Efforts to reduce the prevalence of smoking should continue as tobacco use is a risk factor.

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APPENDIX A – BLADDER CANCER: OVERVIEW

Background

Anatomy of bladder

The urinary bladder is located in the pelvis and consists of three layers: the epithelium and subepithelial connective tissue, the muscle layer (muscularis) and the perivesical fat layer (Figure 11). Bladder cancer can present as a papillary (finger-like) lesion, as a flat pre-malignant (in-situ) lesion 'carcinoma in-situ' (CIS) or as an infiltrating cancer penetrating the muscle layer which can spread to the surrounding lymph nodes and then spread (metastasize) to distant sites.

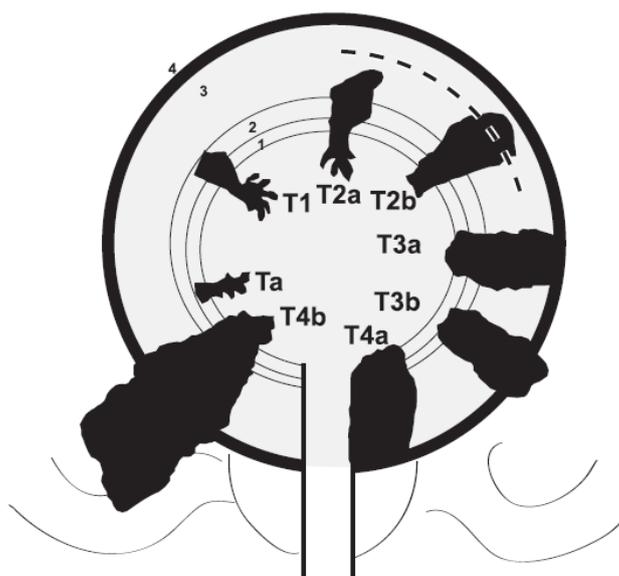


Figure 11: Bladder cancer: The extent (T) of the primary bladder cancer: Ta (confined to mucosa), T1 (extends to submucosa), T2-T4a (invades bladder muscle and surrounding fatty tissue)

1. epithelium 2. subepithelial connective tissue 3. muscle 4. perivesical fat

Bladder cancer

The most common cell type is known as transitional cell carcinoma (TCC). Less than 10% of bladder cancers are adenocarcinoma or squamous cell carcinoma or other less common cell types.

Approximately 70% of patients with bladder cancer present with a disease that is confined to the bladder mucosa-Stage (Ta, CIS) or submucosa T1. These categories are grouped together as non-muscle invasive bladder cancer (NMIBC) while T2-T4 tumours are classified as muscle invasive (MIBC). NMIBC are more common and have a lower risk of progression than MIBC which has poorer survival.

Bladder tumours are generally categorised by stage and grade. The internationally-agreed UICC TNM Staging Classification defines the T (Tumour) category, N (regional nodes) category and M (metastases) category to give an overall stage of disease (Stage 1-Stage 4). Grade describes the tumour behaviour ie. how aggressive the tumour is likely to be. Grade and stage are prognostic factors which influence choice of treatment and determine outcomes.

APPENDIX A – BLADDER CANCER: OVERVIEW

Risk factors

Tobacco smoking is the most important risk factor for bladder cancer^{22,23} causing 50-65% of male cases and 20-30% of female cases. The incidence of bladder cancer is directly related to the duration of smoking and number of cigarettes smoked per day.

Bladder cancer was one of the first cancers shown to be industrially associated with occupational exposure to chemicals present in dyes, paints and plastics being the second most important risk factor²⁴ accounting for 20-25% of all cases. These can cause bladder cancer 5-50 (typically, 10-15) years later. The highest risk is associated with aromatic amines which were found in dyes, paints and plastics and are currently found in diesel exhaust fumes and other industrial by-products. Occupations associated with increased risk include work in textile, dyestuffs, chemical or plastics industries; tyre and rubber manufacture; truck and taxi driving; painting and printing; metalwork; work in the cable industry; leather work and hairdressing. These chemicals have contributed minimally to the current incidence of bladder cancer in western countries because of more stringent occupational regulations.

Bladder schistosomiasis (a parasitic disease) is associated with a five-fold increased risk of urinary bladder cancer. Infections with schistosomiasis affect about 600 million people in Africa, Asia, South America, and the Caribbean, but is not a risk-factor in N. Ireland. Other causes of bladder cancer include previous treatment for cancer- in particular, radiotherapy to the pelvis and some forms of chemotherapy.

Bladder cancer is much more common in men 2.6:1 and this higher incidence is likely related to lifestyle/occupational factors.

Common Symptoms

Haematuria is the most common symptom in bladder cancer. Stage Ta and T1 tumours do not cause bladder pain and rarely present with lower urinary tract symptoms (LUTS) while muscle invasive tumours (T2-T4) present commonly with haematuria and other symptoms such as urinary frequency, urgency, dysuria (pain passing urine) and pelvic pain relating to urinary obstruction.

Screening

At the moment there is no reliable screening test for bladder cancer. Testing for blood in the urine would not be a useful screening test for the general population as small amounts of blood in urine can be caused by infections or kidney problems. Also, the low rate of bladder cancer in the population would impair the feasibility and cost-effectiveness of screening.

APPENDIX A – BLADDER CANCER: OVERVIEW

Investigation and diagnosis

*Cancer Services: Investing for the Future. Cancer Working Group Sub-group report on urology cancers*³ recommended that “Rapid access haematuria clinics could be provided in a range of acute hospitals, including hospitals which are not cancer units, provided they have strong links with a cancer unit and have the appropriate expertise available.” The NICE guidance⁶, recommends that patients with visible haematuria should be referred urgently within two weeks to a dedicated haematuria clinic, so that if bladder cancer is diagnosed primary treatment can be started within two months. Ideally, sufficient tests to determine whether cancer is present can be carried out during a single visit, but in some cases more sophisticated imaging may need to be carried out in a radiology department.

Haematuria clinics should offer the following:

1. Physical examination, which can identify a palpable pelvic mass, i.e. locally advanced tumour.
2. Urine testing. Urinary cytology has a high sensitivity for detecting high-grade tumours and good specificity for all tumours. It can also detect invisible tumours missed by cystoscopy (see below).
3. Cystoscopy is where a scope (cystoscope) is passed through the urethra to examine the inner lining of the bladder. Cystoscopy has good sensitivity for detecting bladder cancer. Fluorescence cystoscopy under blue/violet light, which causes tumours to fluoresce, improves the detection rate, particularly in CIS.
4. Biopsy by transurethral resection of the bladder (TURB, see below).
5. Rapid access, if required, for:
 - a. Ultrasound imaging.
 - b. Intravenous urography (IVU) which is a general X-ray examination to look at the whole of the urinary system, in order to see what is causing symptoms.

Transurethral resection of the bladder (TURB)

Transurethral resection of the bladder (TURB) is a procedure where a resection loop is passed through the cystoscope into the bladder in order to remove/biopsy a bladder lesion. The goal of the TURB is to make a correct diagnosis, and in NMIBC to remove all visible lesions (including any CIS). Any abnormal areas of epithelium should also be sampled as they can be indistinguishable from CIS. When urine cytology is positive, but no visible lesions are present, random biopsies should be taken, as well as upper-tract diagnostics performed. The prostatic urethra should be sampled when any of the following occurs: abnormal tissue in urethra, CIS is suspected in bladder, positive cytology, tumours located at trigone or bladder neck or multiple tumours in bladder.

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When NMIBC (Ta, T1) has been found a second resection is recommended because there is high-risk of residual disease (33-53%), or under-staging (4-25%). Treatment of a Ta/T1 high-grade tumour and a T2 tumour is completely different, hence the importance of staging. The second resection decreases the probability of recurrence, especially when the first TURB is incomplete or lacking sufficient muscle or when T1 or grade 3 disease is diagnosed. The second TURB should take place within 2-6 weeks.

Multidisciplinary team meeting

Patients with cancer often have complex care needs that cannot be addressed by a single specialty or discipline. This has led to the development of multi-disciplinary teams within the Cancer Network to ensure a consistent and equitable approach to planning and managing care. Supporting this approach, there is a role for a Clinical Nurse Specialist to coordinate care between settings and providing support, advice and information for patients and their carers throughout their illness. Rigorous clinical audit is crucial to maintaining and improving quality of outcomes.

Treatment

Non-muscle invasive bladder cancer (NMIBC)⁹

Patients with bladder cancer that has not invaded the bladder muscle (CIS, Ta, T1) should be stratified into one of three risk groups that will facilitate treatment recommendations based on the probabilities of recurrence and progression. Bladder tumours can be risk-stratified into:

1. Low: primary and solitary Ta tumour < 3 cm size, with G1 tumour grade, and no associated CIS.
2. Intermediate: any tumour not in low or high risk group.
3. High: Any of the following: T1 tumour, G3 tumour grade, associated CIS, multiple and recurrent and large Ta tumour with G1 or G2 grade.

For patients with low-risk Ta tumours one immediate postoperative instillation of intravesical chemotherapy (chemotherapy instilled into bladder cavity) is recommended.

For patients with intermediate-risk Ta T1 tumours one immediate postoperative instillation of intravesical chemotherapy should be followed by one year full dose BCG* immunotherapy or further installation of chemotherapy for a maximum of 1 year.

Patients with high-risk tumours should receive intravesical full dose BCG installations for 1-3 years or cystectomy in highest risk tumours or tumours that are BCG refractory.

*Bacillus Calmette-Guérin (BCG)

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Treatment: muscle invasive bladder cancer (MIBC)¹⁰

Patients with MIBC should be referred to the specialist team. MRI or CT scan, if MRI is not available should be performed to assess the extent of invasive tumours before radical treatment. MRI provides better resolution to assess invasion in the bladder muscle.

- The treatment of choice for MIBC is cystectomy and is indicated for T2-T4a tumours in the absence of metastatic disease.
- Neoadjuvant cisplatin-containing chemotherapy should be considered in suitable patients.
- A higher surgical case load reduces morbidity and mortality of cystectomy
- Delay in cystectomy for more than 3 months from diagnosis increases risk of progression and cancer-specific death.
- Lymph node dissection should be an integral part of cystectomy

Urinary diversion after radical cystectomy

Radical cystectomy and urinary diversion are two steps in the one operation. The type of urinary diversion procedure depends on patient comorbidities, functional status and patient preference.

Three alternatives are presently used after cystectomy:

1. *Abdominal diversion:* urethrocutaneostomy, ileal or colonic conduit and various forms of a continent pouch.
2. *Urethral diversion:* various forms of gastrointestinal pouches attached to the urethra as a continent orthotopic urinary diversion (neobladder).
3. *Rectosigmoid diversion:* procedures such as uretero-rectostomy.

Treatment for non-resectable tumours

For patients with locally-advanced tumours (T4b, invading the pelvic or abdominal wall), primary radical cystectomy is not a curative option, but can be used to palliate symptoms such as bleeding, pain, dysuria and urinary obstruction. Cystectomy in patients with locally-advanced disease gives rise to post-operative morbidity and mortality. Advanced muscle invasive disease can lead to ureteral obstruction requiring permanent nephrostomy.

Bladder-preserving treatment

For patients who are unsuitable for cystectomy, multimodal therapy (TURB, radiotherapy or chemoradiotherapy) is the preferred curative therapeutic approach as it is more effective than radiotherapy alone. The rationale for TURB followed by radiation is to achieve local tumour control while cisplatin-containing chemotherapy aims at eradication of micrometastasis. Cisplatin-based chemotherapy in combination with radiotherapy following TURB results in a complete response rate of 60-80%.

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Metastatic Disease

About 10-15% of bladder cancer patients have metastatic disease at diagnosis and approximately half relapse following cystectomy. Local recurrence accounts for 30% of relapses while distant metastases are more common. Cisplatin-containing chemotherapy can achieve median survival of up to 14 months. In patients unfit for cisplatin therapy treatment with carboplatin-containing combination chemotherapy is a therapeutic option.

APPENDIX B – COMPONENTS OF THE CHARLSON COMORBIDITY SCORE

Charlson score components - comorbidity and age

Components	Score
Comorbidity component	
Cerebrovascular Disease	1
Chronic Pulmonary Disease	1
Congestive Heart Failure	1
Connective Tissue Disease	1
Dementia	1
Diabetes Without Complications	1
Liver Disease	1
Myocardial Infarction	1
Peptic Ulcer	1
Peripheral Vascular Disease	1
Cancer	2
Diabetes With Complications	2
Hemiplegia Or Paraplegia	2
Leukaemia	2
Lymphoma	2
Renal Disease	2
Severe Liver Disease	3
HIV	6
Metastatic Cancer	6
Age component	
Age <40 years	0
41—50	1
51—60	2
61—70	3
71—80+	4

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