

**The cost of treatment and its related complications for men who receive surgery or radiation therapy for prostate cancer**

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**Abstract**

**Introduction:** We sought to examine the costs related to treatment and treatment-related complications for patients treated with surgery or radiation for localized prostate cancer.

**Methods:** We performed a population-based, retrospective cohort study of men who underwent open radical prostatectomy or radiation from 2004–2009 in Ontario, Canada. Costs, including initial treatment and inpatient hospitalization, emergency room visit, outpatient consultation, physician billings, and medication costs, were determined for five years following treatment using a validated costing algorithm. Multivariable negative binomial regression was used to assess the association between treatment modality and costs.

**Results:** A total of 28 849 men underwent treatment for localized prostate cancer from 2004–2009. In the five years following treatment, men who underwent radiation (n=12 675) had 21% higher total treatment and treatment-related costs than men who underwent surgery (\$16 716/person vs. \$13 213/person). Based on multivariable analysis, while men who underwent XRT had a lower relative cost in their first year after treatment (relative rate [RR] 0.97; 95% confidence interval [CI] 0.94–1.0; p=0.025), after year 2, annual costs were significantly higher in the radiation group compared to the surgery group (total cost for year 5, RR 1.44; 95% CI 1.17–1.76; p<0.0001). Our results were similar when restricted to young, healthy men and to older men.

**Conclusions:** Men who undergo radiation have significantly higher five-year total treatment-related costs compared to men who undergo open radical prostatectomy. While surgery was associated with slightly higher initial costs, radiotherapy had higher costs in subsequent years.

## Introduction

The treatment options for patients diagnosed with localized prostate cancer include surgery or radiation therapy.<sup>1,2</sup> Results from the largest study to date that randomized patients between surgery and radiation reported similar mortality rates.<sup>1</sup> Thus, treatment choices for patients with localized disease continue to rely on patient and physician factors.<sup>3</sup> The initial treatment can also have long-term consequences that result in complications that require additional treatments.

We previously described high rates of treatment-related complications (other than urinary incontinence and erectile dysfunction) among men in Ontario who were treated with surgery or radiation<sup>4,5</sup>. Subsequent studies have confirmed our initial findings that treatment related complications are common to both treatments, with many patients experiencing a peak in complication rates at 2 years after treatment<sup>6,7</sup>. Furthermore, validation of these results using an American cohort found that treatment related complications frequently recur, with a mean number of complications of 2.6 per patient<sup>7</sup>. While such complications affect patient survivorship, they may also place a burden on the healthcare system.

To date, while the economic effect of incontinence and erectile dysfunction related to treatment of prostate cancer have been well studied,<sup>8-12</sup> the costs associated with other treatment-related complications have not been examined. These costs, unlike those related to incontinence and erectile dysfunction, which are often incurred by the patient, are usually incurred by the health care system through government or third party payers. In order to better understand the costs of treatment of localized prostate cancer while considering treatment-related complications, we examined the absolute and relative 5-year health care utilization costs (consisting of treatment and treatment-related complications costs) for men undergoing surgery or radiation for localized prostate cancer among a large population-based cohort.

## Methods

### *Study subjects*

We performed a retrospective cohort study using a previously described cohort of men undergoing treatment for non-metastatic prostate cancer<sup>4</sup>. We excluded patient's who underwent treatment from January 1 2002 – December 31 2003 due to a paucity of available costing data. In brief, we included men over the age of 18 who had undergone either open radical prostatectomy or radiation therapy (external beam or brachytherapy) between January 1 2004 – December 31 2009 in Ontario, Canada. We excluded patients who underwent minimally invasive surgery (either robotic or laparoscopic) as these procedures were not well established in Ontario

during the study treatment period. Furthermore, while the use of robotic radical prostatectomy has expanded over the past decade, within Canada approximately 70% of radical prostatectomies are performed using open technique<sup>13</sup>. We excluded patients who underwent both radiation and surgery. After their initial treatment, patients were followed for 5 years or until death. Research ethics approval was obtained at the participating institute.

### ***Patient selection***

We identified patients diagnosed with prostate cancer using the Ontario Cancer Registry (OCR), a database of all newly diagnosed invasive cancers. We then linked treatment-related fee codes to identify patients who underwent treatment (surgery or radiation) within 1 year of diagnosis. The Ontario Health Insurance Plan (OHIP) is a government-run health insurance system that is used for physician fee reimbursement. For open radical prostatectomy, we used the fee code S651. For patients who underwent radiation therapy, planning codes (X310, X311, X312 and X313) and radiation follow up codes (A343, A340, A341, K013) were used for identification as previously described<sup>4</sup>. To exclude patients who may have received radiation as palliative therapy, we excluded patients who were initially diagnosed with or who developed metastatic disease during the study period.

### ***Cost determinants***

We determined the total 5-year costs for treatment and treatment related complications for localized prostate cancer. We defined total costs as health care utilization costs due to: hospital admissions, same day surgeries, emergency department visits, visits to a provincially recognized cancer center (for treatment, consultation and/or follow up), drug prescriptions (as captured through the Ontario Drug Benefit (ODB) program) and physician billings as a result of a complication.

We accessed data on hospital admissions, same day surgeries, emergency department visits and cancer clinic visits by linking to the Canadian Institute for Health Information (CIHI) Discharge Abstract Database, the National Ambulatory Care Reporting System, the Ontario Drug Benefit (ODB) program database and OHIP physician records. In Year 1, costs of the initial treatment were included. Years 2 – 5 included follow up as well as costs related to treatment related complications.

As we wanted to examine costs related to complications from treatment (including standard treatment follow up), we only included costs linked to specific OHIP fee codes. These fee codes included consultations, surgeries, and small procedures related to known urinary, rectal and anal complications from treatment. A complete list of included OHIP billing codes can be found in Supplementary Table 3.

### *Derivation of cost estimations*

#### *Hospital inpatient admissions, same day surgery clinics, emergency department and cancer clinic visits*

We examined patient-level healthcare utilization costs within 5 years after initial treatment for prostate cancer. The cost for each patient was determined using costing methods developed for healthcare administrative data<sup>14</sup>. This method of patient costing has been extensively validated and used for several diseases including chronic diseases, critical care, spinal cord injury and trauma<sup>15-18</sup>. Costs are calculated using the CIHI resource intensity weight (RIW) value and multiplying it by cost-per weighted case (CPWC), which is averaged across the province<sup>14,19,20</sup>. These costs are calculated annually and do not include physician OHIP billings. All dollar figures are reported in 2015 Canadian dollars.

#### *Ontario drug benefit program*

Prescription medications and associated pharmacy costs covered by the Ontario Drug Benefit Program (ODB) for patients 65 years of age or older, or under specific circumstances. We included medications that were related to prostate cancer treatment and complications (See Supplementary Table 4).

### *Statistical analysis*

#### *Primary analysis*

Starting from the date of their initial treatment, patients were considered at risk for complications. They were followed until death or the last date of follow up for the study (obtained from the Registered Persons Database). Year 1 included treatment-related costs. Costs were compared using absolute and relative costs. Patients with missing costing data were excluded from the analysis. Study was reported as per the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines<sup>21</sup>.

#### *Absolute costs*

Absolute costs of treatment and treatment-related complications were defined as all costs based on health care utilization for patients in each primary treatment group. Cumulative and annual costs were calculated for each treatment group.

#### *Relative costs*

In order to compare annual per patient complication costs between patients who had primary surgery or radiation, we performed a multivariate negative binomial regression accounting for the dependence of matched data, for each year after treatment. This gave us the relative cost of radiation treated patients compared to surgically treated patients (expressed as the relative rate). For example, a relative cost of 1.5 for radiation means that patients treated with radiation cost on average 50% more than patients treated with surgery. Covariates included in the model were patient age, comorbidity, patient location and year of treatment.

To address differences in baseline characteristics between patients treated with surgery and those treated with radiotherapy, we performed propensity score matching. The propensity score was determined based on a logistic regression model accounting for the following independent variables: age, comorbidity score (ADG), year of treatment, income quintile. Patients were matched 1:1 using the greedy algorithm.

Statistical significance was set at  $p < 0.05$  based on a two-tailed comparison. All statistical analyses were performed in SAS Version 9.4.

### *Sub-analyses*

We performed sub analyses looking at two distinct populations to account for differences in health care resource use due to age and comorbidities. To minimize the effects of selection bias, we examined a subgroup of the youngest and healthiest patients (aged 55 to 65, and  $ADG \leq 5$ ). Also, because the cost of prescription medication is covered by the government only for patients aged 65 years or more, we examined a subgroup of patients older than 65.

## **Results**

Overall, 28,849 men underwent treatment for localized prostate cancer during the study period. Of these men, 16,174 underwent open radical prostatectomy and 12,675 underwent radiation therapy. Men in the surgery group were younger, from higher social economic status, and healthier than patients in the radiation group (Table 1).

### *Absolute costs*

#### *Total treatment-related complication costs over 5 years*

The total 5-year per patient cost was \$13,213 for men who were treated with radical prostatectomy and \$16,716 for men treated with radiation therapy (difference \$3,503, 21%). For patients who underwent surgery and radiation, 74% and 63% of their total costs were incurred within the first year respectively. Annual costs were higher for patients who received radiation therapy for all 5 years (Table 2).

#### *Cost breakdown by category*

When we examined the costs by individual category, the highest cost was the inpatient category for the surgery group (\$7,927/patient over 5 years), while outpatient cancer management costs were the highest for patients who received radiation (\$9,912/patient over 5 years, Table 3). After Year 1, inpatient costs, emergency department visit costs and Ontario Drug Benefit costs were higher in men who underwent radiation (Table 3).

### *Relative costs*

#### *Multivariate analysis*

After controlling for patient age, comorbidities, patient location and year of treatment, patients who received radiation had a significantly lower total cost relative to those who underwent

surgery in the first year after treatment (RR=0.82, 95% CI 0.8-0.84,  $p<0.0001$ , Table 4). Total costs for patients who received radiation were significantly higher from Year 2 onwards (Table 4).

When we restricted the study to patients who are young and healthy (aged between 55 – 65 years, ADG  $\leq 5$ ), and to patients aged  $> 65$  years, we found no change in the effect direction (Table 4).

#### *Propensity matched multivariate analysis*

In our propensity matched analysis, the results were similar. In the first year after treatment, the total costs among patients who received radiation were significantly lower than those who received surgery (RR=0.97, 95% CI 0.94-1.0,  $p=0.025$ ). In Years 3 – 5, the total costs among patients who received radiation were significantly higher than those who received surgery ( $<0.05$  for all, Table 5). Inpatient visits, same day surgeries and emergency department visit costs were significantly lower in men treated with radiation in Year 1 ( $p<0.0001$  for all). In Years 2 to 5, these costs became significantly higher in the radiation group ( $p<0.0001$  for all). Ontario Drug Benefit costs were higher for all years in the radiation group relative to the surgery group (Table 5). By Year 5, outpatient cancer management costs were significantly lower in men who received radiation compared to surgery (RR=0.78 (0.67 – 0.9,  $p<0.002$ ).

#### **Discussion**

In this population-based analysis, men who underwent open radical prostatectomy had 21% lower treatment-related health care expenditures over 5 years, compared with men who underwent radiation treatment for the treatment of localized prostate cancer. By the fifth year after treatment, men who underwent radiation cost almost twice as much per person annually (\$1,450/patient vs. \$800/patient), compared to men who underwent surgery. These differences in costs persisted among young, healthy men and among older men.

To our knowledge, this is the first analysis to compare costs between treatments for prostate cancer, while accounting for treatment related complications. Currently, the literature on treatment costs for localized prostate cancer treatment is limited, consisting mainly of decision analytic models. Gordon et al. determined the costs of prostate cancer treatment using a Markov model and demonstrated that surgery had a lower cost compared to radiation<sup>22</sup>. Cooperberg et al. determined that all forms of radiotherapy were associated with higher lifetime costs compared with any surgical approach<sup>11</sup>. Dorth et al. compared radiation therapy plus androgen deprivation therapy (ADT) to surgery plus radiation and found improved quality adjusted life expectancy but higher costs in the radiation group<sup>23</sup>. While helpful, these models did not include treatment related complication costs. Other cost effectiveness studies did not differentiate between treatment type in their models<sup>9,24,25</sup>.

Perlroth et al. found that the mean medical expenditures following the diagnosis of localized prostate cancer were \$96,300 USD for intensity-modulated radiation therapy, \$67,700 for brachytherapy and \$49,800 for radical prostatectomy<sup>26</sup>. These differences persisted when the

authors accounted for age and comorbidities. The authors concluded that U.S health expenditures could be reduced by up to \$14.5 billion by shifting patients away from radiation therapy <sup>26</sup>.

Costs were highest in the first year of treatment regardless of treatment modality (surgery \$9,739.70/per person, radiation \$10,606.49/per person). First year costs comprised 74% of total costs for patients treated with surgery and 63% of total costs for those treated with radiotherapy. This is to be expected as our first year costs included the initial cost of treatment. For patients treated with radical prostatectomy, inpatient costs drove a significant proportion of overall costs in the first year, but a relatively small amount in subsequent years (less than \$450/per person annually).

Outpatient cancer management costs accounted for the vast majority of costs in the first year among the radiation group (\$8,987/per person) due to the frequent cancer clinic visits for radiation treatment planning and delivery. However, cancer clinic visit costs and OHIP billings from radiation oncologists sharply decreased after Year 1 (see Supplementary Table 1 and Table 2). In contrast, cancer clinic visits from men who underwent surgery had a more gradual decrease, and OHIP physician billings from urologists remained constant throughout the 5 years.

In contrast to the first year where costs are driven by the initial treatment, costs in subsequent years were driven by treatment-related complications. While patients who undergo surgery tend to experience most complications either immediately after surgery or within the first 2 years after treatment <sup>7</sup>, many radiation associated complications, including radiation cystitis/proctitis, fistulae and secondary malignancies <sup>27-29</sup>, have a delayed manifestation. This is consistent with our observation that costs for radiation were higher from Years 3 to 5.

An important strength of this analysis is the ability to determine costs at the population level using a previously validated costing method <sup>14-16,18</sup>. Also, our study used a large, population-based cohort, allowing for generalizations to a larger group of men with prostate cancer. Despite these strengths, our study has limitations. First, this analysis was performed in a single-payer, universal health insurance system. These results may not be generalizable to areas with alternative health care funding arrangements. Further, indirect costs were not considered. Our analysis did not consider robotic prostatectomy. While the robotic platform has been widely disseminated in the United States, the same has not happened in Canada, likely due to our publically funded healthcare system. As of 2016, only 4 provinces had robotic systems <sup>13</sup>. Based on a recent article by Childers et al., robotic surgery adds approximately \$3,500 per case <sup>30</sup>. It is unknown how robotic surgery would affect our costing analysis, as the literature is mixed as to whether the advantages of minimally invasive surgery (lower blood loss and decreased length of stay) outweigh the added cost of the robotic platform <sup>31</sup>.

In addition, we only examined patients who received either radiation or surgery. We did not look at patients who underwent combination therapy (salvage radiation or salvage prostatectomy). While we recognize that this subset of patients will have higher rates of complications and subsequent costs, the majority of men with localized prostate cancer will not have biochemical recurrence <sup>32-34</sup>. Comparative costs are poorly studied in men who receive

salvage treatments and it is unknown how including these patients would effect our analysis. We also did not include costs related to infrastructure, including costs of equipment and maintenance and annual running costs of the operating room and radiation center. As OHIP only covers certain medications and patients older than 65, we could not capture all medications (ex. Phosphodiesterase type 5 inhibitors). Thus, these costs are likely underestimated.

**Conclusion**

We found that patients treated with radiotherapy for localized prostate cancer had significantly higher treatment-attributable costs in the 5 years following treatment, compared with those who underwent open radical prostatectomy. While surgery was associated with slightly higher initial costs, costs associated with radiation treatment were higher in subsequent years.



## References

1. Hamdy FC, Donovan JL, Lane JA, et al. 10-Year Outcomes after Monitoring, Surgery, or Radiotherapy for Localized Prostate Cancer. *N Engl J Med*. 2016;375(15):1415-1424.
2. Dahm P, Yeung LL, Chang SS, Cookson MS. A Critical Review of Clinical Practice Guidelines for the Management of Clinically Localized Prostate Cancer. *The Journal of Urology*. 2008;180(2):451-460.
3. Smith AB, Mancuso P, Sidhom M, et al. Prostatectomy versus radiotherapy for early-stage prostate cancer (PREPaRE) study: protocol for a mixed-methods study of treatment decision-making in men with localised prostate cancer. *BMJ Open*. 2017;7(11).
4. Nam RK, Cheung P, Herschorn S, et al. Incidence of complications other than urinary incontinence or erectile dysfunction after radical prostatectomy or radiotherapy for prostate cancer: a population-based cohort study. *The Lancet Oncology*. 2014;15(2):223-231.
5. Wallis CJD, Herschorn S, Saskin R, et al. Complications After Radical Prostatectomy or Radiotherapy for Prostate Cancer: Results of a Population-based, Propensity Score-matched Analysis. *Urology*. 2015;85(3):621-628.
6. Wallis CJD, Mahar AL, Cheung P, et al. Hospitalizations to Manage Complications of Modern Prostate Cancer Treatment in Older Men. *Urology*. 2016;96:142-147.
7. Wallis CJD, Mahar A, Cheung P, et al. New Rates of Interventions to Manage Complications of Modern Prostate Cancer Treatment in Older Men. *European Urology*. 2016;69(5):933-941.
8. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. *CA: A Cancer Journal for Clinicians*. 2016;66(1):7-30.
9. Krahn MD, Zagorski B, Laporte A, et al. Healthcare costs associated with prostate cancer: estimates from a population-based study. *BJU International*. 2010;105(3):338-346.
10. Wilson LS, Tesoro R, Elkin EP, et al. Cumulative cost pattern comparison of prostate cancer treatments. *Cancer*. 2007;109(3):518-527.
11. Cooperberg MR, Ramakrishna NR, Duff SB, et al. Primary treatments for clinically localized prostate cancer: a comprehensive lifetime cost-utility analysis. *BJU international*. 2013;111(3):437-450.
12. Fradet Y, Klotz L, Trachtenberg J, Zlotta A. The burden of prostate cancer in Canada. *Canadian Urological Association Journal*. 2009;3(3 Suppl 2):S92-S100.
13. Health Quality O. Robotic Surgical System for Radical Prostatectomy: A Health Technology Assessment. *Ont Health Technol Assess Ser*. 2017;17(11):1-172.
14. Wodchis WP BK, Nikitovic M, McKillop I. Guidelines on PersonLevel Costing Using Administrative Databases in Ontario. *Working Paper Series*. Vol 1. Toronto: Health System Performance Research Network; 2013.
15. Munce SE, Wodchis WP, Guilcher SJ, et al. Direct costs of adult traumatic spinal cord injury in Ontario. *Spinal Cord*. 2013;51(1):64-69.
16. Wodchis WP, Austin PC, Henry DA. A 3-year study of high-cost users of health care. *CMAJ : Canadian Medical Association Journal*. 2016;188(3):182-188.

17. Chaudhuri D, Tanuseputro P, Herritt B, D'Egidio G, Chalifoux M, Kyeremanteng K. Critical care at the end of life: a population-level cohort study of cost and outcomes. *Critical Care*. 2017;21:124.
18. Pincus D, Wasserstein D, Nathens AB, Bai YQ, Redelmeier DA, Wodchis WP. Direct medical costs of motorcycle crashes in Ontario. *Canadian Medical Association Journal*. 2017;189(46):E1410.
19. Chen A, Bushmeneva K, Zagorski B, Colantonio A, Parsons D, Wodchis WP. Direct cost associated with acquired brain injury in Ontario. *BMC Neurology*. 2012;12:76-76.
20. Information ClfH. Patient Cost Estimator Methodological Notes and Glossary. 2013(MIS and Costing, Health Spending and Strategic Initiatives):11.
21. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet*. 2007;370(9596):1453-1457.
22. Gordon LG, Tuffaha HW, James R, et al. Estimating the healthcare costs of treating prostate cancer in Australia: A Markov modelling analysis. *Urologic Oncology: Seminars and Original Investigations*. 2017.
23. Dorth JA, Lee WR, Chino J, Abouassaly R, Ellis RJ, Myers ER. Cost-Effectiveness of Primary Radiation Therapy Versus Radical Prostatectomy for Intermediate- to High-Risk Prostate Cancer. *International Journal of Radiation Oncology\*Biophysics*. 2018;100(2):383-390.
24. Murray DK, Karen EB, Brandon Z, et al. Health Care Costs for State Transition Models in Prostate Cancer. *Medical Decision Making*. 2013;34(3):366-378.
25. Stokes ME, Black L, Benedict A, Roehrborn CG, Albertsen P. Long-term medical-care costs related to prostate cancer: estimates from linked SEER-Medicare data. *Prostate Cancer Prostatic Dis*. 2010;13(3):278-284.
26. Perlroth DJ, Goldman DP, Garber AM. The potential impact of comparative effectiveness research on U.S. health care expenditures. *Demography*. 2010;47 Suppl:S173-190.
27. Bassett MR, Santiago-Lastra Y, Stoffel JT, et al. Urinary Diversion for Severe Urinary Adverse Events of Prostate Radiation: Results from a Multi-Institutional Study. *The Journal of Urology*. 2017;197(3, Part 1):744-750.
28. Nieder AM, Porter MP, Soloway MS. Radiation Therapy for Prostate Cancer Increases Subsequent Risk of Bladder and Rectal Cancer: A Population Based Cohort Study. *The Journal of Urology*. 2008;180(5):2005-2010.
29. Wallis CJD, Mahar AL, Choo R, et al. Second malignancies after radiotherapy for prostate cancer: systematic review and meta-analysis. *BMJ : British Medical Journal*. 2016;352:i851.
30. Childers CP, Maggard-Gibbons M. Estimation of the Acquisition and Operating Costs for Robotic Surgery. *JAMA*. 2018;320(8):835-836.
31. Schroeck FR, Jacobs BL, Bhayani SB, Nguyen PL, Penson D, Hu J. Cost of New Technologies in Prostate Cancer Treatment: Systematic Review of Costs and Cost Effectiveness of Robotic-assisted Laparoscopic Prostatectomy, Intensity-modulated Radiotherapy, and Proton Beam Therapy. *Eur Urol*. 2017;72(5):712-735.

32. Pound CR, Partin AW, Eisenberger MA, Chan DW, Pearson JD, Walsh PC. Natural history of progression after PSA elevation following radical prostatectomy. *JAMA*. 1999;281(17):1591-1597.
33. Kestin LL, Vicini FA, Ziaja EL, Stromberg JS, Frazier RC, Martinez AA. Defining biochemical cure for prostate carcinoma patients treated with external beam radiation therapy. *Cancer*. 1999;86(8):1557-1566.
34. Wallis CJD, Cheung P, Herschorn S, et al. Complications following surgery with or without radiotherapy or radiotherapy alone for prostate cancer. *Br J Cancer*. 2015;112(6):977-982.

## Figures and Tables

<b>Table 1. Patient demographic data of men who underwent treatment for localized prostate cancer in Ontario from 2004–2009</b>				
	<b>Treatment type</b>			
<b>Variable</b>	<b>Radical prostatectomy n=16 174</b>	<b>Radiation therapy n=12 675</b>	<b>Total n=28 849</b>	<b>p</b>
Age				<b>&lt;0.001</b>
<55	2489 (15.4%)	473 (3.7%)	2962 (10.3%)	
55–59	3467 (21.4%)	974 (7.7%)	4441 (15.4%)	
60–64	4476 (27.7%)	1651 (13.0%)	6127 (21.2%)	
65–69	4064 (25.1%)	2591 (20.4%)	6655 (23.1%)	
70–74	1527 (9.4%)	3688 (29.1%)	5215 (18.1%)	
75+	151 (0.9%)	3298 (26.0%)	3449 (12.0%)	
Income quintile				<b>&lt;0.001</b>
Missing	43 (0.3%)	36 (0.3%)	79 (0.3%)	
1	2102 (13.0%)	2004 (15.8%)	4106 (14.2%)	
2	2822 (17.4%)	2504 (19.8%)	5326 (18.5%)	
3	3, 22 (19.3%)	2506 (19.8%)	5628 (19.5%)	
4	3701 (22.9%)	2606 (20.6%)	6307 (21.9%)	
5	4384 (27.1%)	3019 (23.8%)	7403 (25.7%)	
Total ADG				<b>&lt;0.001</b>
0–3	3823 (23.6%)	2615 (20.6%)	6438 (22.3%)	
4–5	5958 (36.8%)	4057 (32.0%)	10 015 (34.7%)	
6–7	3918 (24.2%)	3210 (25.3%)	7128 (24.7%)	
8+	2475 (15.3%)	2793 (22.0%)	5268 (18.3%)	
Treatment year				<b>&lt;0.001</b>
2004	1717 (10.6%)	1370 (10.8%)	3087 (10.7%)	
2005	2617 (16.2%)	2054 (16.2%)	4671 (16.2%)	
2006	3031 (18.7%)	2238 (17.7%)	5269 (18.3%)	
2007	3081 (19.0%)	2436 (19.2%)	5517 (19.1%)	
2008	2960 (18.3%)	2339 (18.5%)	5299 (18.4%)	
2009	2768 (17.1%)	2238 (17.7%)	5006 (17.4%)	

<b>Table 2. Absolute 5-year per person costs for treatment and treatment-related complications of men who received surgery or radiation therapy for prostate cancer</b>		
<b>Year since treatment</b>	<b>Radical prostatectomy n=16 174</b>	<b>Radiation therapy n=12 675</b>
1	\$9739.70	\$10 606.49
2	\$1021.74	\$1564.61
3	\$836.71	\$1563.86
4	\$814.61	\$1531.15
5	\$799.80	\$1450.35
Overall	\$13 212.56	\$16 716.47

\*Total costs consist of inpatient hospitalizations, cancer clinic, same day surgery, Ontario Drug Benefit, emergency department visits costs, and OHIP billings. Costs are presented in 2015 Canadian dollars.

<b>Table 3. Annual per person treatment-related complication costs by costing category in men who underwent either radical prostatectomy or radiation therapy for prostate cancer</b>		
<b>Year post-treatment</b>	<b>Radical prostatectomy</b>	<b>Radiation therapy</b>
<b>Inpatient hospitalization costs per person per year</b>		
1	\$6527	\$1071
2	\$272	\$786
3	\$320	\$972
4	\$389	\$1066
5	\$420	\$998
Total	\$7927	\$4892
<b>Same day surgery costs per person per year</b>		
1	\$166	\$83
2	\$77	\$149
3	\$63	\$113
4	\$62	\$86
5	\$58	\$73
Total	\$426	\$504
<b>Emergency department visit costs per person per year</b>		
1	\$58	\$44
2	\$14	\$38
3	\$12	\$29
4	\$14	\$28
5	\$15	\$28
Total	\$113	\$167
<b>Cancer treatment and followup costs per person per year*</b>		

1	\$2939	\$8987
2	\$599	\$290
3	\$383	\$237
4	\$286	\$206
5	\$237	\$192
Total	\$4444	\$9912
<b>Ontario Drug Benefit program cost per person per year</b>		
1	\$50	\$421
2	\$60	\$302
3	\$58	\$213
4	\$63	\$145
5	\$71	\$159
Total	\$301	\$1240

\* Costs include cancer clinic costs and OHIP physician billings related to treatment, followup, and treatment-related complications.

<b>Table 4. Multivariate negative binomial regression comparing 5-year total costs of treatment and treatment related complications in men who received surgery to men who received radiation therapy for treatment of localized prostate cancer</b>					
<b>Group</b>	<b>Year 1</b>	<b>Year 2</b>	<b>Year 3</b>	<b>Year 4</b>	<b>Year 5</b>
<b>Entire cohort</b>					
Surgery	1.00	1.00	1.00	1.00	1.00
Radiation therapy	0.82 (0.8–0.84) p<0.0001	1.01 (0.95–1.07) p=0.76	1.17 (1.1–1.25) p<0.0001	1.29 (1.2–1.37) p<0.0001	1.30 (1.21–1.39) p<0.0001
<b>Men aged 55–65 and ADG ≤5</b>					
Surgery	1.00	1.00	1.00	1.00	1.00
Radiation therapy	0.88 (0.84–0.91) p<0.0001	0.96 (0.88–1.04) p=0.31	0.91 (0.83–1.00) p=0.04	1.5 (1.33–1.62) p<0.0001	1.4 (1.29–1.6) p<0.0001
<b>Men aged &gt;65 years</b>					
Surgery	1.00	1.00	1.00	1.00	1.00
Radiation therapy	0.81 (0.79–0.84) p<0.0001	1.11 (1.04–1.18) p<0.0001	1.44 (1.35–1.54) p<0.0001	1.28 (1.19–1.38) p<0.0001	1.28 (1.18–1.38) p<0.0001

Data are relative rates (RR), (95% confidence interval [CI]). Multivariate model also includes age, comorbidity (ADG case mix), year of treatment, and income.

**Table 5. Propensity-scored matching negative binomial regression comparing 5-year total costs of treatment and treatment related complications in men who received surgery to men who received radiation therapy for treatment of localized prostate cancer**

Group	Year 1	Year 2	Year 3	Year 4	Year 5
<b>Total cost</b>					
Surgery	1.00	1.00	1.00	1.00	1.00
Radiation therapy	0.97 (0.94–1.0) p=0.025	1.12 (0.98–1.29) p=0.096	1.28 (1.07–1.54) p=0.007	1.26 (1.03–1.54) p=0.025	1.44 (1.17–1.76) p<0.0001
<b>Inpatient costs</b>					
Surgery	1.00	1.00	1.00	1.00	1.00
Radiation therapy	0.11 (0.1–0.13) p<0.0001	2.23 (1.66–2.99) p<0.0001	1.97 (1.44–2.7) p<0.0001	1.76 (1.25–2.46) p=0.001	1.98 (1.43–2.74) p<0.0001
<b>Same day surgery</b>					
Surgery	1.00	1.00	1.00	1.00	1.00
Radiation therapy	0.57 (0.51–0.64) p<0.0001	1.49 (1.31–1.71) p<0.0001	1.44 (1.25–1.67) p<0.0001	1.17 (0.99–1.38) p=0.06	1.02 (0.85–1.23) p=0.83
<b>Emergency department visits</b>					
Surgery	1.00	1.00	1.00	1.00	1.00
Radiation therapy	0.54 (0.46–0.63) p<0.0001	1.89 (1.4–2.56) p<0.0001	1.76 (1.34–2.33) p<0.0001	1.54 (1.19–2.01) p=0.001	1.55 (1.17–2.05) p=0.003
<b>Cancer treatment and followup costs per person per year<sup>§</sup></b>					
Surgery	1.00	1.00	1.00	1.00	1.00
Radiation therapy	2.8 (2.7–2.89) p<0.0001	0.43 (0.39–0.48) p<0.0001	0.58 (0.51–0.65) p<0.0001	0.63 (0.56–0.72) p<0.0001	0.78 (0.67–0.9) p=0.002
<b>Ontario drug benefit program</b>					
Surgery	1.00	1.00	1.00	1.00	1.00
Radiation therapy	3.95 (3.23–4.82) p<0.0001	2.33 (1.9–2.87) p<0.0001	2.05 (1.67–2.52) p=0.001	1.21 (0.88–1.67) p=0.24	1.44 (1.1–1.88) p=0.009

Data are relative rates (RR), (95% confidence interval [CI]). Patients are matched 1:1. Propensity score was calculated based on patient's age, income quintile, ADG and year of diagnosis.

<sup>§</sup>Costs include cancer clinic visits costs and OHIP physician billings related to treatment, followup, and treatment-related complications.

**Supplementary Table 1. Annual 5-year per person cancer clinic visit costs for men who were treated with surgery or radiation therapy for localized prostate cancer**

<b>Year post-treatment</b>	<b>Radical prostatectomy (\$)</b>	<b>Radiation therapy (\$)</b>
Year 1	982.77	7778.17
Year 2	384.36	41.08
Year 3	197.21	22.41
Year 4	123.82	24.25
Year 5	84.93	21.75
<b>Total</b>	<b>1773.09</b>	<b>7887.66</b>

**Supplementary Table 2. Annual number of OHIP billings for urologists and radiation oncologists for men who were treated with surgery or radiation for localized prostate cancer**

	<b>Surgery, urology* (% of year 1)</b>	<b>Radiation therapy, radiation oncology** (% of year 1)</b>
Year 1	9738 (100)	8513 (100)
Year 2	10 127 (104)	6522 (77)
Year 3	9409 (97)	5945 (70)
Year 4	8657 (89)	5198 (61)
Year 5	8019 (82)	4640 (55)

\*Urology billings include OHIP fee codes A353, A354, A355. \*\*Radiation oncology billings include OHIP fee codes A348, X313, A340, A343, A341. OHIP: Ontario Health Insurance Plan.



<b>Supplementary Table 3. List of Ontario Health Insurance Plan (OHIP) physician fee codes that were included in determining treatment and treatment-related complication costs in treatment for localized prostate cancer</b>	
<b>Fee code</b>	<b>Description of code</b>
A001	Minor assessment – family practitioner
A003	General assessment – family practitioner
A004	General re-assessment – family practitioner
A005	Consultation – family medicine
A008	Mini assessment – family practitioner
A015	Consultation – anesthesia
A033	Specific assessment – general surgery
A034	Partial assessment – general surgery
A035	Consultation – general surgery
A036	Repeat consultation – general surgery
A131	Complex medical specific re-assessment – internal and occupational medicine
A133	Medical specific assessment – internal and occupational medicine
A134	Medical specific re-assessment – internal and occupational medicine
A340	Medical specific re-assessment – radiation oncology
A341	Complex medical specific re-assessment – radiation oncology
A343	Medical specific assessment – radiation oncology
A345	Consultation – radiation oncology
A346	Re-consultation – radiation oncology
A348	Partial assessment – radiation oncology
A353	Specific assessment – urology
A354	Partial assessment – urology
A355	Consultation – urology
A356	Re-consultation – urology
A411	Complex medical specific re-assessment – gastroenterology
A413	Medical specific assessment – gastroenterology
A414	Medical specific re-assessment – gastroenterology
A415	Consultation – gastroenterology
A418	Partial assessment – gastroenterology
A441	Complex medical specific re-assessment – medical oncology
A443	Medical specific assessment – medical oncology
A444	Medical specific re-assessment – medical oncology
A445	Consultation – medical oncology
A448	Partial assessment – medical oncology
A473	Medical specific assessment – internal medicine
A474	Medical specific re-assessment – internal medicine

A585	Diagnostic consultation – pathology
A745	Limited consultation – radiation oncology
A771	Pronouncement of death
A888	Partial assessment – emergency department equivalent
A935	Preamble – special surgical consultation
C012	Subsequent hospital visit up to 5 weeks – anesthesia
C013	Special assessment – anesthesia
C018	Concurrent hospital care – anesthesia
C032	Subsequent hospital visit up to five weeks – general surgery
C038	Concurrent hospital care – general surgery
C101	Intensive care unit premiums
C122	Most responsible physician
C123	Most responsible physician
C124	Day of discharge visit – most responsible physician
C342	Subsequent hospital visit – radiation oncology
C352	Subsequent hospital visit – urology
C353	Specific hospital assessment – urology
C354	Specific hospital re-assessment – urology
C355	Hospital consultation – urology
C358	Concurrent hospital care – urology
C412	Subsequent hospital visits – gastroenterology
C418	Concurrent care
C990	Special hospital inpatient visit
C994	Special hospital inpatient visit
C995	Special hospital inpatient visit
E022	Anaesthesia extra units
E023	Anaesthesia basic units
E082	Admission assessment by most responsible physician
E083	Subsequent visit by the most responsible physician, to subsequent visit, c122, c123, c124, c142, c143, c882 or c982
E702	Oesophagoscopy with multiple biopsies
E705	Digestive system – intestinal endoscopy into terminal ileum, add on
E717	Colonoscopy – biopsy/coagulation of lesion
E720	Colonoscopy – excision of polyp
E740	Intestine endoscopy – sigmoid to splenic flexure, add on
E741	Intestine endoscopy – sigmoid to hepatic flexure, add on
E746	Sigmoidoscopy – performed outside of hospital
E747	Intestine endoscopy – sigmoid.to caecum add to z512/z555
E749	Digestive system – when z512,555,580 performed outside of hospital, add on
E787	Cystoscopy with resection or incision of bladder neck, male, add on

E797	Management of upper or lower gastrointestinal bleeding by any technique
G009	Urinalysis routine
G010	Urinalysis
G192	Video fluoroscopic multichannel urodynamic assessment
G224	Nerve block
G247	Nerve block – hospital visits
G339	Chemotherapy – single-agent intravenous chemotherapy
G379	Adult intravenous
G381	Intravenous chemotherapy
G382	Supervision of chemotherapy by telephone, monthly
G395	Critical care first ¼ hour
G401	Critical intensive care
G475	Cystometrogram & or voiding pressure
G511	Telephone management of palliative care at home
G512	Palliative care case management fee
G900	Residual urine measurement
H065	Emergency physician consult
H101	Minor assessment – emergency
H102	Comprehensive assessment and care – emergency medicine
H103	Multiple systems assessment – emergency medicine
H104	Re-assessment – emergency medicine
H105	In-patient interim admission orders
H122	Comprehensive assessment and care – emergency medicine (00:00h–08:00h)
H122	Comprehensive assessment and care – emergency medicine (00:00h–08:00h)
H123	Multiple systems assessment – emergency medicine (00:00h–08:00h)
H124	Re-assessment – emergency medicine (00:00h–08:00h)
H131	Minor assessment – emergency (18:00h–24:00h)
H132	Comprehensive assessment and care – emergency medicine (18:00h–24:00h)
H133	Multiple systems assessment – emergency medicine (18:00h–24:00h)
H134	Re-assessment – emergency medicine (18:00h–24:00h)
H151	Minor assessment – emergency (Holidays)
H152	Comprehensive assessment and care – emergency medicine (holidays)
H153	Multiple systems assessment – emergency medicine (holidays)
H154	Re-assessment – emergency medicine (holidays)
J028	Diagnostic radiology – urethrocystogram
J128	Diagnostic ultrasound – abdominal scan – limited study
J138	Intracavitary ultrasound (transrectal)
J149	Ultrasound guidance of biopsy, aspiration, amniocentesis or drainage procedures
J162	Ultrasound – pelvis complete
J163	Diagnostic ultrasound – pelvis, limited study other than pregnancy

K002	Interviews-relatives on behalf of patient per 1/2 hour
K005	Individual care per 1/2 hour
K013	Counselling one or more people-per 1/2hr.
K015	Counselling relatives on behalf of patient
K070	Home care application
K990	Special visits emergency department premiums
K991	Special visits emergency department premiums
K994	Special visits emergency department premiums
K995	Special visits emergency department premiums
L634	Urine microbiology and culture
Q133	Colorectal screening tracking code
Q142	Colorectal exclusion
Q150	Fecal occult blood distribution and counselling fee
Q200	Per patient rostering fee
S323	Herniotomy
S519	Surgical repair of bladder neck
S532	Transurethral visual urethrotomy
S539	Insertion of artificial urinary sphincter
S548	Urethral sling
S573	Circumcision
S636	Vesiculectomy
S640	Stereotactic prostate brachytherapy
S651	Prostatectomy/vasectomy-retropubic radical
S652	Pelvic lymphadenectomy for prostate cancer
S653	Laparoscopic radical prostatectomy
S655	Transurethral resection of prostate
X310	Radiation treatment planning level 1
X311	Radiation treatment planning level 2
X312	Radiation treatment planning level 3
X313	Radiation treatment planning level 4
Z399	Elective oesophagoscopy
Z400	Endoscopy for active bleeding
Z535	Sigmoidoscopy with or without anoscopy
Z543	Anoscopy
Z555	Colonoscopy into descending colon
Z570	Colonoscopy – excision/fulguration of polyps
Z571	Colonoscopy – excision/fulguration of polyps
Z580	Sigmoidoscopy
Z602	Bladder – catheterization in office
Z606	Cystoscopy

Z607	Cystoscopy – repeat within 30 days
Z608	Manual catheter declotting and irrigation of bladder
Z611	Bladder – catheterization in hospital
Z615	Filiform & follower urethral dilatation
Z619	Dilation of urethral stricture under general anaesthetic, male
Z621	Dilation of urethral stricture under local anaesthetic, male
Z628	Cystoscopy and diagnostic ureteroscopy
Z700	Intracorporeal injection for impotence
Z712	Prostate needle biopsy

**Supplementary Table 4. List of medications that were included in determining treatment and treatment-related complication costs in treatment for localized prostate cancer**

Drug category	Name	Drug ID number
Alpha blocker	Tamsulosin HCL	02362406
Alpha blocker	Tamsulosin HCL	02270102
Alpha blocker	Tamsulosin HCL	09857334
Alpha blocker	Tamsulosin HCL	02340208
Alpha blocker	Tamsulosin HCL	02368242
Alpha blocker	Tamsulosin HCL	02238123
Alpha blocker	Tamsulosin HCL	02298570
Alpha blocker	Tamsulosin HCL	02281392
Alpha blocker	Tamsulosin HCL	02294265
Alpha blocker	Tamsulosin HCL	02319217
Alpha blocker	Sildosin	02361663
Alpha blocker	Sildosin	02361671
Alpha blocker	Alfuzosin	02245565
Alpha blocker	Doxazosin	02240589
Alpha blocker	Doxazosin	02240590
Alpha blocker	Doxazosin	02240588
Alpha blocker	Doxazosin	02242730
Alpha blocker	Doxazosin	02242729
Alpha blocker	Doxazosin	02242728
Alpha blocker	Doxazosin	02244529
Alpha blocker	Doxazosin	02244528
Alpha blocker	Doxazosin	02244527
Alpha blocker	Terazosin	02234504
Alpha blocker	Terazosin	02234505

Alpha blocker	Terazosin	02234503
Alpha blocker	Terazosin	02234502
Alpha blocker	Terazosin	00818658
Alpha blocker	Terazosin	00818666
Alpha blocker	Terazosin	00818682
Alpha blocker	Terazosin	00818674
Alpha blocker	Terazosin	02243520
Alpha blocker	Terazosin	02243519
Alpha blocker	Terazosin	02243518
Alpha blocker	Terazosin	02243521
Alpha blocker	Terazosin	02230806
Alpha blocker	Terazosin	02230805
Alpha blocker	Terazosin	02230808
Alpha blocker	Terazosin	02230807
5ARI	finasteride	02365383
5ARI	finasteride	02405814
5ARI	finasteride	<a href="#">02428148</a>
5ARI	finasteride	02354462
5ARI	finasteride	02355043
5ARI	finasteride	02357224
5ARI	finasteride	02389878
5ARI	finasteride	02356058
5ARI	finasteride	02392631
5ARI	finasteride	02348500
5ARI	finasteride	02320169
5ARI	finasteride	02310112
5ARI	finasteride	02238213
5ARI	finasteride	09857529
5ARI	finasteride	02010909
5ARI	finasteride	02371820
5ARI	finasteride	02306905
5ARI	finasteride	02322579
5ARI	finasteride	02339471
5ARI	finasteride	02428741
5ARI	Dutasteride	02412691
5ARI	Dutasteride	02404206
5ARI	Dutasteride	02247813
5ARI	Dutasteride	02416298
5ARI	Dutasteride	02428873
5ARI	Dutasteride	02393220

5ARI	Dutasteride	02424444
5ARI	Dutasteride	02408287
PD5 inhibitors	Sildenafil	02239767
PD5 inhibitors	Sildenafil	02239766
PD5 inhibitors	Sildenafil	02239768
PD5 inhibitors	Tadalafil 20 mg	02421933
PD5 inhibitors	Tadalafil 10 mg	02248088
PD5 inhibitors	Tadalafil 5mg	02296896
PD5 inhibitors	Tadalafil 2.5 mg	02296888
PD5 inhibitors	Vardenafil 10 mg	02250470
PD5 inhibitors	Vardenafil 20 mg	02250489
PD5 inhibitors	Vardenafil 5 mg	02250462
Beta 3 agonist	mirabegron 50 mg	02402882
Beta 3 agonist	Mirabegron 25 mg	02402874
Anti-muscarinic	Darifenacin	02273225
Anti-muscarinic	Darifenacin	02273217
Anti-muscarinic	Fesoterodine	02380048
Anti-muscarinic	Fesoterodine	02380021
Anti-muscarinic	Oxybutynin	01924753
Anti-muscarinic	Oxybutynin	02223376
Anti-muscarinic	Oxybutynin	02163543
Anti-muscarinic	Oxybutynin	01924761
Anti-muscarinic	Oxybutynin	02230800
Anti-muscarinic	Oxybutynin	02230394
Anti-muscarinic	Oxybutynin	02240550
Anti-muscarinic	Oxybutynin 10% topical gel	02366150
Anti-muscarinic	Solifenacin	02422247
Anti-muscarinic	Solifenacin	02422239
Anti-muscarinic	Solifenacin	02424339
Anti-muscarinic	Solifenacin	02424347
Anti-muscarinic	Solifenacin	02417731
Anti-muscarinic	Solifenacin	02417723
Anti-muscarinic	Solifenacin	02437988
Anti-muscarinic	Solifenacin	02437996
Anti-muscarinic	Solifenacin	02399040
Anti-muscarinic	Solifenacin	02399032
Anti-muscarinic	Solifenacin	02397919
Anti-muscarinic	Solifenacin	02397900
Anti-muscarinic	Solifenacin	02277263

Anti-muscarinic	Solifenacin	02277271
Anti-muscarinic	Tolterodine	02244612
Anti-muscarinic	Tolterodine	02244613
Anti-muscarinic	Tolterodine	02404184
Anti-muscarinic	Tolterodine	02404192
Anti-muscarinic	Tolterodine	02413159
Anti-muscarinic	Tolterodine	02413140
Anti-muscarinic	Tolterodine	02412195
Anti-muscarinic	Tolterodine	02412209
Anti-muscarinic	Tolterodine	02369680
Anti-muscarinic	Tolterodine	02369699
Anti-muscarinic	Tolterodine	02239065
Anti-muscarinic	Tolterodine	02239064
Anti-muscarinic	Tolterodine	02423308
Anti-muscarinic	Tolterodine	02423316
Anti-muscarinic	Tolterodine	02299593
Anti-muscarinic	Tolterodine	02299607
Anti-muscarinic	Tospium	02275066
Anti-androgens	Bicalutamide	02296063
Anti-androgens	Bicalutamide	02325985
Anti-androgens	Bicalutamide	02184478
Anti-androgens	Bicalutamide	02274337
Anti-androgens	Bicalutamide	02357216
Anti-androgens	Bicalutamide	02270226
Anti-androgens	Bicalutamide	02275589
Anti-androgens	Bicalutamide	02371324
Anti-androgens	Bicalutamide	02276089
Anti-androgens	Bicalutamide	02428709
Anti-androgens	Enzalutamide	02407329
Anti-androgens	Flutamide	02059673
Anti-androgens	Nilutamide	02221861
GnRH agonists	Leuprolide	02239834
GnRH agonists	Leuprolide	02230248
GnRH agonists	Leuprolide	00884502
GnRH agonists	Leuprolide	02239833
GnRH agonists	Leuprolide	00836273
GnRH agonists	Goserelin	02049325
GnRH agonists	Triptorelin	02240000
GnRH agonists	Triptorelin	02243856
GnRH agonists	Triptorelin	02412322



GnRH agonists	Buserelin	02225166
GnRH agonists	Buserelin	02225158
GnRH agonists	Histrelin	02278383
GnRH antagonists	Degarelix	02337029
GnRH antagonists	Degarelix	02337037
CYP3A4 inhibitors	Abiraterone	02371065
Chemotherapy	Docetaxel	02177099
Chemotherapy	Docetaxel	02177080
Chemotherapy	Carbazitaxel	02369524
Chemotherapy	Mitoxantrone	02244614
Bisphosphonates	Zoledronic acid	02248296
Steroids	Prednisone	00598194
Steroids	Prednisone	00550957
Steroids	Prednisone	00312770
Steroids	Prednisone	00021695
Steroids	Prednisone	00868426
Steroids	Prednisone	00868434
Steroids	Prednisone	00868442
Steroids	Prednisone	00607517
Steroids	Prednisone	00156876
Steroids	Prednisone	00021695
Steroids	Prednisone	00232378
Steroids	Dexamethasone	02250055
Steroids	Dexamethasone	02261081
Steroids	Dexamethasone	00617210
Steroids	Dexamethasone	00349119
Steroids	Dexamethasone	00598542
Steroids	Dexamethasone	00250325
Steroids	Dexamethasone	00308455
Steroids	Dexamethasone	02387743
Steroids	Dexamethasone	00416010
Steroids	Dexamethasone	00874582
Steroids	Dexamethasone	00664227
Steroids	Dexamethasone	01977547
Steroids	Dexamethasone	02204266
Steroids	Dexamethasone	02204274
Steroids	Dexamethasone	02239534
Steroids	Dexamethasone	00627763
Steroids	Dexamethasone	02237044
Steroids	Dexamethasone	02237045

Steroids	Dexamethasone	02237046
Steroids	Dexamethasone	02260298
Steroids	Dexamethasone	02260301
Steroids	Dexamethasone	01946897
Steroids	Dexamethasone	01964976
Steroids	Dexamethasone	01964968
Steroids	Dexamethasone	01964070