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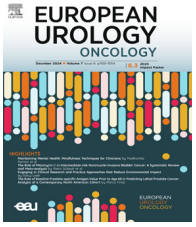

European Association of Urology

Original articles

Achieving Benchmarks for National Quality Indicators Reduces Recurrence and Progression in Non–muscle-invasive Bladder Cancer

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Abstract

Background: Noncompliance with evidence-based interventions and guidelines contributes to significant and variable recurrence and progression in patients with non–muscle-invasive bladder cancer (NMIBC). The implementation of a quality performance indicator (QPI) programme in Scotland's National Health Service (NHS) aimed to improve cancer outcomes and reduce nationwide variance.

Objective: To evaluate the effect of hospitals achieving benchmarks for two specific QPIs on time to recurrence and progression in NMIBC.

Design, setting, and participants: QPIs for bladder cancer (BC) were enforced nationally in April 2014. NHS health boards collected prospective data on all new BC patients. Prospectively recorded surveillance data were pooled from 12 collaborating centres.

Intervention: QPIs of interest were (1) hospitals achieving detrusor muscle (DM) sampling target at initial transurethral resection of bladder tumour (TURBT) and (2) use of single instillation of mitomycin C after TURBT (SI-MMC).

Outcome measurements and statistical analysis: The primary and secondary endpoints were time to recurrence and progression, respectively. Kaplan-Meier and Cox multivariable regression analyses were performed.

Key findings and limitations: Between April 1, 2014 and March 31, 2017, we diagnosed 3899 patients with new BC, of which 2688 were NMIBC . With a median follow up of

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60.3 mo, hospitals achieving the DM sampling target had a 5.4% lower recurrence rate at 5 yr than hospitals not achieving this target (442/1136 [38.9%] vs 677/1528 [44.3%], 95% confidence interval [CI] = 1.6–9.2, $p = 0.005$). SI-MMC was associated with a 20.4% lower recurrence rate (634/1791 [35.4%] vs 469/840 [55.8%], 95% CI = 16.4–24.5, $p < 0.001$). On Cox multivariable regression, meeting the DM target and SI-MMC were associated with significant improvement in recurrence (hazard ratio [HR] 0.81, 95% CI = 0.73–0.91, $p = 0.0002$ and HR 0.66, 95% CI = 0.59–0.74, $p < 0.004$, respectively) as well as progression-free survival (HR 0.62, 95% CI = 0.45–0.84, $p = 0.002$ and HR 0.65, 95% CI = 0.49–0.87, $p = 0.004$, respectively). We did not have a national multicentre pre-QPI control.

Conclusions: Within a national QPI programme, meeting targets for sampling DM and SI-MMC in the real world were independently associated with delays to recurrence and progression in NMIBC patients.

Patient summary: Following the first 3 yr of implementing a novel quality performance indicator programme in Scotland, we evaluated compliance and outcomes in non–muscle-invasive bladder cancer. In 2688 patients followed up for 5 yr, we found that achieving targets for sampling detrusor muscle and the single instillation of mitomycin C during and after transurethral resection of bladder tumour, respectively, were associated with delays in cancer recurrence and progression.

1. Introduction

Bladder cancer (BC) poses a significant burden to patients, carers, and the already stretched healthcare system [1,2]. Non–muscle-invasive bladder cancer (NMIBC) encompassing over 75% of all BC cases [1] has a significant risk of recurrence and progression, thus necessitating (often) life-long surveillance and repeat interventions (surgical and intravesical treatment). This leads to a considerable strain on both health-related quality of life and finances [3,4].

Despite the knowledge of this burden, evidence-based interventions and guidelines are not adopted widely, that is, efficacy has not been translated adequately to effectiveness [5–7]. Why spend millions on clinical trials when real-world patients are not benefitting from these? Variation in clinical practice also contributes to suboptimal [8] as well as heterogeneous outcomes [6]. In NMIBC, it is well recognised that there are often poor compliance to guidelines [5] and ineffective initial interventions, necessitating additional surgery [9]. Unified approaches are required to address this knowledge-practice divide—for example, the IMAGINE project designed to improve guideline compliance [10]. Quality indicators (QIs), conversely, both evaluate healthcare quality and (putatively) drive standards for better patient outcomes [11–13].

In 2008, The Scottish Government, recognising the need to improve cancer survival and address healthcare inequalities/variance across the country, published "*Better Cancer Care, An Action Plan*" [14], mapping out key priorities and action plans; this included introduction of QIs. Scotland's quality performance indicator (QPI) programme aimed to foster a culture of continuous quality improvement by a regular review of real-time data and consequently implement changes to improve patient-centred care, whilst reducing variance.

As part of the Scottish BC Quality Performance Indicators influencing Outcomes, Prognosis and Surveillance (*Scot BC Quality OPS*) series [15], we aimed to prospectively assess the effect of hospitals achieving benchmarks for two specific QPIs related to the initial transurethral resection of bladder tumour (TURBT) on the time to recurrence and progression in NMIBC. The secondary aims included determining the utility of these QPIs within a prognostic calculator.

2. Patients and methods

Under the auspices of Scotland's three regional cancer networks, the Information Services Division (ISD), and Healthcare Improvement Scotland (HIS), development of QPIs for BC (SBC-QPIs) began in December 2012. A multidisciplinary panel of specialists and patient representatives evaluated the literature and guidelines to produce 12 QPIs (Supplementary material), with details of data definitions, targets, and measurability criteria [16]. QPIs, each with a specific purpose, were designed to be reviewed every 3 yr, ensuring responsiveness to changes in clinical practice and emerging evidence [16]. The governance aspects, policies, and protocols are published [16]. SBC-QPIs were enforced nationally in April 2014. National Health Service (NHS) health boards collected data prospectively on all new BC patients, including patient/tumour demographics, QPI variables, and pathology reports (using the Royal College of Pathologists' checklist [17]) and have accountability for QPI compliance. Data acquisition and analyses of compliance to QPIs by NHS data/audit personnel are independent of clinicians by design. A mandatory regional review of data is undertaken annually for accuracy and compliance, and then published online by each network as snapshots, that is, 2014/15, 2015/16, and 2016/17, and were first collated nationally in 2018 [18].

2.1. Follow up data

The clinical arm of this project was conceived at the time of SBC-QPI development, forming the Scot BC Quality OPS clin-

ical project [15], essentially a phase T4 translational project gauging outcomes through clinical audit of national policy [19]. Following initial treatment, patients received risk-adapted surveillance and adjuvant intravesical treatment according to the European Association of Urology (EAU) guidelines [20] with multidisciplinary team (MDT) input. MDT meetings occur weekly, attended by urologists, oncologists, uroradiologists, uropathologists, clinical nurse specialists, trainees, and audit personnel. Clinical findings from surveillance were prospectively recorded electronically (and paper) in each hospital and then pooled centrally as part of the collaborative, once in 2019 [21] for early outcomes and then on October 29, 2021 for the current analysis of long-term outcomes. Data were recorded using a standard operative proforma as a QPI requirement (Supplementary material) [16,21].

Only patients diagnosed with new NMIBC between April 2014 and March 2017 were included in the current set of analyses [15,21].

The exclusion criteria for the analysis of endpoints are as follows:

1. Muscle-invasive and nonurothelial BC
2. Synchronous upper tract urothelial carcinoma (UTUC) at the time of diagnosis
3. Patients scheduled for palliative care only
4. MDT and/or comprehensive geriatric assessment (CGA) recommendation that regular surveillance was not in the patient's best interest.

The specific QPIs of interest in this study are surrogates for reducing recurrence in NMIBC by influencing the initial TURBT:

1. Sampling of detrusor muscle (DM) in the initial TURBT specimen [22,23]. The target for each hospital is 80%.
2. Use of a single instillation of Mitomycin C (SI-MMC) within 24 h following the initial TURBT [24]. The target for each hospital is 60%.

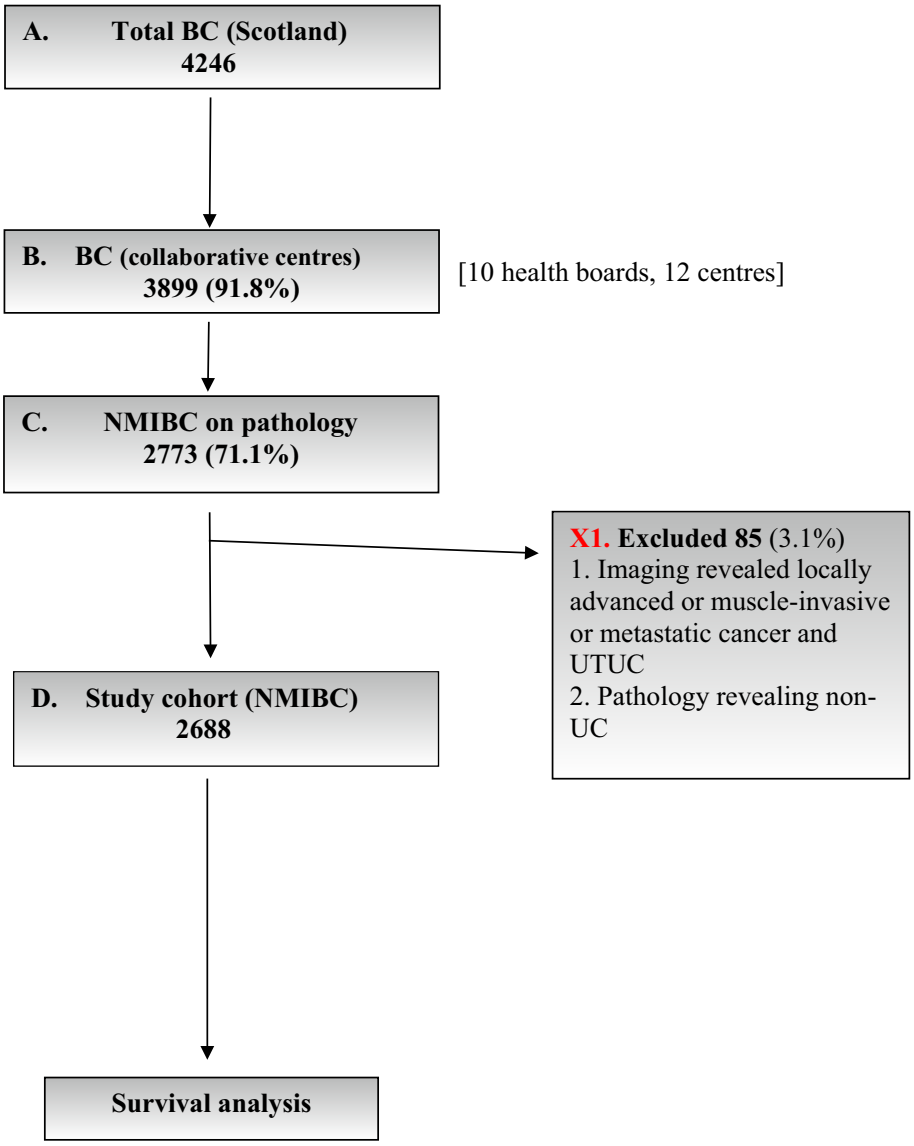

Fig. 1 – Study profile. BC = bladder Cancer; NMIBC = non–muscle-invasive bladder cancer; UC = urothelial carcinoma; UTUC = upper tract urothelial carcinoma.

Definitions used have been published previously [21] and the relevant ones are the following:

1. Compliance—percentage (%) of patients achieving a particular QPI.
2. Recurrence—biopsy-proven cancer or a lesion that has been fulgurated at the time of cystoscopic follow-up. When biopsies have not been taken, the assumption is that the pathology of the lesion is the worst grade/stage of tumour identified previously.
3. Progression—recurrence where the pathology reveals a higher grade (either low grade to high grade or cis; or G1 to G2/ G3 or G2 to G3) and/or higher stage (from pTa to pT1/pT2 or pT1 to pT2). Pathological grades were described using both the 1973 and the 2004 World Health Organization (WHO) classifications.
4. MDT—when used in the exclusion criteria for follow-up, this team includes oncological MDT and/or CGA.
5. Trainee seniority—we agreed at the time of QPI development that all trainees undertaking initial TURBT would be supervised by a consultant [16]. Trainee seniority was defined similar to our previous work [21–23], where senior specialist trainees are those in years 5 onwards, whilst the specialist trainees are below 5 yr in urology training.

The endpoints are the following:

1. Time to recurrence
2. Time to progression

The analysis was based on an "intention to treat" within the QPI framework and related clinical principles.

2.2. Statistical methodology

A Kaplan-Meier analysis of recurrence and progression in a univariate manner has been presented as failure plots with associated log-rank statistics, after excluding patients without follow-up, to show the effect of stratification variables. Rates of recurrence/progression have been compared at 5 yr from TURBT using a binomial test for the comparison of proportions and presented with the difference in percentage, 95% CI for the difference.

A multivariate analysis of recurrence and progression used Cox proportional-hazard modelling. For this, we have considered tumour size (<3 or ≥3 cm), tumour number (single or multiple), WHO 2004 grade (low or high), stage (T1 or Ta), concomitant cis (yes or no), DM sampled (yes or no), Mitomycin C use (yes or no), hospital achieving target DM sampling (yes or no), hospital achieving target bladder diagram usage (yes or no), hospital achieving target SI-MMC (yes or no), sex (male or female), smoking status (current, ex, or non), and age group (≤70 or >70 yr). The initial model consisted of variables that reached statistical significance ($p < 0.05$) in the univariate analysis, and any nonsignificant variables were removed sequentially to return a model containing only those variables reaching statistical significance when other variables are taken into account. An analysis was completed using SAS V 9.4 (SAS Institute Inc., Cary, NC, USA).

NHS Lothian R&D provided funding for statistical analysis.

3. Results

A total of 4246 consecutive patients had a new BC diagnosis in Scotland (April 2014 and March 2017) [18]. Of these patients, 3899 (91.8%) were diagnosed in the collaborating centres with 2773 (71.1%) having NMIBC on pathology. After excluding 85 patients with imaging evidence of muscle-invasive, locally advanced, or metastatic BC, or UTUC and pathological nonurothelial carcinoma, the total number of NMIBC patients in the study cohort was 2688 (Fig. 1).

Table 1 describes patient/tumour characteristics at the time of initial TURBT or biopsy. Approximately 30% of patients never smoked, and where documented, 75% TURBT operations were undertaken by consultants or senior trainees.

A bladder diagram and standard operative description were used in 2090/2688 (77.8%) NMIBC patients. DM was sampled in 73% patients, whilst SI-MMC was utilised in 67% patients (Table 1).

Table 1 – Patient and tumour characteristics with surgeon categories at the time of initial TURBT

Variable		Number (% of total)
Total patients included into NMIBC analysis (*N*)		2688
Patient age (yr), mean (range)		72.0 (21.8–97.7)
Patient age, median (IQR)		73.2 (65.5–79.9)
Sex, *n* (%)	Female	785 (29.2)
	Male	1903 (70.8)
Smoking status, *n* (%)	Never	805 (29.9)
	Ex-smoker	1252 (46.6)
	Current smoker	606 (22.6)
	Unknown	25 (0.9)
Tumour size, *n* (%)	Small (<3 cm)	1821 (67.8)
	Large (≥3 cm)	783 (29.1)
	Not clearly specified/missing	84 (3.1)
Tumour multiplicity, *n* (%)	Single	1816 (67.6)
	Multiple	851 (31.7)
	Not clearly specified/missing	21 (0.8)
Primary tumour grade (WHO 2004 classification), *n* (%)	Low grade	1457 (54.2)
	High grade	1210 (45.0)
	Cis	21 (0.8)
Primary tumour stage, *n* (%)	Ta	1910 (71.1)
	T1	757 (28.2)
	Tis	21 (0.8)
Detrusor muscle sampled, *n* (%)	Yes	1961 (73.0)
	No	696 (25.9)
	Not applicable (biopsy only)	31 (1.2)
Single postoperative instillation of Mitomycin C, *n* (%)	Yes	1797 (66.9)
	No	853 (31.7)
	Felt not applicable by surgeon	26 (1.0)
	Not documented	12 (0.5)
Operating surgeon category, *n* (%)	Consultant	1490 (55.4)
	Senior specialist trainee	536 (19.9)
	Specialist trainee	225 (8.4)
	Not clearly specified/missing	437 (16.3)

IQR = interquartile range; NMIBC = non–muscle-invasive bladder cancer; TURBT = transurethral resection of bladder tumour; WHO = World Health Organization.

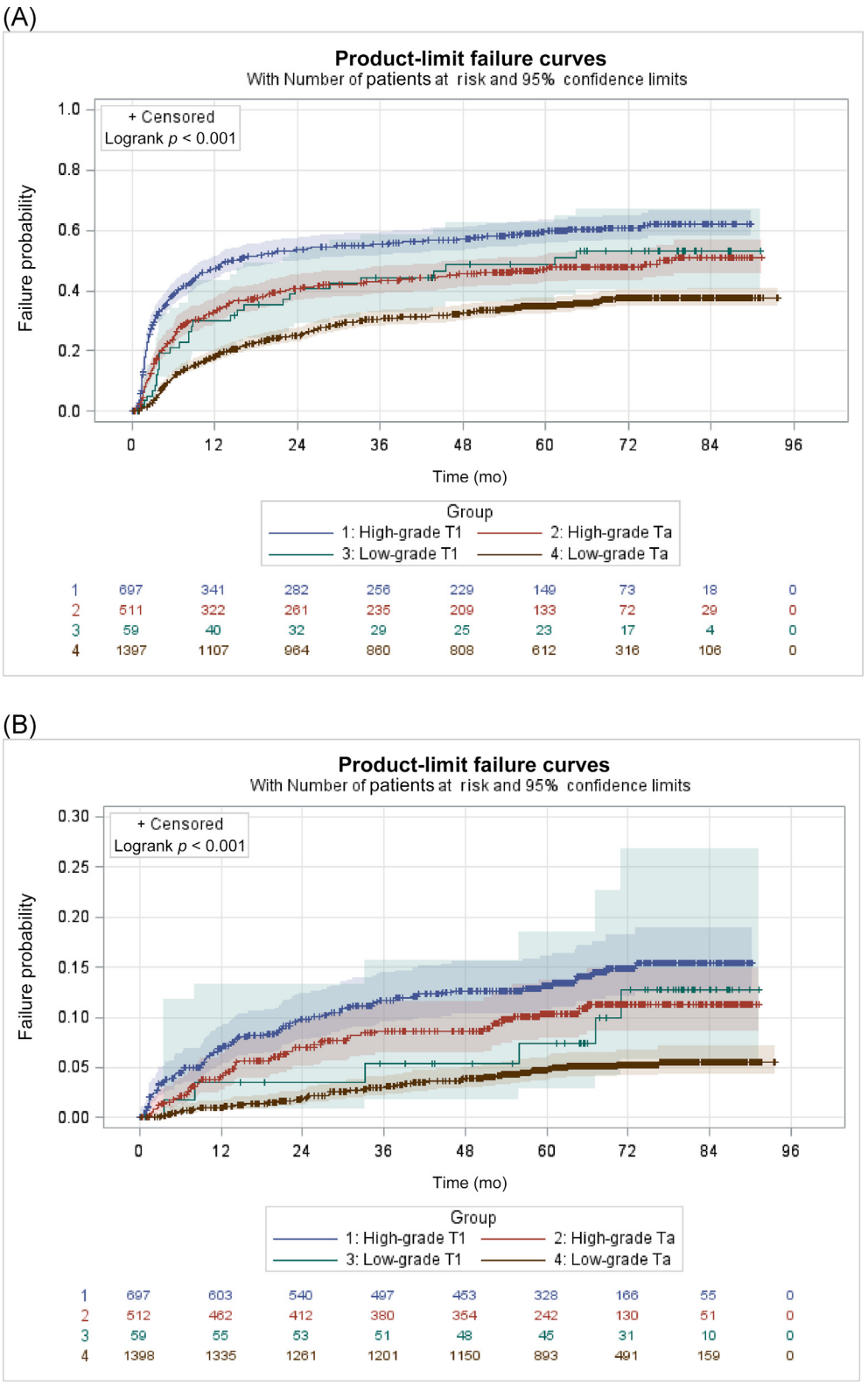

Fig. 2 – Time to (A) recurrence and (B) progression stratified by initial tumour grade and stage in NMIBC patients (shaded areas denote 95% confidence intervals). NMIBC = non–muscle-invasive bladder cancer.

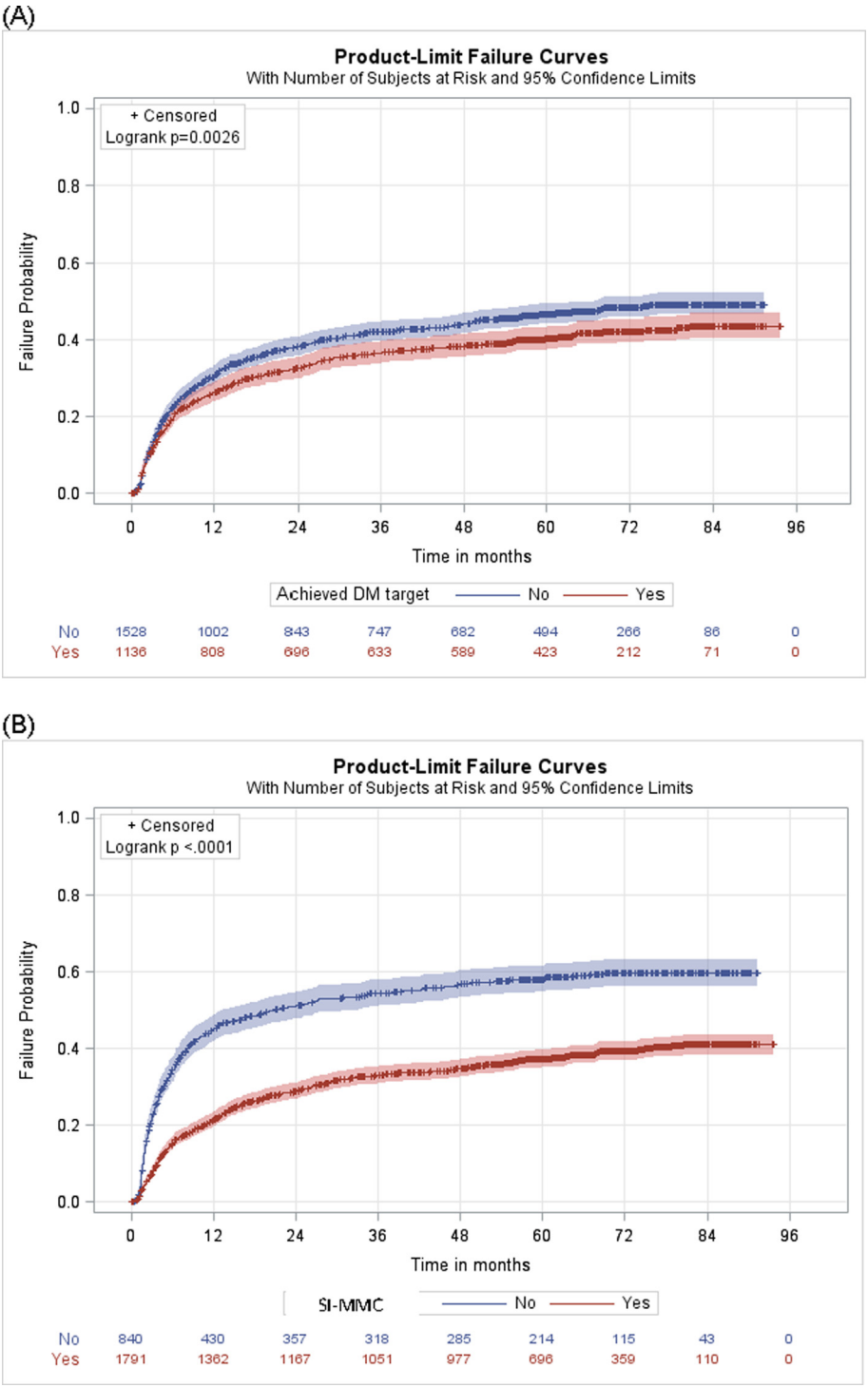

Fig. 3 – Time to recurrence between (A) Centres achieving the DM target and those that did not, and (B) Patients who received SI-MMC and those who did not. DM = detrusor muscle; SI-MMC = single instillation of Mitomycin C.

3.1. Hospital compliance to QPI targets

3.1.1. Sampling DM

Four hospitals (accounting for 1149/2688 [42.8%] patients) achieved the DM target of 80%. Adjuvant intravesical BCG was used in 248/1149 (21.6%) and 383/1539 (24.9%) patients in centres achieving and not achieving the DM target, respectively. An adjuvant course of Mitomycin C was used in 121/1149 (10.5%) and 153/1539 (9.9%) patients in centres achieving and not achieving the DM target, respectively. Re-TURBT for patients with high-grade (HG) Ta/T1 cancer was undertaken in 364/516 (70.5%) and 451/691 (65.3%) patients in centres achieving and not achieving the DM target, respectively.

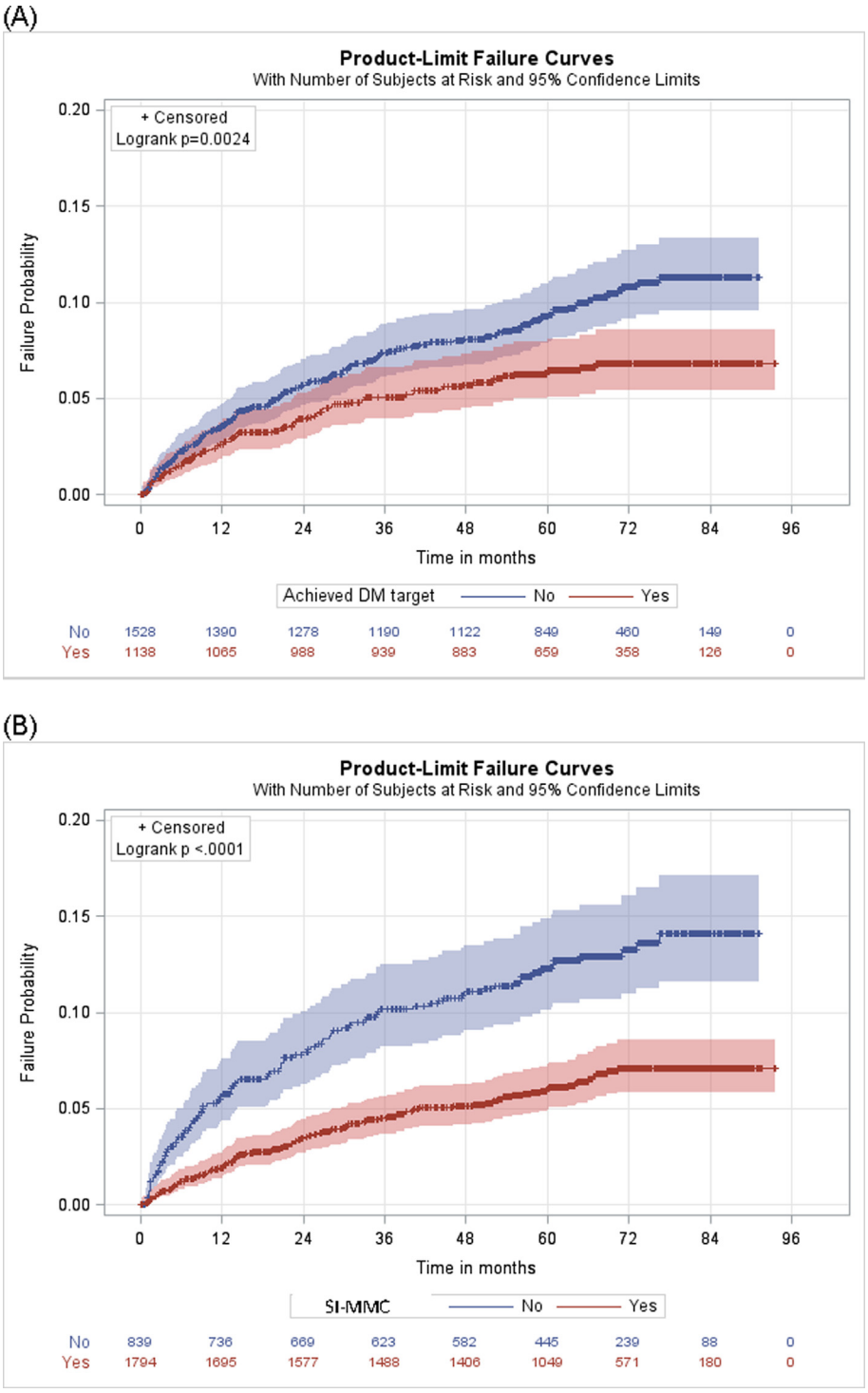

Fig. 4 – Time to progression between (A) Centres achieving the DM target and those that did not, and (B) Patients who received SI-MMC and those who did not. DM = detrusor muscle; SI-MMC = single instillation of Mitomycin C.

3.1.2. SI-MMC

Only one hospital did not achieve the 60% target for this QPI.

3.2. Time to recurrence and progression

Kaplan-Meier curves in Figure 2 reveal time to recurrence (Fig. 2A) and time to progression (Fig. 2B) stratified by tumour grade and stage. At 5 yr, the estimated rates of recurrence for patients with low-grade (LG) Ta, LGT1, HGTa, and HGT1 were 463/1397 (33.1%; 95% CI = 30.7–35.7), 27/59 (45.8%; 95% CI = 32.7–59.2), 226/511 (44.2%; 95% CI = 39.9–48.7), and 393/697 (56.4%; 95% CI = 52.6–60.1), respectively (Fig. 2A). Conversely, the rates of progression at 5 yr in these patients were 59/1398 (4.2%; 95% CI = 3.2–5.4), 4/59 (6.8%; 95% CI = 1.9–16.5), 47/512 (9.2%; 95% CI = 6.8–12.0),

Table 2 – Cox multivariable regression analysis for recurrence and progression

Parameter		*p* value	Hazard ratio	95% hazard ratio confidence limits	
Recurrence					
Tumour size	Large	<0.0001	1.468	1.310	1.646
Tumour number	Multiple	<0.0001	1.281	1.148	1.430
Grade (WHO 2004)	High	<0.0001	1.352	1.174	1.557
Stage (pT)	1	0.0179	1.194	1.031	1.382
Concomitant CIS	Yes	0.0025	1.290	1.094	1.522
SI-MMC	Yes	<0.0001	0.664	0.594	0.742
Centre achieving DM target	Yes	0.0002	0.813	0.729	0.906
Age group (yr)	>70	<0.0001	1.395	1.248	1.561
Progression					
Tumour number	Multiple	0.0428	1.357	1.010	1.823
Grade (WHO 2004)	High	<0.0001	1.921	1.386	2.663
Concomitant CIS	Yes	0.0007	1.870	1.303	2.684
SI-MMC	Yes	0.0039	0.651	0.486	0.871
Centre achieving DM target	Yes	0.0023	0.617	0.452	0.842
Age group (yr)	>70	0.0282	1.407	1.037	1.908

CIS = carcinoma in situ; DM = detrusor muscle; SI-MMC = single instillation of Mitomycin C; WHO = World Health Organization. Large tumour is > or = 3cm and multiple tumours is more than 1.

and 83/697 (11.9%; 95% CI = 9.6 - 14.5), respectively (Fig. 2B).

3.3. Primary endpoints

Hospitals achieving the DM sampling target were associated with a statistically significant 5.4% (absolute) lower recurrence rate at 5 yr when compared with the hospitals not achieving this target (yes = 442/1136 [38.9%], no = 677/1528 [44.3%], 95% CI = 1.6–9.2, p = 0.005; Fig. 3A). This equated to a 12.2% relative reduction in recurrence.

Time to recurrence was significantly shorter in the only centre that did not achieve the SI-MMC target than in the other 11 centres (log-rank p = 0.015; Supplementary Fig. 1). As there are small numbers of patients in this single centre, we describe this endpoint comparing patients who received SI-MMC with those who did not—Figure 3B reveals a 20.4% (absolute) lower recurrence rate at 5 yr in favour of patients receiving SI-MMC (yes = 634/1791 [35.4%], no = 469/840 [55.8%], 95% CI = 16.4–24.5, p < 0.001; Fig. 3B). This equated to a 36.6% relative reduction.

3.4. Secondary endpoints

Figure 4A reveals a significantly lower 5-yr progression rate by an absolute 3% for patients treated in hospitals achieving the DM target compared with the hospitals that do not (yes = 69/1138 [6.1%], no = 136/1528 [8.9%], 95% CI = l.8–4.8, p = 0.005). The relative reduction was 31.5%.

SI-MMC was associated with a significant 6% absolute reduction in 5-yr progression compared with those who did not receive SI-MMC (yes = 103/1794 [5.7%], no = 97/839 [11.6%], 95% CI = 3.4–8.2, p < 0.001; Fig. 4B). The relative reduction was 50.9%.

Table 2 reveals the multivariable Cox regression analysis with the univariate analyses included in Supplementary Tables 1 and 2. After sequential exclusion of variables not reaching statistical significance, the multivariable model includes previously known variables (tumour size, number, grade, stage, age, and concomitant cis), with now the inclusion of "centre meeting the DM target" and "use of SI-MMC" as independent predictors of recurrence and progression (Table 2). Hazard ratios (HRs) are included.

4. Discussion

"*I have been impressed with the urgency of doing. Knowing is not enough; we must apply. Being willing is not enough; we must do*"—Leonardo da Vinci

Scotland's QPI programme, to our knowledge, is the first and only national initiative that has implemented QIs, together with the evaluation of compliance within a framework of robust governance, MDT input, good documentation, standard pathology reporting, and prospective audit-feedback processes, with state-provider accountability. Through the Scot BC Quality OPS clinical project, we have demonstrated, for the first time, that achieving prospectively evaluated benchmark targets for specific NMIBC QIs that influence the initial TURBT is associated with delays to recurrence and progression, augmenting proportional hazard models.

The building blocks for this large clinical project were developed circa 2006/2007 within the Edinburgh Bladder Cancer Surgery's Effectiveness & Efficiency Programme (EBCS-EEP), where prospectively collected real-world data helped develop surrogates for quality control [22] and benchmarking [23] amongst others. The SBC-QPI provided opportunity to introduce and validate these evidence-based benchmarks through a national programme [16]. Whilst a multicentre national pre-QPI cohort was not designed for comparison, a published analysis from a unicentre EBCS-EEP work package of 302 new NMIBC patients undergoing white light TURBT between 2007 and 2008, that is, before QPI, is available [25,26], where the proforma (Supplementary material) was completed and all patients presented to MDT. SI-MMC was used in almost all patients, and 62% of the patients had DM sampled at initial TURBT. The 3-yr recurrence and progression rates of 55.3% and 13.3%, respectively [26], appear significantly higher than in the current QPI cohort.

Challenges in NMIBC include variability in initial interventions [8], and the QPI programme, with in-built audit feedback within a robust governance framework, is designed to reduce variability and consequently improve outcomes. Processes that incorporate "audit and feedback" can putatively improve outcomes within healthcare systems [27], and perhaps "scrutiny" within large public healthcare systems, such as the NHS, favours better outcomes when performance targets are also applied [28]. Our targets were developed considering the previous EBCS-EEP work:

1. The centre's DM target had to be higher than the 68% in our initial study [22], which revealed differences in early recurrence between patients with DM sampled and not. With a retrospective study around the time of our QPI development

showing a 79% DM sampling rate in their centre and no difference in early recurrence weather DM was sampled or not [29], we took 80% as our target.
2. For the SI-MMC target we considered the following:
   (a) The 69% NMIBC prevalence in our previous publication [25]
   (b) The accuracy of predicting NMIBC from cystoscopic appearance alone [30]
   (c) Contraindications for SI-MMC (bleeding or perforation) [21].

A conservative target of 60% was chosen. Targets, by design, were to be reviewed at the formal review upon completing the first 3-yr cycle.

Developing and implementing achievable QIs is complex [31], having to take into account multiple facets (including behavioural) in addressing knowledge-practice gaps [32,33], with multilayered interventions required to improve compliance [27,34]. The Donabedian [11] principles—*structure, process*, and *outcome*—are embedded in our 12 QPIs. Despite the absence of clinical outcomes, to our knowledge, from any other BC QI programme, support for QI adoption into clinical practice is abundant [12,13,35–37]. A systematic approach to quality of cancer care, including measuring performance against benchmarks, is paramount to ensuring the best possible care [38,39]. Our programme has a robust regional and national governance framework assuring quality of cancer services with published details [16]. The Regional Cancer Advisory Group (RCAG) reviews an annual regional comparative report and produces action plans for NHS health boards to address the highlighted areas of variance in QPI compliance. If progress with action plans remains unacceptable, the RCAG will escalate to Board Chief Executives and HIS when necessary [16].

Recurrence in NMIBC as the primary endpoint is recommended by the International Bladder Cancer Group (IBCG) [40]. Attention to detail [41] with good documentation using a proforma/diagram [20], sampling of DM [22,23], as well as SI-MMC [24] can reduce recurrence. In the "centre achieving DM target", we introduce a novel entity wherein the quality of a centre's performance appears to influence recurrence and progression—this is possibly consequent to, and becomes a surrogate of, the combined (1) attention to detail, being practiced [41]; (2) emphasis being placed on accurate clearance/staging; (3) good governance with regular audit and feedback; and (4) overall credence given to NMIBC within the centre. Perhaps this could be considered as a benchmark for selection of centres to participate in clinical trials. Our Scottish dataset [18] reveals an exceptionally high use of the single post-TURBT chemotherapy instillation compared with other European, Australian, and North American data [5]. We report, possibly for the first time, the positive association between SI-MMC and reduction in progression. Whilst further confirmatory analyses are required, we postulate that this observation is likely secondary to adopting the more contemporary IBCG definition of progression [40]. Our large sample size with standardised quality and higher event rate, consequent to this definition, is likely to have facilitated this observation. Additionally, if SI-MMC reduces recurrence rates even beyond 3 yr [24], and "prior recurrence rate" is an established predictor of progression [42], then by extension, reduction in prior recurrence should reduce the rates of progression.

Another observation challenging clinical dogma is that tumour stage no longer appeared to predict progression in the multivariable regression model despite a univariate association (HR = 2.3, 95% CI = 1.7–3.1, $p < 0.001$). The a priori reasons are that the novel inclusion of "achieving DM target" and SI-MMC appear stronger predictors of progression when the current IBCG definition is used, particularly when historical cohorts in risk calculators not only use muscle-invasive bladder cancer as the endpoint, but also did not emphasise TURBT quality [42].

At QPI inception, the protocol defined "all NMIBC patients" as denominators for calculating percentages of DM sampling and SI-MMC based on our work [22,23] and EAU guidelines of 2013 [20]—the current outcome analyses must reflect this policy. More recent guidelines and evidence [24] have informed our first formal review in 2018, with consequent modifications to the QPIs, including changing the DM sampling and SI-MMC denominators to high-grade NMIBC and low-grade Ta, respectively. Targets have been increased accordingly, and outcome analyses from the second cycle (patients diagnosed between April 2017 and March 2020) through Scot BC Quality OPS [15], including comparison between the cohorts, are underway. The maturity of this process has allowed many lessons to be learnt over 9 yr [18], and with granular data from over 12 000 patients, we hope to better understand real-world treated natural history, including prognostic prediction, and validate observed associations between SI-MMC and stage on progression, amongst others. The current analyses focused on the impact of QPIs influencing the initial TURBT and further reports on other QPIs, including the value of re-TURBT, and our "Scottish NMIBC risk calculator" will be part of separate reports.

4.1. Limitations

We lacked a planned national multicentre pre-QPI cohort—the study was designed to perform internal comparisons, and emphasise the clinical utility of achieving benchmarks and consequently provide vital evidence to support compliance and inform 3-yearly formal reviews. Furthermore, being prospectively audited, the Hawthorne effect would likely improve outcomes over any historical cohort. As the EBCS-EEP pre-QPI cohort mentioned previously is being prepared for publication, including a detailed comparative analysis in this manuscript is inappropriate and will remove agreed anonymity of centres [21]. Treatment beyond the initial TURBT relied on MDT-guided clinical management—we accept this as representing pragmatic real-world practice, encouraged by the high utilisation of MDT meetings in Scotland [18], and are confident that standard evidence-based adjuvant treatments were being adopted [18]. A central pathologist was not utilised; however, in our opinion, regional uropathologists reporting all biopsies, use of the Royal College of Pathologists' checklist [17], and multidisciplinary overview facilitated uniform standards.

5. Conclusions

Within Scotland's national QPI programme for BC, achievement of benchmarks for sampling of DM and utilisation of a single post-TURBT instillation of Mitomycin C in the real world were independently associated with delays to recurrence and progression in patients presenting with NMIBC. We would encourage wider adoption of these principles into clinical practice, prognostic evaluation and clinical trial design.

Author contributions: Paramananthan Mariappan had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Acquisition of data: Mariappan, Johnston, Trail, Hamid, Hollins, Dreyer, Ramsey, Padovani, Garau, Enriquez, Boden, Maresca, Simpson, Hasan, Sharpe, Thomas, Chaudhry, Khan, Bhatt, Ahmad, Nandwani, Dimitropoulos, Hendry.
Analysis and interpretation of data: Mariappan, Graham.
Drafting of the manuscript: Mariappan, Graham.
Critical revision of the manuscript for important intellectual content: Mariappan, Graham, Hendry, Ahmad, Makaroff, Shaw.
Statistical analysis: Graham.
Obtaining funding: Mariappan.
Administrative, technical, or material support: Mariappan, Hendry, Ahmad, Hollins, Ramsey, Simpson, Thomas, Khan, Nandwani, Dimitropoulos, Chaudhry, Graham.
Supervision: Mariappan, Hendry, Ahmad, Hollins, Ramsey, Simpson, Thomas, Khan, Nandwani, Dimitropoulos, Chaudhry, Graham.
Other: None.

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Ethics statement: This is an audit of clinical practice.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.euo.2024.01.012.

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