

## **Reducing delays in the diagnosis and treatment of muscle-invasive bladder cancer using simulation modelling**

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## **Abstract**

### *Objective*

To develop a simulation model to identify key bottlenecks in the bladder cancer pathway at Royal Cornwall Hospital, and predict the impact of potential changes to reduce these delays.

### *Materials and methods*

The diagnosis and treatment of muscle-invasive bladder cancer can suffer numerous delays which can significantly affect patient outcomes. We developed a Discrete Event computer simulation model of the flow of patients through the bladder cancer pathway at the hospital, using anonymised patient records from 2014 and 2015. The changes tested in the model were for patients suspected to have muscle-invasive disease on flexible cystoscopy. Those patients were “fast-tracked” to receive their Transurethral Resection of Bladder Tumour (TURBT) treatment using operating slots kept free for these patients. A staging CT scan was booked in the haematuria clinic. Pathology requests were marked as 48 hour turn around. The nurse specialist would then speak to the patient whilst they are on the ward following their TURBT to give information about their ongoing treatment and provide support.

### *Results*

The model predicted that if the changes were implemented, delays in the system could be reduced by around five weeks. The changes were implemented, and analysis of three months of the data post-implementation shows that the average time in the system has reduced by five weeks. The environment created by the changes in the pathway improved referral to treatment times in both muscle invasive and non-muscle invasive groups.

### *Conclusion*

The simulation model proved an invaluable tool for facilitating the implementation of changes. Simple changes to the pathway led to significant reductions in delays for bladder cancer patients at Royal Cornwall Hospital.

**Keywords :** Simulation, Operational Research, Bladder Cancer

A Level of Evidence is not applicable for this study.

## **Introduction**

Bladder cancer is the seventh most common cancer in the UK with about 10,000 new cases each year <sup>1</sup>. 20-25% of these cancers involve the muscle wall of the bladder at diagnosis <sup>1</sup>, which confers a worse prognosis. In this group of patients, despite treatment, five year survival is only around 50% <sup>2</sup>. The standard definitive treatment of non-metastatic muscle invasive bladder cancer is radical cystectomy with the use of neoadjuvant cisplatin-based combination chemotherapy in appropriate cases. In patients who are unfit for or unwilling to undergo surgery, radiotherapy is a viable alternative option. Delays to definitive treatment are associated with worse outcomes in this aggressive cancer <sup>3-8</sup>.

In bladder cancer the “stop the clock” treatment in the 31 and 62 day pathways has been the TURBT. In muscle invasive disease the TURBT can be seen as merely a biopsy and not the definitive treatment. This has meant that, as in the case of our institution and region, the cancer pathway targets can be met while there is a pronounced delay to definitive treatment in the muscle invasive group<sup>9</sup>.

The diagnostic pathway for patients with muscle invasive bladder cancer (MIBC) is complex and involves multiple investigations, and the potential significant delays in this pathway have been demonstrated <sup>9</sup>. Simulation modelling methods allow us to identify bottlenecks in real world systems and explore the potential impact of changes to the system without the cost and safety risks associated with trialling real-world changes without evidence <sup>10</sup>. Such methods are increasingly being used to improve the efficiency of patient pathways to generate better patient outcomes, and have led to significant increases in stroke patients receiving life-changing treatment <sup>11</sup>, improvements to the organisation of networks for neonatal care <sup>12</sup> and a better understanding of the demand for urgent and emergency care <sup>13</sup>.

In this paper we describe the development and implementation of a Discrete Event Simulation model of the bladder cancer pathway at Royal Cornwall Hospital (RCHT), Treliske in the UK. We also present results of an analysis of three months of data collected after real-world changes were made, and discuss the impact these changes have had for the system and for patients.

## **Materials and Methods**

We developed an in-silico Discrete Event Simulation <sup>14</sup> model of the bladder cancer pathway at RCHT Treliske using Simul8 Professional software (SIMUL8; SIMUL8 Corporation, Boston, MA; [www.Simul8.com](http://www.Simul8.com)). This type of simulation is useful for modelling patient pathways and changes to these pathways because it allows for a system’s discrete, sequential events and their associated queues to be captured.

### *Model Structure*

In our model, patients are referred into the system and first wait to receive a renal tract ultrasound and flexible cystoscopy. Once a tumour has been confirmed they are referred for a Transurethral Resection of Bladder Tumour (TURBT) to remove or reduce any tumours identified. The histology from the TURBT allows the clinician to identify whether the patient's bladder cancer is muscle-invasive. Once a diagnosis of muscle-invasion is made, the patient's case is referred for discussion at the local and specialist Multi-Disciplinary Team meetings, and a nurse specialist and / or urologist contacts the patient to discuss the diagnosis and their treatment options. Once both of these things have happened, the case is formally referred to Derriford Hospital in Plymouth for consideration of cystectomy and to the local oncologist to discuss neoadjuvant chemotherapy. Figure 1 shows an overview of the processes captured by the model.

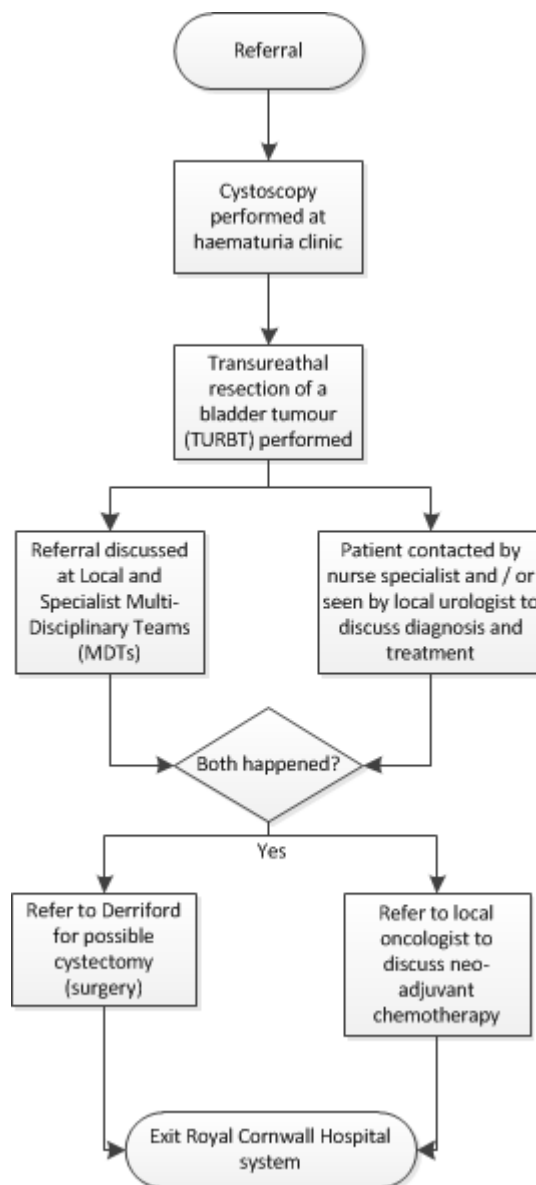


Figure 1. Overview of the processes captured by the simulation model.

Some intermediate steps in the real-world process were not explicitly included in the model due to lack of data, but are still represented in terms of the delays between the activities included in the simulation.

### *Parameterisation of the Model*

We were provided with two years of pseudo-anonymised patient data for bladder cancer patients referred to RCHT Treliske, comprising 408 records over 2014 and 2015. The average time between referrals in the 2014 and 2015 data was 3.6 days (standard deviation of 4.9 days). We used an exponential distribution with mean 3.6 days to represent the time between referrals in our model. The waits in the system were represented in the model by using distributions that best fit the pattern of the data, and were determined using Stat-Fit software (Stat::Fit; Geer Mountain Software Corporation; <http://www.geerms.com/>) as follows :

- The time between referral and cystoscopy was fitted to a Log Normal distribution with mean of 15.5 days and standard deviation of 32.5 days.
- The time between cystoscopy and TURBT was fitted to a Log Normal distribution with mean of 43.2 days and standard deviation of 43.9 days.
- The time between TURBT and discussion at the MDT was fitted to a Pearson Type VI Distribution with  $\alpha_1$  of 30.7,  $\alpha_2$  of 4.54, and  $\beta$  of 2.31.
- The time between TURBT and the specialist nurse / urologist contacting the patient was fitted to a Pearson Type V Distribution with  $\alpha$  of 4 and  $\beta$  of 75.5.
- Once both the case has been discussed at the MDT and the patient has been contacted, the wait for a referral to Derriford Hospital was fitted to a Log Normal distribution with mean of 17.7 days and standard deviation of 19.9 days, and the wait for a referral to the oncologist was fitted to a Log Normal distribution with mean of 12.3 days and standard deviation of 20.8 days

In each case, the simulation was run for a simulated period of 10 years. Each scenario was tested by running the simulation five times and taking average results over these simulation runs. This number was calculated by the Simul8 software as being sufficient to ensure 95% confidence intervals on the output mean.

### *Scenarios Tested*

The simulation was first tested with the 'base case' scenario – a representation of what is happening now in the real world system. By running this scenario in front of oncologists and urologists at the hospital, we were able to visually demonstrate in the simulation that there were two key bottlenecks in the system – patients waiting for their TURBT, and patients waiting for a nurse specialist or oncologist to speak to them to discuss their diagnosis and treatment options.

Consequently, the group discussed how they might reduce these bottlenecks and suggested practical changes that they could make:

- fast-tracking patients with suspected muscle-invasion at their flexible cystoscopy to receive their TURBT as quickly as they receive a cystoscopy after referral
- booking staging CT urogram plus thorax in suspected muscle invasive disease straight from haematuria clinic

- fast tracking TURBT pathology specimens (48 hour turn around for suspected MIBC)
- asking the nurse specialist to speak to the patient about their diagnosis and treatment options whilst they are on the ward for their TURBT

Therefore, we tested the impact of these changes as our second scenario by using the same distribution for both the wait for cystoscopy and the wait for TURBT, and by reducing the wait for contact by specialist nurse / urologist to zero.

For each scenario run in the model, we recorded the average time spent in the system (from initial referral to referral to Derriford Hospital).

## **Results**

### *Predictions from the Simulation Model*

The model predicts that, on average, the time from referral by GP to referral to Derriford was 112 days in the base case scenario (95% Confidence Intervals (CI), 109 days to 114 days).

If the wait for a TURBT was reduced to the same as the wait for cystoscopy after referral, and there was no wait to speak to a nurse specialist after the TURBT, the model predicts that, on average, the time from referral to referral to Derriford would be 75 days (95% CI, 71 days to 78 days). This represents a predicted reduction of 37 days (over five weeks) for the average patient.

### *Real World Changes from Model Predictions*

Given the model predicted a significant reduction to delays in the system if the proposed changes were implemented, the consultants at RCHT Treliske were keen to implement the changes as quickly as possible. Within 24 hours from the presentation of the results in November 2016, a new protocol was written by the Cancer Lead for Urology instructing clinicians to identify any patients suspected to have a muscle-invasive tumour on flexible cystoscopy and who would be a candidate for cystectomy to have a fast track pre-assessment and TURBT within two weeks. All haematuria clinic flexible cystoscopies at the Royal Cornwall Hospital are performed by a consultant urologist or registrar. The protocol also dictates that the nurse specialist should see the patient on the ward during their admission.

The trust collected three months of data following the change, consisting of 32 patient records, including seven who were fast-tracked. We analysed this data to assess whether there had been a reduction in the time from initial referral to TURBT and from initial referral to date contacted by the nurse specialist, for both fast-track patients and across all bladder cancer patients.

### *Results from the Post-Change Data Analysis*

The mean time from initial referral to TURBT has reduced from 57 days (max = 433 days, min = 8 days) before the changes to 48 days (max = 96 days, min = 21 days) across all bladder cancer patients, and 32 days (max = 42 days, min = 21 days) for patients who have been fast-tracked. This represents an average reduction of 9 days across all bladder cancer patients, and 25 days (three and a half weeks) for fast-tracked patients.

The mean time from initial referral to date contacted by the nurse specialist has reduced from 78 days (max = 408 days, min = 19 days) before the changes to 67 days (max = 142 days, min = 14 days) across all bladder cancer patients, and 43 days (max = 70 days, min = 14 days) for patients who have been fast-tracked. This represents an average reduction of 11 days across all bladder cancer patients, and 35 days (five weeks) for fast-tracked patients.

The number of tertiary referrals generated in the post-change cohort was very small (1 in the fast-track group and 1 in the non-fast-track group) so it was not possible to comment in a meaningful way on the time to either tertiary referral or definitive treatment. We assume that by making relatively large improvements in the earlier steps of the pathway the time to definitive treatment will improve accordingly.

## **Discussion**

Our simulation model identified two key bottlenecks in the bladder cancer pathway at RCHT Treliske - the wait for a patient to receive a TURBT and the wait for a patient to be contacted by the nurse specialist to discuss their diagnosis and treatment options. With the current strain on the NHS waiting lists for surgery are increasing under pressure. The process by which all TURBTs are listed with the same clinical priority is potentially disadvantaging those with more aggressive disease. Facilitating an early meeting between the CNS and patient allows for a relationship to be forged and clinical information given. It makes it easier to have subsequent communication by telephone, allowing the patients to be quickly placed into the correct clinic setting while avoiding patient confusion and unnecessary outpatient appointments.

By using the simulation model as both a visualisation tool to clearly show the nature and extent of these bottlenecks and facilitate discussion, and as a predictive tool to allow "what if" scenarios identified by the collaborators to be tested, a hugely convincing case was made to implement specific, simple, immediate and cost-neutral changes to the pathway. Assessment of the data three months following the implementation indicates that, as predicted by the model, these changes have had a significant impact for bladder cancer patients, reducing the time from initial referral to discussion of their diagnosis and treatment options by five weeks for patients who have been fast-tracked, and over one and half weeks across all bladder cancer patients.

Multiple studies have shown that in an aggressive cancer like MIBC any delay to definitive treatment is likely to affect outcome<sup>3-8</sup>. Therefore, these findings are significant and imply that patient's outcomes are highly likely to have been improved by these changes, potentially significantly. One concern was that, by concentrating on the suspected muscle invasive cases, the rest of the new bladder cancer patients would be disadvantaged by having their treatment delayed. It is therefore reassuring to observe that there has been a reduction in waiting times across all bladder cancer patients and not just those that have been fast-tracked. It is possible that the project's engagement with a multitude of clinicians involved across the bladder cancer pathway across the trust (including consultants, surgeons and nurse specialists) helped to increase awareness of the delays in the system and instil an increased motivation to improve the efficiency of the system.

The preliminary analysis of post-implementation impact of the changes made is encouraging, although we should be a little cautious here. This is only a three month analysis, and as such only includes 36 patients, of whom 7 were fast-tracked. Further analysis will be necessary after six and / or 12 months to allow more patients to be included and give greater power to the analysis. It will also be important to observe whether the impact of the changes have been sustained, or whether some momentum has been lost over time. Nevertheless, it is very encouraging to see such a direction and extent of travel in outcomes for all bladder cancer patients in the months immediately following the implementation of these changes. There is also a further question as to how good clinicians are at identifying muscle invasive disease at the initial flexible cystoscopy, particularly as a failure to identify a high risk patient may also affect their pathway negatively. Our initial analysis indicates that all seven fast-tracked patients had clinically significant cancers, and two of the seven were identified as being muscle-invasive. However, the numbers are too small to draw any conclusions from this, and a separate study would be warranted to assess effectiveness of identifying muscle-invasive patients at flexible cystoscopy. Nevertheless, we do know that there has been a universal reduction in delays, and so outcomes are likely to have improved regardless.

The majority of patients with muscle-invasive bladder cancer at RCHT Treliske are referred to Derriford Hospital in Plymouth for their definitive treatment, as cystectomy is not currently offered in Cornwall. Therefore, we next intend to explore whether there are delays in the system once patients have been referred to Derriford, and identify whether a similar simulation modelling approach could be used to reduce any bottlenecks in this part of the system, in order to further reduce to the time from referral to treatment for muscle-invasive bladder cancer patients.

## **Conclusions**

Simulation modelling methods offer an effective means of identifying bottlenecks in a system and predicting the impact of various efforts to reduce such bottlenecks. The model in this project was used to facilitate discussion about delays in the system, and the evidence from the model was the primary motivation for effecting rapid and cost-neutral change in the system that has led to significant improvements for patients.

In these times of increasing financial pressures, cost-neutral changes that improve patient outcomes and potentially save on treatment resources by avoiding more complex outcomes will be vital in ensuring sustainable services. We would strongly encourage others to explore simulation methods to assess how their own bladder cancer pathways might be improved, and urge NHS clinicians and decision-makers alike to increase their engagement with operational research more widely.

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