BMJ Open

# Complications after surgery for benign prostatic enlargement: a population-based cohort study in Ontario, Canada

Rano Matta ,[1,2] Erind Dvorani,[3] Christopher Wallis,[1,2] Amanda Hird,[1,2] Joseph LaBossiere,[4] Girish Kulkarni,[1,5] Ronald Kodama,[1,6] Lesley Carr,[1,6] Sidney B Radomski,[1,5] Refik Saskin,[2,3] Sender Herschorn,[1,6] Robert K Nam[1,2,3,6]

**To cite:** Matta R, Dvorani E, Wallis C, *et al*. Complications after surgery for benign prostatic enlargement: a population-based cohort study in Ontario, Canada. *BMJ Open* 2019;**9**:e032170. doi:10.1136/bmjopen-2019-032170

► Prepublication history and additional material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2019-032170).

Received 11 June 2019
Revised 09 November 2019
Accepted 04 December 2019



[1]Surgery, Division of Urology, University of Toronto, Toronto, Ontario, Canada
[2]Institute of Health Policy Management and Evaluation, University of Toronto, Toronto, Ontario, Canada
[3]Institute for Clinical Evaluative Sciences, Toronto, Ontario, Canada
[4]Division of Urology, University of Alberta, Edmonton, Alberta, Canada
[5]Division of Urology, University Health Network, Toronto, Ontario, Canada
[6]Division of Urology, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada

**Correspondence to**
Dr Rano Matta;
rano.matta@mail.utoronto.ca

## ABSTRACT

**Objectives** To examine the complication rates after benign prostatic enlargement (BPE) surgery and the effects of age, comorbidity and preoperative medical therapy.

**Design** A retrospective, population-based cohort study using linked administrative data.

**Setting** Ontario, Canada.

**Participants** 52 162 men≥66 years undergoing first BPE surgery between 1 January 2003 to 31 December 2014.

**Intervention** Medical therapy preoperatively and surgery for BPE.

**Primary and secondary outcome measures** The primary outcome was overall 30-day postoperative complication rates. Secondary outcomes included BPE-specific event rates (bleeding, infection, obstruction, trauma) and non-BPE specific event rates (cardiovascular, pulmonary, thromboembolic and renal). Multivariable analysis examined the association between preoperative medical therapy and postoperative complication rates.

**Results** The 30-day overall complication rate after BPE surgery was 2828 events/10 000 procedures and increased annually over the study period. Receipt of preoperative α-blocker monotherapy (relative rate (RR) 1.05; 95% CI 1.00 to 1.09; p=0.033) and antithrombotic medications (RR 1.27; 95% CI 1.22 to 1.31; p<0.0001) was associated with increased complication rates. Among the ≥80-year-old group, the rate of complications increased by 39% from 2003 to 2014 (RR 1.39; 95% CI 1.21 to 1.61; p<0.0001). The mean duration of medical and conservative management increased by a mean of 2.1 years between 2007 and 2014 (p<0.0001 for trend).

**Conclusions** Thirty-day complication rates after BPE surgery have increased annually between 2003 and 2014. Preoperative medical therapy with alpha blockers or antithrombotics was independently associated with higher rates of complications. Over this time, the duration of conservative therapy also increased.

## Strengths and limitations of this study

- A major strength of this study includes population-level data with the ability to follow patients after their index procedure irrespective of where complications are managed within the province.
- There is potential for misclassification using administrative data to identify outcomes.
- Although we adjust for geography and income, the regional variations within Ontario might limit the generalisability of our results to other jurisdictions.
- We do not have data on prostate size, urinary symptoms, extent of resection during the index procedure and the specific technology used for resection beyond electrical, laser or open surgery.
- We were unable to evaluate postoperative functional outcomes besides urinary obstruction.

## INTRODUCTION

Medical therapy as first-line treatment for patients with lower urinary tract symptoms (LUTS) from benign prostatic enlargement (BPE) has enabled men to delay or avoid surgery.[1 2] Watchful waiting (conservative management) is also a reasonable management option.[3] Some men with BPE will develop progression of their disease as the severity of LUTS,[4] the size of the prostate[5] and the cumulative incidence of urinary retention[6] increase with time and age. When medical or conservative therapy for patients eventually becomes ineffective, surgery is offered. The recommended surgical treatments for patients with urinary symptoms secondary to BPE are either endoscopic resection, vapourisation or enucleation or simple prostatectomy.[7] By this point, patients are often older and more frail,[8 9] which may increase the rate of perioperative complications.[10]

Studies evaluating surgical therapy for BPE have reported rates of postoperative morbidity greater than 10%.[10–12] However, there are few clinical studies evaluating the effects of medical therapy on perioperative outcomes, and these have been highly controlled with small sample sizes.[8 9 13] To our knowledge, there are no large, population-based studies examining the effect of medical management on surgical complications. Thus, we evaluated the trends in 30-day complications and re-operation following BPE surgery, and the factors

Table 1 Baseline characteristics of men undergoing benign prostatic enlargement (BPE) surgery from 2003 to 2014 in Ontario, Canada

| | Total cohort | |
|---|---|---|
| Variable | n=52 162 | |
| Mean age (years; SD) | 75.76 | ±6.41 |
| Intervention type (N, %) | | |
| TURP | 45 463 | 87.2% |
| Laser | 5925 | 11.4% |
| Open | 774 | 1.5% |
| Preoperative urinary obstruction* (N, %) | 25 779 | 49.4% |
| 5ARI medication (only) in year prior to surgery (N, %) | 2378 | 4.6% |
| α-blocker medication (only) in year prior to surgery (N, %) | 20 600 | 39.5% |
| 5ARI and α-blocker in year prior to surgery (N, %) | 14 450 | 27.7% |
| No BPE medications prior to surgery (N, %) | 14 734 | 28.2% |
| Antithrombotic in year prior to surgery (N, %) | 12 837 | 24.6% |
| Charlson Comorbidity Index (N, %) | | |
| 0 | 40 694 | 78.0% |
| 1 | 3961 | 7.6% |
| 2+ | 7507 | 14.4% |
| Income quintile (N, %) | | |
| Missing | 167 | 0.3% |
| 1 | 9553 | 18.3% |
| 2 | 10 728 | 20.6% |
| 3 | 10 263 | 19.7% |
| 4 | 10 689 | 20.5% |
| 5 | 10 762 | 20.6% |
| Rural residence (N, %) | 7264 | 13.9% |

*Preoperative urinary obstruction events include: urinary retention, bladder neck obstruction or obstructive uropathy.
ARI, α-reductase inhibitor; TURP, Transurethral resection of the prostate.

associated with these outcomes, in a population-based sample of patients≥66 years old in Ontario, Canada.

## METHODS

### Data sources and setting

A population-based, retrospective cohort study of all men≥66 years old who underwent BPE surgery in Ontario, Canada was conducted with linked health administrative databases. In Ontario, all necessary healthcare services, physician services and prescription medication information are recorded and held at the Institute for Clinical Evaluative Sciences (ICES; http://www.ices.on.ca). ICES is an independent, non-profit research institute whose legal status under Ontario's health information privacy law allows it to collect and analyse healthcare and demographic data, without consent, for health system evaluation and improvement. Each of the data sources used has been validated previously (online supplementary data sources). All analyses were performed between June 2018 and January 2019 and were consistent with Strengthening the Reporting of Observational Studies in Epidemiology reporting guidelines.

### Study subjects

All individuals≥66 years old who had BPE surgery from 1 January 2003 to 31 December 2014 were eligible (supplementary eTable 1 for cohort selection). We included only the first procedure (index procedure) for each patient, which included transurethral resection of the prostate (TURP) using electrocautery, transurethral laser surgery (including enucleation or vapourisation using any laser modality) or simple prostatectomy. These were captured using intervention codes during their hospitalisation (see supplementary eTable 2). Individuals were followed from the date of index procedure to 30 days post procedure.

To determine the duration of time between initiating BPE medication and surgical therapy, we restricted the cohort to men≥80 years old to ensure a 15-year look-back period to age 65, since the cost of prescription medication in Ontario is covered for all patients starting at this age and therefore dispensing records are available.

### Exposure

The primary independent variable was receiving a prescription for medical therapy for BPE. We captured this using prescription claims for 5α-reductase inhibitors (5ARI) and α-blockers indicated for BPE, in the year prior to surgery (see supplementary eTable 3 for list of medications).

### Covariates

We collected information on important covariates that may confound the association between medication use and postoperative outcomes including age at surgery, year of surgery, Charlson Comorbidity Index-based hospitalisations in the 5 years preceding the index procedure, prescription claims for antithrombotics (see supplementary eTable 3 for list of medications), geographical region of residence (Local Health Integration Network) and income quintile.

We also identified patients who had a urinary obstruction event (urinary catheterisation, bladder neck obstruction or obstructive uropathy) in the 2 years prior to their index surgery (see supplementary eTable 4 for codes).

In our subcohort of men restricted to >80 years, we identified their first BPE medication prescription and determined the total time from initial prescription to the index BPE surgery.

### Outcomes

The primary outcome was 30-day overall complications. Secondary outcomes were the specific categories of BPE

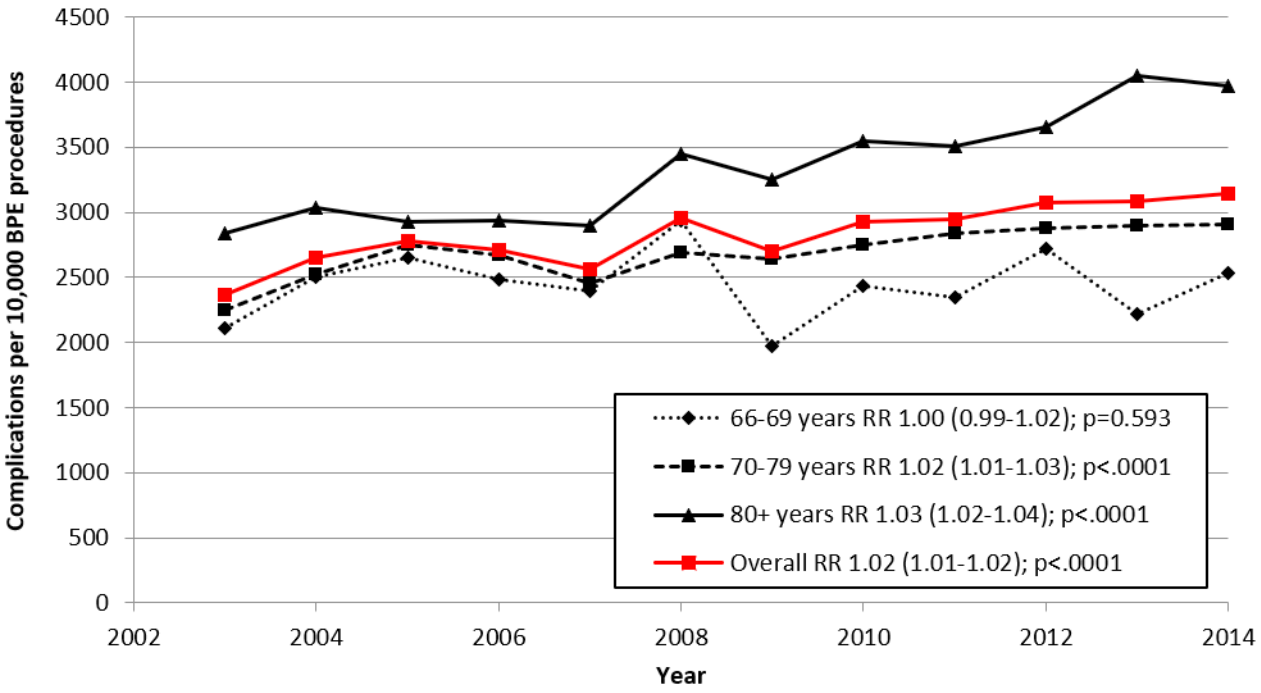


**Figure 1** Thirty-day complication rates by age group and year of surgery following benign prostatic enlargement (BPE) surgery. RR, relativerate.

(obstruction, bleeding, trauma, infection) and non-BPE (cardiovascular, pulmonary, thromboembolic and renal) perioperative complications. These outcomes were captured using diagnostic and procedure codes, as well as billing records for physician services (See supplementary eTable 4 for complete list of complications and codes).

To operationalise complications, if a patient had any code recorded within an individual complication category (eg, bleeding, infection, cardiovascular, etc) during the follow-up period, he was considered to have had a unique complication event. Repeated events within the same complication category were not counted separately, regardless of timing within the follow-up period, to avoid overestimating the rate of complications in a single category. The complication rate was calculated as the cumulative number of complication events per procedure during the follow-up period.

Other secondary outcomes included 30-day and 1-year reoperation. Reoperation was defined as receiving any BPE surgery during the follow-up after the index surgery. Since reoperation was a binary measure, the effect is reported as a relative risk, rather than rate.

### Statistical analysis

To test the association between preoperative covariates and our primary outcome of 30-day overall complications, unadjusted and adjusted relative rates (RRs) were computed using Poisson regression. To determine if there was a trend in complication rates over time, we included the year of surgery as an ordinal variable in the Poisson model. Since these models evaluated uniformly defined outcomes, they were not offset.

We conducted exploratory analysis evaluating the association of preoperative covariates and individual BPE and non-BPE specific outcomes, as well as other secondary outcomes using log-binomial multivariate regression. Rather than formal hypothesis testing, the exploratory analyses were hypothesis generating and thus, a p value of $<0.05$ was considered significant, without adjustment for multiple comparisons. We also stratified our analysis by age group to evaluate differences in the effects of covariates between age groups.

To evaluate the trend in duration of conservative therapy, we modelled the preoperative treatment time, from initiation of medical therapy until BPE surgery, by year of surgery using linear regression.

Statistical analyses were performed using Enterprise Guide V.6.1 (SAS Institute).

### Patient and public involvement

This research was done without patient involvement. Patients were not invited to comment on the study design and were not consulted to develop patient relevant outcomes or interpret the results. Patients were not invited to contribute to the writing or editing of this document for readability or accuracy.

## RESULTS

We identified 52 162 men who underwent BPE surgery. Most of these men underwent a TURP (n=45 463, 87%; table 1). The proportion of patients undergoing a TURP decreased over time from 95% in 2003 to 78% in 2014 (supplementary eTable 5). In the year prior to surgery,

40% (n=20 600) of patients received a prescription for α-blocker monotherapy, 5% (n=2378) received a prescription for 5ARI monotherapy and 28% (n=14 450) of patients received both medications. Within 2 years preceding surgery, 49% (n=25 779 patients) experienced a preoperative urinary obstruction event (requiring urinary catheterisation or developing obstructive uropathy), and this percentage did not change on an annual basis throughout the study period (supplementary eTable 6). Most patients had a Charlson Comorbidity Index of zero (78%) and the proportion of patients undergoing surgery with a Comorbidity Index ≥2 increased gradually over time (14% in 2003 to 15% in 2014).

The crude rate of 30-day complications increased from 2363 events/10 000 BPE procedures in 2003 to 3145 events/10 000 in 2014 (figure 1). The rates of complications also increased by age group, with the highest rate of complications among the ≥80-year group (4050 events/10 000 procedures in 2013; figure 1). The ≥80-year group also had the largest increase in complication rate over time (p<0.0001; figure 1), with the rate of complications increasing by 39% from 2003 to 2014 (RR=1.39; 95% CI 1.21 to 1.61; p<0.0001). For the 70–79 year group, the complication rate increased by 30% over the same time period (RR=1.30; 95% CI 1.16 to 1.46; p<0.0001) and for the 66–69 year group, the complication rate increased by 20% (RR=1.20; 95% CI 0.99 to 1.45; p=0.07). Of the BPE complications, the most common were urinary obstruction complications (1273 events/10 000 BPE procedures; table 2). Of the non-BPE complications, the most common were cardiovascular complications (179 events/10 000 procedures).

In multivariable Poisson regression analysis, the RR of complications increased with age (RR 1.01 per year; 95% CI 1.01 to 1.02; p<0.0001), Charlson Comorbidity Index (RR 1.06 per unit increase; 95% CI 1.04 to 1.07; p<0.0001) and with year of surgery (RR 1.02 per year increase; 95% CI 1.01 to 1.02; p<0.0001). Other factors associated with an increased rate of complications included having a preoperative urinary obstruction event, a non-TURP procedure and geographical location (table 3). When we further stratified our multivariate analysis (table 3), the RR of complications was the highest for the ≥80-year group (table 3).

Receipt of an α-blocker prescription in the year prior to surgery was associated with an increased 30-day complication rate (RR 1.05; 95% CI 1.01 to 1.09; p=0.033). We did not observe an association between receipt of 5ARI or dual therapy and complications (table 3). In exploratory analysis, we evaluated the association between receipt of preoperative medication and procedure-specific complications following BPE surgery (table 4). Receipt of a prescription for α-blockers (RR 1.13; 95% CI 1.06 to 1.19; p<0.0001) and antithrombotics (RR 1.11; 95% CI 1.05 to 1.17; p<0.0001) was associated with a significantly increased risk of urinary obstruction, while receipt of 5ARI alone was not. Receipt of an antithrombotic prescription was significantly associated with an increased risk of bleeding complications (RR 1.48; 95% CI 1.39 to 1.58; p<0.0001).

**Table 2** Unadjusted rates of complications and secondary outcomes following benign prostatic enlargement (BPE) procedures

| | Total cohort (n=52 162) |
|---|---|
| Primary outcome: 30-day complications | |
| All complications | 2827.9 |
| Bleeding* | **814.6** |
| Infection† | **225.3** |
| Obstruction‡ | 1273.0 |
| Trauma§ | **75.7** |
| Renal¶ | **107.6** |
| Cardiovascular** | **179.3** |
| Pulmonary†† | **42.4** |
| Thromboembolic‡‡ | **37.6** |
| Secondary outcomes | |
| 30-day reoperation | **72.7** |
| 1-year reoperation | **404.3** |

Complication rates are reported per 10 000 BPE procedures.
*Bleeding complications include: haematuria (with or without manual catheter or cystoscopy clot evacuation), and haematuria requiring blood transfusion and/or hospital admission.
†Infection complications include: cystitis/urinary tract infection (UTI), kidney infection, prostatitis and/or prostate abscess, orchitis/epididymitis, sepsis and septic shock.
‡Obstruction complications include: urinary retention, bladder neck obstruction, obstructive uropathy and urethral stricture.
§Trauma complications include: urethral or vesical fistula, paraphimosis and incontinence.
¶Renal complications include: impaired renal function, acute renal failure and ureteric obstruction/hydroureter.
**Cardiovascular complications include: myocardial infarction, stroke and cardiac arrest requiring cardiopulmonary resuscitation(CPR).
††Pulmonary complications include: pneumonia and requiring a ventilator for more than 48 hours.
‡‡Thromboembolic complications include: pulmonary embolism and deep vein thrombosis.

The risk of 30-day reoperation was not associated with preoperative medication use, age or comorbidity, but it was associated with preoperative urinary obstruction (RR 1.48; 1.20 to 1.82; p=0.0003; table 4). The risk of 1-year reoperation was reduced with receipt of a α-blocker alone (RR 0.89; 95% CI 0.80 to 0.99; p=0.03), combination therapy (α-blocker and 5ARI; RR 0.85; 95% CI 0.76 to 0.96; p=0.0081), and antithrombotic medications (RR 0.87; 95% CI 0.78 to 0.96; p=0.0073) and was slightly increased with age (RR 1.01 per 1 year increase; 95% CI 1.00 to 1.02; p=0.0049) and year of surgery (RR 1.02; 95% CI 1.00 to 1.03; p=0.0098).

We examined the amount of time from medical therapy initiation to surgery among the ≥80-year-old group since this age group had the highest rate of complications (figure 1) and we could lookback over

**Table 3** Multivariable Poisson regression analysis of predictors of 30-day complications following benign prostatic enlargement surgery, in the complete cohort and stratified by age group

| | Full cohort | | | 66–69 years | | | 70–79 years | | | 80+ years | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Variable** | **aRR** | **95% CI** | **P value** | **aRR** | **95% CI** | **P value** | **aRR** | **95% CI** | **P value** | **aRR** | **95% CI** | **P value** |
| Age at procedure | 1.01 | 1.01 to 1.02 | <0.0001 | 1.03 | 0.99 to 1.07 | 0.1109 | 1.01 | 1 to 1.01 | 0.2232 | 1.01 | 1 to 1.02 | 0.0025 |
| Year of surgery | 1.02 | 1.01 to 1.02 | <0.0001 | 1 | 0.99 to 1.02 | 0.5931 | 1.02 | 1.01 to 1.03 | <0.0001 | 1.03 | 1.02 to 1.04 | <0.0001 |
| Preoperative urinary obstruction | 1.23 | 1.19 to 1.27 | <0.0001 | 1.16 | 1.07 to 1.26 | 0.0004 | 1.23 | 1.17 to 1.29 | <0.0001 | 1.28 | 1.21 to 1.36 | <0.0001 |
| 5ARI prescription | 0.95 | 0.87 to 1.03 | 0.2104 | 1 | 0.81 to 1.24 | 0.9907 | 0.96 | 0.85 to 1.08 | 0.5138 | 0.9 | 0.78 to 1.04 | 0.1631 |
| α-blocker prescription | 1.05 | 1 to 1.09 | 0.0335 | 0.99 | 0.9 to 1.09 | 0.8121 | 1.06 | 1 to 1.12 | 0.0645 | 1.05 | 0.98 to 1.13 | 0.1472 |
| Both 5ARI and α-blocker prescription | 1.02 | 0.97 to 1.07 | 0.463 | 0.96 | 0.86 to 1.08 | 0.5264 | 0.99 | 0.93 to 1.06 | 0.7626 | 1.08 | 1 to 1.17 | 0.0487 |
| Antithrombotic prescription | 1.27 | 1.22 to 1.31 | <0.0001 | 1.35 | 1.22 to 1.5 | <0.0001 | 1.28 | 1.21 to 1.34 | <0.0001 | 1.22 | 1.15 to 1.3 | <.0001 |
| Charlson Comorbidity Index | 1.06 | 1.05 to 1.07 | <0.0001 | 1.05 | 1.02 to 1.09 | 0.0037 | 1.07 | 1.05 to 1.09 | <0.0001 | 1.04 | 1.02 to 1.06 | <.0001 |
| Income quintile | | | | | | | | | | | | |
| 1 | Referent | | | Referent | | | Referent | | | Referent | | |
| 2 | 1.01 | 0.96 to 1.07 | 0.6615 | 1.07 | 0.94 to 1.21 | 0.3279 | 1.01 | 0.94 to 1.09 | 0.8196 | 0.99 | 0.91 to 1.09 | 0.8901 |
| 3 | 0.98 | 0.93 to 1.03 | 0.3801 | 1.03 | 0.91 to 1.17 | 0.6221 | 0.96 | 0.89 to 1.04 | 0.3239 | 0.97 | 0.88 to 1.06 | 0.4915 |
| 4 | 1 | 0.95 to 1.05 | 0.9921 | 0.93 | 0.82 to 1.06 | 0.2654 | 1.02 | 0.95 to 1.1 | 0.5603 | 1.01 | 0.92 to 1.11 | 0.8281 |
| 5 | 1.02 | 0.97 to 1.07 | 0.4711 | 0.97 | 0.86 to 1.11 | 0.6946 | 1.04 | 0.97 to 1.12 | 0.2856 | 1.02 | 0.93 to 1.11 | 0.7306 |
| Intervention type | | | | | | | | | | | | |
| TURP | Referent | | | Referent | | | Referent | | | Referent | | |
| Laser | 1.15 | 1.09 to 1.21 | <0.0001 | 1.17 | 1.04 to 1.32 | 0.0108 | 1.18 | 1.1 to 1.27 | <0.0001 | 1.09 | 0.99 to 1.19 | 0.0675 |
| Simple | 1.22 | 1.08 to 1.38 | 0.0016 | 1.4 | 1.08 to 1.82 | 0.0105 | 1.22 | 1.03 to 1.45 | 0.022 | 1.07 | 0.83 to 1.37 | 0.5948 |

Models are adjusted for Local Health Integration Network (not shown).
5ARI, 5α-reductase inhibitor; aRR, adjusted relative rate; TURP, transurethral resection of the prostate.

**Table 4** Multivariable log-binomial regression analysis of predictors of 30-day obstruction, bleeding and reoperation complications

| | Obstruction | | | Bleeding | | | 30-day reoperation | | |
|---|---|---|---|---|---|---|---|---|---|
| **Variable** | **aRR** | **95% CI** | **P value** | **aRR** | **95% CI** | **P value** | **aRR** | **95% CI** | **P value** |
| Age at procedure | 1.01 | 1.01 to 1.02 | <0.0001 | 1.01 | 1 to 1.01 | 0.0064 | 1 | 0.99 to 1.02 | 0.7487 |
| Year of surgery | 1 | 0.99 to 1.01 | 0.8181 | 1.03 | 1.02 to 1.04 | <0.0001 | 1.01 | 0.98 to 1.04 | 0.495 |
| Preoperative urinary obstruction | 1.42 | 1.36 to 1.49 | <0.0001 | 1.04 | 0.98 to 1.1 | 0.2143 | 1.48 | 1.2 to 1.82 | 0.0003 |
| 5ARI prescription | 1 | 0.89 to 1.13 | 0.9663 | 1.08 | 0.94 to 1.25 | 0.2702 | 0.94 | 0.55 to 1.6 | 0.8135 |
| α-blocker prescription | 1.13 | 1.06 to 1.19 | <0.0001 | 1.05 | 0.97 to 1.13 | 0.2051 | 1.07 | 0.83 to 1.38 | 0.5911 |
| Both 5ARI and α-blocker prescription | 1.08 | 1.01 to 1.15 | 0.0219 | 1.01 | 0.93 to 1.09 | 0.8651 | 0.91 | 0.68 to 1.22 | 0.5147 |
| Antithrombotic prescription | 1.11 | 1.06 to 1.17 | <0.0001 | 1.48 | 1.39 to 1.58 | <0.0001 | 0.97 | 0.76 to 1.24 | 0.8046 |
| Charlson Comorbidity Index | 1 | 0.98 to 1.02 | 0.7621 | 1.02 | 1 to 1.05 | 0.038 | 0.92 | 0.83 to 1.01 | 0.078 |
| Income quintile | | | | | | | | | |
| 1 | Referent | | | Referent | | | Referent | | |
| 2 | 1.03 | 0.96 to 1.11 | 0.4281 | 1.04 | 0.95 to 1.14 | 0.4272 | 0.8 | 0.58 to 1.11 | 0.1843 |
| 3 | 0.98 | 0.91 to 1.05 | 0.588 | 1.04 | 0.95 to 1.14 | 0.423 | 0.91 | 0.66 to 1.26 | 0.571 |
| 4 | 0.99 | 0.92 to 1.06 | 0.7191 | 1.01 | 0.92 to 1.11 | 0.8236 | 0.94 | 0.68 to 1.29 | 0.6966 |
| 5 | 1.05 | 0.98 to 1.13 | 0.18 | 1.06 | 0.97 to 1.16 | 0.2205 | 0.99 | 0.72 to 1.36 | 0.9626 |
| Intervention type | | | | | | | | | |
| TURP | Referent | | | Referent | | | Referent | | |
| Laser | 1.43 | 1.34 to 1.53 | <0.0001 | 0.91 | 0.82 to 1 | 0.0536 | 1.13 | 0.82 to 1.57 | 0.4555 |
| Simple | 1.12 | 0.94 to 1.32 | 0.2075 | 1.09 | 0.86 to 1.37 | 0.49 | 1.36 | 0.68 to 2.75 | 0.3849 |

Models are also adjusted for Local Health Integration Network (not shown).
5ARI, 5α-reductase inhibitor; aRR, adjusted relative risk; TURP, transurethral resection of the prostate.

at least a 15-year period of potential time since initiating medical therapy. Between 2007 and 2014, there was an annual mean increase of 3.1 months per year (95% CI 2.6 to 3.7; p<0.0001) in the duration of time from initiating BPE medical therapy to surgery. In 2007, the mean duration of therapy was 4.5 years (95% CI 4.3 to 4.8), reaching 6.4 years (95% CI 6.1 to 6.7; p<0.0001; figure 2) in 2014.

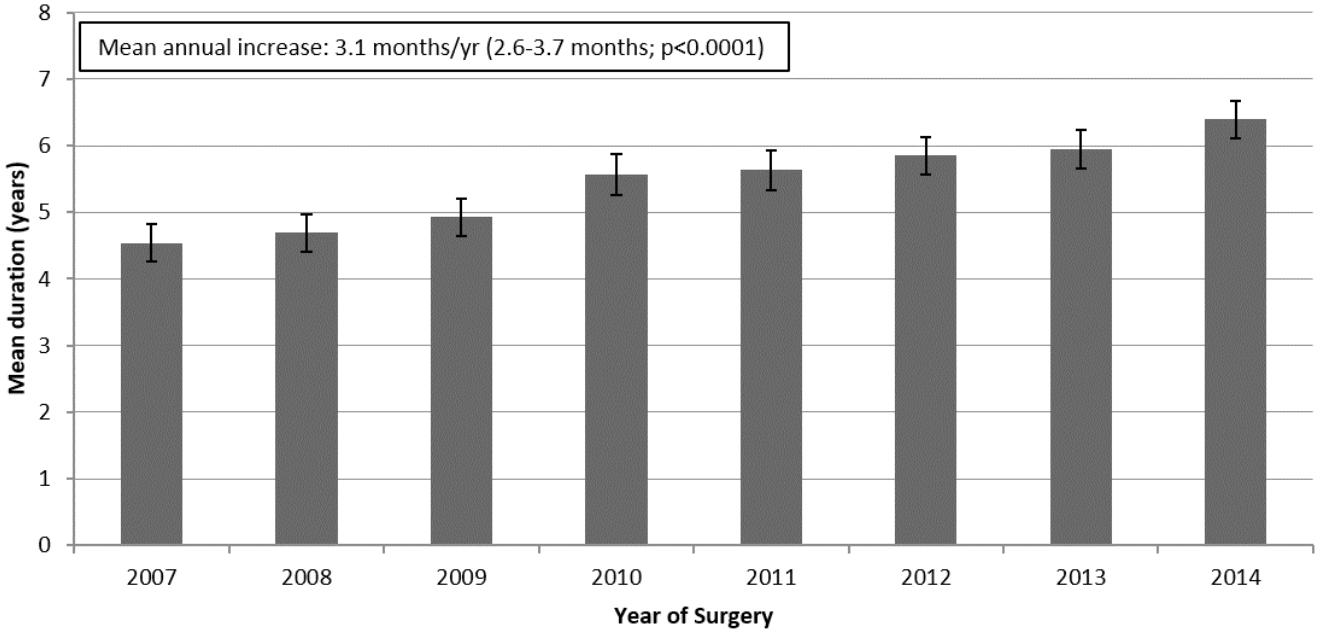


**Figure 2** Mean duration of time from first 5-α reductase inhibitor or α-blocker prescription to benign prostatic enlargement surgical treatment by year of surgery for patients ≥80 years old at surgery.

## DISCUSSION

Between 2003 and 2014, among elderly men who underwent BPE surgery, 30-day complication rates increased by year of surgery, and with age, comorbidity, and receipt of an α-blocker or antithrombotic medication in the year prior to surgery. The most common type of complication was urinary obstruction. Among the ≥80-year-old group, the 30-day relative complication rate increased significantly by 39%. This occurred concurrently with an increasing duration of medical therapy or conservative management over time.

To our knowledge, this is the first population-based study assessing the role of preoperative BPE medication use on BPE surgery outcomes, while accounting for other important preoperative variables. It appears paradoxical that the rate of postoperative complications over time increased, while BPE surgical technology continues to advance,[14] the adoption of laser ablative surgery[11] aims to reduce complications and frailty assessment improves patient selection[15] and preoperative medical optimisation of patients. One possible explanation for this finding is that the duration from initiating medical therapy to surgery increased over the study period. Therefore, efforts to improve outcomes may be offset by the progression of BPE and comorbidity during this period of conservative management.

This hypothesis is further strengthened by our finding that the receipt of α-blockers in the year prior to surgery was associated with an increased risk of complications, while receipt of 5ARI medications was not. Conservative therapy and α-blocker monotherapy may have similar effects on BPE progression, and in like manner, BPE surgery complications. From the Medical Therapy of Prostatic Symptoms (MTOPS) study, patients receiving α-blocker monotherapy (with doxazosin) experienced a 24% increase in prostate volume after an average follow-up of 4.5 years, identical to the increase observed in the placebo group. Reich *et al*, in a cohort of 10 564 men, found a strong positive correlation between prostate weight resected, transfusion, TUR syndrome and reoperation rates.[12] Conversely, 5ARIs are known to reduce prostate volume, as seen in the long-term open-label extension of three phase III trials evaluating dutasteride.[16] Both finasteride and dutasteride also decrease vascular endothelial growth factor expression as well as microvessel density in prostatic tissue,[17 18] which has translated to a reduced rate of perioperative bleeding in several clinical trials.[19] This was also observed in our data where patients receiving 5ARI in the year prior to surgery did not have an increased rate of complications, including bleeding.

Previous studies attempting to address the effect of BPE medications on surgical outcomes have been limited. Izard and Nickel, in their institutional series, found that as BPE medication use increased between 1998 and 2008, there was a substantial rise in the percentage of men presenting to their institution with preoperative acute or chronic urinary retention, and hydronephrosis.[8] As well, the number of patients discharged with a catheter increased over the two decades. Similarly, in a pooled analysis of postoperative outcomes from randomised controlled trials between 1997 to 2007, the postoperative failure-to-void rate of patients worsened over time compared with two large cohort landmark studies of successive preceding decades.[20] In these two studies, the duration of medical therapy, however, was not directly measured, but rather inferred based on the era of treatment.

We found that bleeding complications represented the second highest rate of procedure-specific complications. The American College of Chest Physicians antithrombotic guidelines identify BPE surgery, specifically TURP, as having a high rate of bleeding.[21] We also found that the receipt of antithrombotic medications, including anticoagulation and antiplatelet therapy, significantly increased the rate of 30-day overall complications and 30-day bleeding complications following BPE surgery. In keeping with this, Wallis *et al* previously identified that the use of antithrombotic medications, compared with non-use, was significantly associated with higher rates of haematuria-related complications.[22]

### Strengths and limitations

A major strength of this study includes the availability of population-based data. In Ontario, the sole provider of health insurance, the Ontario Health Insurance Plan (OHIP), covers nearly all healthcare services for ~13 million people. This allows the ability to follow patients after their index procedure irrespective of where complications are managed within the province.

A general limitation of all studies using administrative databases is the potential for misclassification. There is also potential for selection bias. Although we adjust for geography and income, the regional variations within Ontario might limit the generalisability of our results. The absence of information on prostate size, urinary symptoms, extent of resection during the index procedure and the specific technology used for resection (monopolar or bipolar TURP, or type of laser and whether it was enucleation or vapourisation) are important limitations that may contribute to early morbidity. Also, we were unable to evaluate postoperative functional outcomes, besides urinary obstruction, which may be increased because of prolonged conservative or medical management of BPE.[20]

## CONCLUSION

Elderly men receiving BPE surgery between 2003 and 2014 had increasing annual rates of 30-day complications, with an increased rate of complications for older and more comorbid men. There was a concurrent increase in the duration between initiating medical therapy and surgery over this time period. Patients receiving α-blocker monotherapy had an increased rate of 30-day overall complications. Patients receiving preoperative 5ARI monotherapy and combination therapy did not have an increased rate of complications.

**Twitter** Rano Matta @ranomatta

**Contributors** All authors designed the study. SH and RKN obtained funding for the study. All authors drafted the manuscript, revised it and approved the final version to be published.

**Funding** This study was supported by ICES, which is funded by an annual grant from the Ontario Ministry of Health and Long-Term Care. This study also received funding from: Functional Urology Research Program at the University of Toronto and the Ajmera Family Chair in Urologic Oncology awarded to RKN.

**Disclaimer** The analyses, conclusions, opinions and statements expressed herein are solely those of the authors and do not reflect those of the funding or data sources; no endorsement is intended or should be inferred.

**Competing interests** SH has received grants and personal fees from Astellas, Allergan, and Ipsen and personal fees from Pfizer and Duchesnay. SBR has acted as an advisory board member for Astellas, Pfizer, Merus, Allergan and participated in research for Astellas and Allergan. LC has participated in research and advisory board meetings for Cook MyoSite, and also serves on speakers boards for Astellas, Allergan, Pfizer, Duchesney USA and Ferring Pharmaceuticals.

**Patient consent for publication** Not required.

**Ethics approval** The Sunnybrook Health Sciences Centre Research Ethics Board approved this study protocol.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data availability statement** The dataset from this study is held securely in coded form at the Institute for Clinical Evaluative Sciences (ICES). While data sharing agreements prohibit ICES from making the dataset publicly available, access may be granted to those who meet pre-specified criteria for confidential access, available at www.ices.on.ca/DAS. The full dataset creation plan and underlying analytic code are available from the authors upon request, understanding that the computer programs may rely upon coding templates or macros that are unique to ICES and are therefore either inaccessible or may require modification.



**ORCID iD**

Rano Matta http://orcid.org/0000-0002-1414-4991

## REFERENCES

1 McConnell JD, Roehrborn CG, Bautista OM, *et al*. The long-term effect of doxazosin, finasteride, and combination therapy on the clinical progression of benign prostatic hyperplasia. *N Engl J Med* 2003;349:2387–98.
2 Roehrborn CG, Siami P, Barkin J, *et al*. The effects of combination therapy with dutasteride and tamsulosin on clinical outcomes in men with symptomatic benign prostatic hyperplasia: 4-year results from the combat study. *Eur Urol* 2010;57:123–31.
3 Wei JT, Miner MM, Steers WD, *et al*. Benign prostatic hyperplasia evaluation and management by urologists and primary care physicians: practice patterns from the observational BPH registry. *J Urol* 2011;186:971–6.
4 Jacobsen SJ, Girman CJ, Guess HA, *et al*. Natural history of prostatism: longitudinal changes in voiding symptoms in community dwelling men. *J Urol* 1996;155:595–600.
5 Lieber MM, Rhodes T, Jacobson DJ, *et al*. Natural history of benign prostatic enlargement: long-term longitudinal population-based study of prostate volume doubling times. *BJU Int* 2010;105:214–9.
6 Jacobsen SJ, Jacobson DJ, Girman CJ, *et al*. Natural history of prostatism: risk factors for acute urinary retention. *J Urol* 1997;158:481–7.
7 Benign Prostatic Hyperplasia (BPH) Guideline - American Urological Association. Available: https://www.auanet.org/guidelines/benign-prostatic-hyperplasia-(bph)-guideline [Accessed 7 May 2019].
8 Izard J, Nickel JC. Impact of medical therapy on transurethral resection of the prostate: two decades of change. *BJU Int* 2011;108:89–93.
9 Vela-Navarrete R, Gonzalez-Enguita C, Garcia-Cardoso JV, *et al*. The impact of medical therapy on surgery for benign prostatic hyperplasia: a study comparing changes in a decade (1992-2002). *BJU Int* 2005;96:1045–8.
10 Bhojani N, Gandaglia G, Sood A, *et al*. Morbidity and mortality after benign prostatic hyperplasia surgery: data from the American College of surgeons national surgical quality improvement program. *J Endourol* 2014;28:831–40.
11 Gilfrich C, Leicht H, Fahlenbrach C, *et al*. Morbidity and mortality after surgery for lower urinary tract symptoms: a study of 95 577 cases from a nationwide German health insurance database. *Prostate Cancer Prostatic Dis* 2016;19:406–11.
12 Reich O, Gratzke C, Bachmann A, *et al*. Morbidity, mortality and early outcome of transurethral resection of the prostate: a prospective multicenter evaluation of 10,654 patients. *J Urol* 2008;180:246–9.
13 Bansal A, Arora A. Transurethral resection of prostate and bleeding: a prospective, randomized, double-blind placebo-controlled trial to see the efficacy of short-term use of finasteride and dutasteride on operative blood loss and prostatic microvessel density. *J Endourol* 2017;31:910–7.
14 Rassweiler J, Teber D, Kuntz R, *et al*. Complications of transurethral resection of the prostate (TURP)--incidence, management, and prevention. *Eur Urol* 2006;50:969–80.
15 Hall DE, Arya S, Schmid KK, *et al*. Association of a frailty screening initiative with postoperative survival at 30, 180, and 365 days. *JAMA Surg* 2017;152:233–40.
16 Debruyne F, Barkin J, van Erps P, *et al*. Efficacy and safety of long-term treatment with the dual 5 alpha-reductase inhibitor dutasteride in men with symptomatic benign prostatic hyperplasia. *Eur Urol* 2004;46:488–95.
17 Busetto GM, Giovannone R, Antonini G, *et al*. Short-Term pretreatment with a dual 5α-reductase inhibitor before bipolar transurethral resection of the prostate (B-TURP): evaluation of prostate vascularity and decreased surgical blood loss in large prostates. *BJU Int* 2015;116:117–23.
18 Pareek G, Shevchuk M, Armenakas NA, *et al*. The effect of finasteride on the expression of vascular endothelial growth factor and microvessel density: a possible mechanism for decreased prostatic bleeding in treated patients. *J Urol* 2003;169:20–3.
19 Zhu Y-P, Dai B, Zhang H-L, *et al*. Impact of preoperative 5α-reductase inhibitors on perioperative blood loss in patients with benign prostatic hyperplasia: a meta-analysis of randomized controlled trials. *BMC Urol* 2015;15:47.
20 Mayer EK, Kroeze SGC, Chopra S, *et al*. Examining the 'gold standard': a comparative critical analysis of three consecutive decades of monopolar transurethral resection of the prostate (TURP) outcomes. *BJU Int* 2012;110:1595–601.
21 Douketis JD, Spyropoulos AC, Spencer FA, *et al*. Perioperative management of antithrombotic therapy: antithrombotic therapy and prevention of thrombosis, 9th ED: American College of chest physicians evidence-based clinical practice guidelines. *Chest* 2012;141:e326S–50.
22 Wallis CJD, Juvet T, Lee Y, *et al*. Association between use of antithrombotic medication and Hematuria-Related complications. *JAMA* 2017;318:1260–71.