# Interventions for obstructive uropathy in advanced prostate cancer: a population-based study

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**ABSTRACT**

**Objectives:**

Upper tract obstructive uropathy (UTOU) is a complication of advanced prostate cancer (PCa) that may require urinary tract decompression. There are no population-based studies on the incidence, treatment, and outcomes of this complication. We developed and validated a coding framework to identify procedures for UTOU in men with locally advanced and metastatic PCa using administrative hospital data to assess clinical outcomes.

**Patients and Methods:**

Patients newly diagnosed with PCa between April 2014 and March 2019 were identified in the English cancer registry. A coding framework based on procedure (OPCS-4) and diagnostic (ICD-10) codes was developed and validated. Subsequent clinical outcomes were determined using Hospital Episodes Statistics (HES) to determine the utility of the intervention.

**Results:**

A total of 77,010 patients newly diagnosed with locally advanced, and 30,083 patients with metastatic PCa were identified. Of these, 1,951 (1.8%) patients underwent an intervention for UTOU according to our coding framework: 830 (42.5%) had locally advanced disease and 1,121 (57.5%) had metastatic disease. 844 (43.3%) had a percutaneous nephrostomy (PCN), 473 (24.2%) had a PCN with antegrade stent and 634 (32.5%) had a retrograde stent. Mean follow-up time was 43.2 months. The cumulative incidence of the use of these interventions at one, three, and five years was 2.5%, 3.6% and 4.2% in men with metastases compared to 0.5%, 0.9% and 1.4% in men with locally advanced disease.

**Conclusion:**

A new coding framework, developed to identify procedures for UTOU. was applied in the largest study to date of UTOU in men with primary locally advanced and metastatic PCa. Results demonstrated that 2% of men with locally advanced PCa and 4% of men with metastatic PCa require an intervention to resolve UTOU within 5 years of their PCa diagnosis.

## INTRODUCTION

Upper tract obstructive uropathy (UTOU) can be a complication of advanced prostate cancer (PCa) patients, with historical data reporting up to 10% of patients require intervention with a percutaneous nephrostomy (PCN) in their final year of life (1). This is a consequence of ureteric compression or infiltration by loco-regional or metastatic retroperitoneal progression of disease. Ureteric obstruction, often complicated by sepsis and acute kidney injury is commonly responsible for renal impairment (2). When UTOU presents in castrate-resistant PCa it is associated with reduced life expectancy (3).

Patients presenting with acute UTOU can be treated with PCN or ureteric stenting but complications of these interventions may result in a prolonged hospital stay or multiple readmissions, which adversely affect quality of life (4). In one study, 50% of patients treated for UTOU required readmission, spending 41% of their post PCN-life in hospital due to PCN tube-related complications such as stent displacement or blockage. The incidence of this was between 18 to 30% (5).

To develop a better understanding of the true incidence and natural history of this condition we used information available in the National Prostate Cancer Audit (NPCA) to evaluate longitudinal data related to a defined population (6). The NPCA database includes over 200,000 men newly diagnosed with PCa in England between 2014 and 2019 with subsequent follow-up.

We developed and validated a coding framework applied to Hospital Episode Statistics (HES), the administrative hospital database of all patient episodes in the English National Health Service (NHS) to identify interventions to manage UTOU in patients diagnosed with metastatic or locally advanced PCa, linking these to the use of a UTOU intervention. We demonstrate how this coding framework can be used to estimate the incidence of UTOU and describe outcomes from the interventions that were used to manage this complication to help validate the framework.

## METHODOLOGY

### Patient population

We identified 213,333 men diagnosed with PCa between 1st April 2014 to 31st March 2019 using the International Classification of Diseases, 10th edition (ICD-10) codes, in the English national cancer registry data (7). Men were categorised according to their risk score at the time of diagnosis using the method developed by the NPCA (8). This modified D'Amico classification is based on criteria recommended by the UK National Institute for Health and Care Excellence (NICE) (9). Following this classification, patients with extra-pelvic spread of cancer were categorised as metastatic (M1), whilst those with positive pelvic lymph nodes (N+), a tumour stage classified as T-stage ≥3, Gleason score ≥8 or PSA level of >20ug/L were categorised as having locally advanced disease (6).

### Data Sources

We used data items from the English national cancer registry to obtain information about prostate cancer characteristics, age at diagnosis, ethnicity, deprivation, TNM stage, Gleason score and PSA. HES was used to retrieve information about diagnoses, procedures, and length of hospital stay. The Office for National Statistics was used to retrieve information about time of death.

### Study Cohort

We included all patients from our dataset with newly diagnosed locally advanced or metastatic PCa, who underwent an intervention related to their first diagnosis of UTOU or who had a first diagnosis, as defined by procedure and diagnostic codes in HES (Appendix 1). Some patients underwent an OTOU-related intervention before their PCa diagnosis and we excluded all patients who had an intervention more than 60 days before their diagnosis, as these were likely unrelated to their cancer. We excluded interventions for benign diagnoses such as urinary tract stones defined by Office of Population, Censuses and Surveys – Classification of Surgical Operations and Procedures 4th edition (OPCS-4) codes N20-23 and non-obstructive diagnoses such as urinary sepsis defined by N39.0 and A41 (10).

### Coding

Our coding framework used ICD-10 diagnostic codes and OPCS-4 procedure codes within the HES database (11). Relevant literature and expert clinicians (MP, HP, NC, JSAG) were consulted to identify relevant ICD-10 and OPCS-4 codes following the steps detailed below (12, 13) (Appendix 1).

***Step 1 – Forward coding***

'Forward coding', defined as using codes pre-specified according to literature and input from the expert clinicians, identified OPCS-4 procedure codes involving PCN and ureteric stenting, and ICD-10 diagnostic codes relating to obstructive uropathy. The presence of PCN and stenting procedures was used as a guide to find patients who had UTOU.

***Step 2 – Backward coding***

'Backward coding', defined as an exploration of the records of patients previously found by forward searching, identified additional common diagnostic and procedure codes that are likely related to the procedure (14). The final coding list comprised all diagnostic and

procedure codes, identified in the forward and backward coding steps likely to be related to PCN or stent intervention for obstructive uropathy.

**Validation and analysis**

Patients were followed from the date of diagnosis until the end of follow-up on 31st March 2020 or death which ever occurred earlier. Cumulative incidence of intervention for UTOU for locally advanced or metastatic patients was plotted. Death was treated as a censoring event. Data analysis was undertaken using Stata version 15 (StataCorp LLC, College Station, TX, USA).

We validated the coding framework using three methods. We initially assessed the consistency and pairing between relevant diagnostic and procedure codes. We then investigated poor consistency by including lower tract decompression interventions such as urinary bladder catheterisation to account for patients with high pressure chronic retention. Following this we compared the time from PCa diagnosis to UTOU between locally advanced and metastatic PCa. Finally, we compared the frequency of the interventions and the related length of stay with results found in the related scientific literature.

## RESULTS

### Patient identification

213,222 men with newly diagnosed PCa were identified. Of these, 21,260 (10.0%) had insufficient information to be assigned a risk score and were excluded. 77,010 (36.1%) had locally advanced PCa, and 30,083 (14.1%) had metastatic disease (Figure 1).

Of the 107,093 patients with locally advanced and metastatic PCa, 3,975 (3.7%) had interventions related to PCN or stenting, at diagnosis, as defined by our coding framework: 3,161 (79.5%) of these patients had their intervention after or within 60 days before their PCa diagnosis. Of the 3,161 patients, 1,210 (38.3%) patients were excluded due to UTOU caused by urolithiasis (n=462), presence of sepsis without obstruction (n=328), or another diagnosis unrelated to obstruction from PCa as discussed in our validation below (n=420). In total 1,951 patients had an intervention for a diagnosis for UTOU related to their PCa diagnosis. Their mean follow-up was 43 months (45 and 42 months for locally advanced and metastatic patients, respectively).

### Validation of the coding framework

Forward coding identified six diagnostic codes and eight procedure codes. Backward coding added two diagnostic and eight procedure codes. Appendix 1 presents a full list of diagnostic and procedure codes used in the framework.

We investigated the consistency between diagnostic and intervention codes (Table 1). 2,371 patients had an intervention related to their PCa as identified by our coding framework. Of these, 1,951 (82.3%) also had a diagnosis of obstructive uropathy. The remaining 420 (17.7%) patients had an intervention for another diagnostic code unrelated to obstruction from PCa.

10,483 patients had a diagnostic code indicative of obstructive uropathy, of whom 8,532 (81.4%) did not have a PCN or stent intervention. Instead, 6,124 (71.8%) had a procedure code for urethral catheterisation (M47) or suprapubic catheterisation (M38.2, M48.1) or a diagnostic code of urinary retention (R33), representing a cohort of patients with lower tract obstruction, decompressed for high pressure urinary retention. In the remaining 2,408 (28.2%) patients, 2,288 (95.0%) did not have a diagnosis of acute kidney injury, representing patients with a minimal degree of obstructive uropathy that did not warrant intervention. From the remaining 120 of these patients, 98 (81.7%) had metastatic disease and they may have been treated with a palliative approach: it was not possible to confirm this. Of the 10,483 patients who had a diagnosis code of UTUO, 6,124 patients (58.4%) had a lower tract intervention and 1,951 (18.6%) had an upper tract procedure.

The most frequent diagnostic code used was “Other and unspecified Hydronephrosis” (N13.3) (66.8%). The most frequent procedure codes used for PCN were “Drainage of kidney” (M13.2) (36.5%) and “Percutaneous insertion of nephrostomy tube” (M13.6) (28.4%). The most frequent code for PCN and antegrade stent (AGS) was “Percutaneous insertion of ureteric stent into ureter NEC” (M33.5) (16.4%). The most frequent code for retrograde stenting (RGS) was “Endoscopic insertion of tubal prosthesis into ureter NEC” (M29.2) (21.6%). Table 2 shows the consistency between specific diagnostic and procedure codes and a complete frequency list of all codes used.

We then compared the incidence of interventions among men with metastatic and locally advanced PCa. The overall incidence of an intervention for UTOU was greater in the metastatic compared with the locally advanced cohort (3.7% vs 1.1%) as was the cumulative incidence of intervention for UTOU (Figure 2). At five-year follow-up, the incidence of intervention for UTOU was 4.4% and 1.6% in men with metastatic and locally advanced PCa, respectively. Furthermore, at the time of diagnosis there was a substantial peak of incidence of intervention for UTOU in metastatic patients: this was not seen in locally advanced patients.

**Interventions**

Table 3 shows the interventions by patient characteristics. PCN was the most frequently used form of initial intervention in UTOU, with 43.3% of patients receiving a PCN, 24.2% receiving both a PCN and AGS and 32.5% receiving an RGS.

Men receiving PCN+AGS were older than those receiving PCN and RGS (73.2, 72.6 and 71.4 respectively). Charlson co-morbidity index score was ≥1 in 41.9%, 44.4% and 34.5% for PCN, PCN+AGS and RGS, respectively. More patients with metastatic disease had PCN and PCN+AGS than those with locally advanced disease (44.4% vs 41.7%, and 26.9% vs 20.7%, respectively), while for RGS the opposite was true (28.7% vs 37.6%).

A smaller proportion of men with locally advanced disease had an intervention earlier compared to men with metastatic disease. Cumulative intervention at one-, three- and five-years was 2.5%, 3.6% and 4.2% in men with metastatic disease compared to 0.5%, 0.9% and 1.4% in men with locally advanced disease. PCN was associated with a mean length of hospital stay of 9.6 (SD: +/-0.5) days, PCN+AGS was 13.5 (SD: +/-0.6) days and RGS was 4.2 (SD: +/-0.3) days.

## DISCUSSION

This is the largest study to date describing the interventions used to manage UTOU in patients with newly presenting locally advanced and metastatic PCa. We developed a novel coding framework to identify such interventions. Further, we describe clinical outcomes related to these interventions to validate the framework. By using a national dataset containing data from over 200,000 patients we were able to identify almost 2,000 men who required urinary tract decompression due to UTOU at or within five years of their initial diagnosis.

We estimated the incidence of these interventions in the first five years after the date of the prostate cancer diagnosis and found it to be more than twice as high in patients diagnosed with metastatic PCa (4%) than in patients diagnosed with locally advanced disease (2%). Historical data has suggested a greater incidence of UTOU ranging between 3% to 16% (15). Our contemporary database includes men who have been diagnosed since 2014 and have been treated with improved therapeutic strategies for advanced prostate cancer such as androgen receptor targeted agents and targeted radiotherapy. Our incidence rates are similar to the 1 to 2% rate of ureteric stenting or nephrostomy use found in the STAMPEDE trial investigating treatment approaches for patients with advanced and metastatic disease (16).

Our validation suggests that this coding framework is sufficiently robust for identification of PCa patients with UTOU and for categorisation of their treatment interventions. One in five patients with a diagnostic code for obstructive uropathy had an upper tract intervention. It was possible to discriminate these patients to those with bladder outlet issues as these patients were treated with lower tract interventions such as catheterisation or they were managed conservatively. Using this methodology, it has been possible to show that the cumulative incidence of intervention at one, three and five years is greater in men with primary metastatic disease compared to those presenting with primary locally advanced PCa.

Current literature relating to UTOU is limited and based mostly on small, retrospective, single-centre studies. The largest systematic review assessing the use of interventions for obstructive uropathy following a PCa diagnosis found 184 patients across seven studies treated with PCN. The mean age of 70 was similar to our cohort (3). Most of the studies only report the use of PCN, irrespective of stent use, for the management of UTOU, largely due to the inferior success rate of RGS (17). In our study, PCN alone was used in most men, with RGS the next most common and PCN followed by AGS used in approximately a quarter of the cases. To our knowledge, there are no other studies that describe all three treatment modalities.

Our study reports a mean length of hospital stay of 10, 14 and 4 days for PCN, PCN followed by AGS and RGS. This is similar to another study that reports length of stay for PCN of 14 days (4). Length of stay may represent the general health of the patient cohort and RGS may have been used in the fitter patients, who required a shorter hospital stay. This notion is further highlighted when comparing the Charlson co-morbidity index scores, with fewer patients undergoing a RGS having a score of ≥1 compared to those undergoing a PCN or PCN and AGS. Men with metastatic disease who underwent an intervention stayed in hospital longer than men with locally advanced disease.

A possible limitation in the development of a coding framework using routinely collected hospital data is that it might be affected by misclassification due to incorrect clinical coding. We have tried to minimise this as much as possible by using a system of forward and backward coding to capture idiosyncratic coding practices that are difficult to predict but are relevant to our framework.

Over 1% of patients with metastatic PCa required an intervention for UTOU at the time of initial diagnosis. This represents an important cohort of men who require intervention at the onset of treatment. Currently there is a lack of consensus about whether interventions are indicated in UTOU secondary to malignancy due to poor quality of life associated with interventions. However, current literature and clinical practice favours the use of decompression interventions (13, 18).

By developing a coding framework to identify PCa patients with UTOU we can now accurately define a population of patients with this condition whose treatment and short- and long-term outcomes can be further studied, enabling urologists, oncologists, and interventional radiologists to better understand the implications of obstructive uropathy. This will help to overcome the current

**Conclusions**

A significant number of men with newly diagnosed with locally advanced or metastatic PCa require intervention for UTOU within five years. This may either be at the time of diagnosis or at some point during their follow-up. We have developed a coding framework that can be used to identify these patients in administrative hospital data, thereby, enabling further research into UTOU and its management including outcomes following intervention and its relationship with prognosis.

## DECLARATIONS

### Ethical Approval

All patient data used is fully anonymised and is therefore exempt from the UK National Research Ethics Committee (NREC) approval.

### Competing Interests

A.S is an employee of Flatiron Health UK and has stock ownership in Roche.
J.N and J.VDM report a contract with the Healthcare Quality Improvement Partnership (HQIP) for the provision of the National Prostate Cancer Audit.
All other authors declare no competing interests.


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### Author Contribution

Study design: A.N, M.M, M.P, J.VDM, J.S.A.G
Data analysis: A.N, M.M, M.P
Article draft: A.N, M.M, M.P, J.VDM, N.C, J.S.A.G
Critical revision: All authors
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