

**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.

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## 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<br/>n=16 174</b> | <b>Radiation therapy<br/>n=12 675</b> | <b>Total<br/>n=28 849</b> | <b>p</b>         |
| <b>Age</b>  |   |                                       |                           | <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%)              |                  |
| <b>Income quintile</b>  |   |                                       |                           | <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%)              |                  |
| <b>Total ADG</b>  |   |                                       |                           | <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<br>(34.7%)         |                  |
| 6–7   | 3918 (24.2%)                              | 3210 (25.3%)                          | 7128 (24.7%)              |                  |
| 8+  | 2475 (15.3%)                              | 2793 (22.0%)                          | 5268 (18.3%)              |                  |
| <b>Treatment year</b>   |   |                                       |                           | <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>Year since treatment</b> | <b>Radical prostatectomy<br/>n=16 174</b> | <b>Radiation therapy<br/>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>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<br>(0.8–0.84)<br>p<0.0001  | 1.01<br>(0.95–1.07)<br>p=0.76   | 1.17<br>(1.1–1.25)<br>p<0.0001  | 1.29<br>(1.2–1.37)<br>p<0.0001  | 1.30<br>(1.21–1.39)<br>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<br>(0.84–0.91)<br>p<0.0001 | 0.96<br>(0.88–1.04)<br>p=0.31   | 0.91<br>(0.83–1.00)<br>p=0.04   | 1.5<br>(1.33–1.62)<br>p<0.0001  | 1.4<br>(1.29–1.6)<br>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<br>(0.79–0.84)<br>p<0.0001 | 1.11<br>(1.04–1.18)<br>p<0.0001 | 1.44<br>(1.35–1.54)<br>p<0.0001 | 1.28<br>(1.19–1.38)<br>p<0.0001 | 1.28<br>(1.18–1.38)<br>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<br>(0.94–1.0)<br>p=0.025   | 1.12<br>(0.98–1.29)<br>p=0.096  | 1.28<br>(1.07–1.54)<br>p=0.007  | 1.26<br>(1.03–1.54)<br>p=0.025  | 1.44<br>(1.17–1.76)<br>p<0.0001 |
| <b>Inpatient costs</b>   |                                 |                                 |                                 |                                 |                                 |
| Surgery  | 1.00                            | 1.00                            | 1.00                            | 1.00                            | 1.00                            |
| Radiation therapy  | 0.11<br>(0.1–0.13)<br>p<0.0001  | 2.23<br>(1.66–2.99)<br>p<0.0001 | 1.97<br>(1.44–2.7)<br>p<0.0001  | 1.76<br>(1.25–2.46)<br>p=0.001  | 1.98<br>(1.43–2.74)<br>p<0.0001 |
| <b>Same day surgery</b>  |                                 |                                 |                                 |                                 |                                 |
| Surgery  | 1.00                            | 1.00                            | 1.00                            | 1.00                            | 1.00                            |
| Radiation therapy  | 0.57<br>(0.51–0.64)<br>p<0.0001 | 1.49<br>(1.31–1.71)<br>p<0.0001 | 1.44<br>(1.25–1.67)<br>p<0.0001 | 1.17<br>(0.99–1.38)<br>p=0.06   | 1.02<br>(0.85–1.23)<br>p=0.83   |
| <b>Emergency department visits</b>   |                                 |                                 |                                 |                                 |                                 |
| Surgery  | 1.00                            | 1.00                            | 1.00                            | 1.00                            | 1.00                            |
| Radiation therapy  | 0.54<br>(0.46–0.63)<br>p<0.0001 | 1.89<br>(1.4–2.56)<br>p<0.0001  | 1.76<br>(1.34–2.33)<br>p<0.0001 | 1.54<br>(1.19–2.01)<br>p=0.001  | 1.55<br>(1.17–2.05)<br>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<br>(2.7–2.89)<br>p<0.0001   | 0.43<br>(0.39–0.48)<br>p<0.0001 | 0.58<br>(0.51–0.65)<br>p<0.0001 | 0.63<br>(0.56–0.72)<br>p<0.0001 | 0.78<br>(0.67–0.9)<br>p=0.002   |
| <b>Ontario drug benefit program</b>  |                                 |                                 |                                 |                                 |                                 |
| Surgery  | 1.00                            | 1.00                            | 1.00                            | 1.00                            | 1.00                            |
| Radiation therapy  | 3.95<br>(3.23–4.82)<br>p<0.0001 | 2.33<br>(1.9–2.87)<br>p<0.0001  | 2.05<br>(1.67–2.52)<br>p=0.001  | 1.21<br>(0.88–1.67)<br>p=0.24   | 1.44<br>(1.1–1.88)<br>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 – urethrocytogram  |
| 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 |

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