Original Study

Healthcare Resource Use and Costs of Localized Prostate Cancer Patients in Finland

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Abstract

This retrospective study estimates healthcare resource utilization and costs of localized prostate cancer (LPC) in Finland based on initial treatment. Using data from university hospitals and the Social Insurance Institution, results show significant cost variations across treatment pathways, with radical prostatectomy and radiotherapy plus androgen deprivation therapy incurring the highest first-year costs. Costs rise substantially before and after metastatic progression, underscoring economic implications.

Background: Prostate cancer is the most prevalent cancer among men in Finland, causing significant healthcare costs. Understanding the economic burden of various treatment pathways is vital for optimizing healthcare strategies. This study aimed at estimating healthcare resource utilization and associated costs for patients with localized prostate cancer (LPC) and locally advanced prostate cancer (LAPC) based on initial treatment decisions in Finland. **Patients and Methods:** A retrospective, noninterventional study was conducted using pseudonymized patient-level data from the 5 University Hospitals and the Social Insurance Institution of Finland. The cohort included 16,212 adults diagnosed with localized prostate cancer (LPC) or locally advanced prostate cancer (LAPC) between 1 July 2010 and 30 June 2021. Patients were categorized into 4 groups: no immediate treatment (NIT), radiotherapy only (RT), radiotherapy combined with androgen deprivation therapy (RT+ADT), and radical prostatectomy (RP). Healthcare resource utilization and costs were analyzed on a per-patient-year basis, considering inpatient admissions, outpatient visits, emergency department visits, and outpatient medication costs. **Results:** The first-year costs were highest for RP (€11,766) and RT+ADT (€10,421), reflecting intensive treatment, followed by RT only (€9,014) and no immediate treatment (NIT) (€4,129). Over time, costs decreased for RP and RT+ADT groups. Emergence of metastatic disease significantly increased costs, particularly due to outpatient medication. Costs began rising 1-2 years before metastasis, indicating early health deterioration. **Conclusion:** This study highlights significant cost variations across different treatment pathways for prostate cancer in Finland and underscores the economic impact of metastatic disease. Early detection and effective management are essential for cost containment.

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Introduction

Prostate cancer (PC) is a significant global health issue and the most prevalent cancer type among men in Finland, with over 5,000 new cases diagnosed annually.[1] Annual incidence has increased since data collection began in 1953. The number of cases and associated healthcare costs are expected to continue rising, as the national cancer burden is projected to nearly double by 2,040 due to an ageing population.

Prostate cancer treatment varies by stage and grade. For low-risk localized prostate cancer (LPC), active surveillance is recommended by European Association of Urology guidelines.[2] For intermediate- and high-risk patients, radical prostatectomy and radiation therapy

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are common treatment modalities. For localized high-risk patients, a combination of radiation therapy and adjuvant androgen deprivation therapy (ADT) is often used with curative intent. The optimal treatment approach is determined based on risk groups, patient profiles, and patient preferences. Recently, abiraterone acetate and enzalutamide, initially approved for the treatment of metastatic prostate cancer, have shown improved outcomes among men with high-risk nonmetastatic PC when combined with ADT and radiation therapy or in men with high-risk biochemical recurrence, respectively.[3] These novel therapies are associated with higher costs, adding to the economic burden of prostate cancer treatment.

There are challenges in risk stratification that can lead to both overtreatment and undertreatment. Hamdy et al.[4] found that while radical treatments reduced the incidence of metastasis, local progression, and long-term ADT use by half compared to active monitoring, these reductions did not translate into differences in mortality. Despite recent advances in early detection and treatment of LPC, the management of the disease remains controversial. Prospective trials have demonstrated that survival from clinically localized prostate cancer remains very high, with around 97% of patients surviving over 15 years, irrespective of treatment allocation.[4] In Finland, the overall survival rate for prostate cancer is high, with 94% of all patients being alive at 5 years after diagnosis.[1]

The economic burden of prostate cancer remains significant. According to the Cancer Foundation Finland,[5] the total cost for malignant neoplasms of male genital organs (C60-C63) was €162 million in 2021, with 58% attributed to medications, 23% to outpatient visits, 8% to inpatient care, 5% to primary care, and the rest to social benefits. Similarly, a Swedish study[6] estimated the direct medical costs of prostate cancer in 2016 to be €162 million, with half of the costs incurred by inpatient and outpatient care. Pharmaceuticals were the largest single category, accounting for 28% of the costs, while primary care and palliative care each accounted for 11% of the costs.

Given the increasing incidence of prostate cancer and the uncertainty surrounding its management and treatment, understanding the cost implications of different treatment options for localized prostate cancer patients is crucial. Currently, there is a lack of comprehensive evidence on the economic implications of various treatment strategies highlighting the need for detailed cost analysis. This study aimed to estimate the healthcare resource utilization and associated costs of LPC patients based on initial treatment decisions in Finland.

Materials and Methods

This study adhered to the strengthening the reporting of observational studies in epidemiology (STROBE)[7] guidelines.

Study Setting

Prostate cancer care in Finland is provided by not-for-profit hospital districts, each with a university or central hospital. Municipalities within a district fund services through taxes, covering costs based on resident usage. University hospitals serve their district's population and offer specialized treatments for referrals from central hospitals. Newer therapies such as androgen receptor pathway inhibitors are reimbursed in Finland for patients with metastatic PC.

Data Sources

This noninterventional register study utilized retrospectively collected pseudonymized patient-level data from all 5 university hospitals in Finland and the Social Insurance Institution (Kela). The dataset included specialized care events from hospitals' records, covering inpatient and outpatient services, radiation therapy, surgical procedures, pathology reports, billing, and medications. Data from Kela provided costs for outpatient medications. Registers were interlinked by Findata using personal identification numbers.

Study Population

The study cohort comprised of adult individuals newly diagnosed with LPC, identified via the international statistical classification of diseases, 10th revision[8] (ICD-10) code C61 from the electronic health records of university hospitals across Finland from 1 July 2010 to 30 June 2021. Exclusion criteria included: (1) treatment across multiple hospital districts; (2) residence outside the treating hospital district's catchment area; (3) any recorded instance of ICD-10 code C61 before 1 July 2010; (4) individuals younger than 18 years at diagnosis; and (5) prior active prostate cancer treatment before 1 July 2010.

Variable Definitions

The index date of PC diagnosis was the earlier of 2 events: the registration of ICD-10 code C61 or the initiation of PC-related active treatment. Criteria for identifying metastasis included: (1) ICD-10 codes indicative of metastasis (C76-C80); (2) code for palliative care (Z51.5); (3) surgical codes for metastasis treatment; (4) mentions of metastasis in patient records' free-text fields; or (5) a prostate-specific antigen (PSA) level $>$ 100 ng/mL. Medications related to treatment were identified using anatomical therapeutic chemical (ATC) codes.[9]

Active interventions were classified into: ADT with agents such as goserelin, leuprorelin, triptorelin, degarelix, bicalutamide, and flutamide; radical prostatectomy; and radiation therapy. Study participants were stratified into groups based on the active treatment received within the first 9 months postdiagnosis: (1) Radiotherapy only (RT) without prior ADT; (2) Radiotherapy and ADT (RT+ADT) for those who received ADT followed by radiotherapy; (3) Radical prostatectomy (RP) with or without concurrent ADT; and (4) No immediate treatment (NIT) for those who did not receive any active treatment within the first 9 months.

Costs and Healthcare Resource Utilization

Cost estimation used billing data from 4 of the 5 university hospitals and prostate cancer prescription data from Kela. One hospital was excluded from cost analyses due to data limitations. Costs were categorized as: (1) Inpatient care, including care and hospital administered medications; (2) Outpatient care, including appointments and radiation therapy; and (3) Emergency department costs. The analysis included all secondary healthcare resource use and costs, not limited to prostate cancer treatment. All costs were adjusted to 2019 prices using Statistics Finland's cost-of-living index.[10] Healthcare resource utilization was categorized as: (1) Inpatient admissions; (2) Outpatient visits; and (3) Emergency department visits. Healthcare resource utilisation data was included from all 5 hospitals.

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Statistical Analyses

Patient demographics and clinical variables were summarized by patient group. Continuous variables were presented as means with standard deviations, and categorical variables as counts and percentages. Costs and healthcare resource utilization were analyzed on a per-patient-year basis, with the year of diagnosis set as the index year. Results were presented based on the number of years since the index date. To avoid end-of-life cost bias in the localized disease analyses, annual cost estimates (for years +1 to +5) were based only on patients with complete follow-up for the respective year, excluding those who died during that year.[11] For example, a patient who died in year 4 was included only in the analyses for years 1 to 3. A cost analysis around metastasis examined costs 3 years before and after emergence of metastatic disease. healthcare resource utilizations and costs were calculated using a complete cases approach, including only uncensored patients alive at the year's end. Statistical analyses were conducted using R version 4.2.2.

Results

Patient Characteristics

Demographic and clinical characteristics of the patients are presented in Table 1. The study cohort included 16,212 patients diagnosed with prostate cancer from treatment pathways: NIT group (n = 5,943, 36.7%), RP group (n = 4,208, 26.0%), RT+ADT group (n = 4,030, 24.9%), and RT only group (n = 2,031, 12.5%).

Mean age at diagnosis was 69.5 years (SD = 8.5), the RP group with the lowest (64.2 years, SD = 6.3) and the RT+ADT group with the highest (72.5 years, SD = 6.6) mean age. PSA levels at diagnosis varied, with the RT+ADT group having the highest mean PSA level (16.3 ng/mL, SD = 15.4) and the NIT group the lowest (7.8 ng/mL, SD = 7.7). The NIT group had a higher proportion of patients with lower Gleason scores (≤6, 36.0%) compared to other treatment groups, with the RT+ADT group having the highest proportion of patients with Gleason scores ≥8 (26.9%). The RP group demonstrated the highest overall survival (OS) rate at 96% and metastasis-free survival (MFS) rate at 89%, though this group also had the lowest mean age. Conversely, the RT+ADT group showed the lowest OS rate at 80% and MFS rate at 73% (Table 2).

Healthcare Resource Use and Costs

The mean first-year postdiagnosis direct healthcare costs per patient across all treatment pathways displayed varying trends across different types of healthcare services from 2011 to 2020, as depicted in Figure 1. The mean inpatient care costs across all treatment

Table 1 Patient Demographics and Clinical Characteristics at Diagnosis

	NIT	RP	RT	RT+ADT	Total
Patients, n (%)	5,943 (36.7)	4,208 (26.0)	2,031 (12.5)	4,030 (24.9)	16,212
Age (year), mean (SD)	70.9 (9.4)	64.2 (6.3)	70.5 (7.7)	72.5 (6.6)	69.5 (8.5)
Risk group, n (%)					
Low or intermediate risk	4,045 (68.1)	2,361 (56.1)	1,131 (55.7)	1,099 (27.3)	8,636 (53.3)
High risk	442 (7.4)	1,289 (30.6)	585 (28.8)	2,444 (60.6)	4,760 (29.4)
Unknown	1,456 (24.5)	558 (13.3)	315 (15.5)	487 (12.1)	2,816 (17.4)
PSA (ng/mL), mean (SD)	7.8 (7.7)	10.1 (8.1)	9.5 (8.7)	16.3 (15.4)	10.9 (11.0)
Gleason Score, n (%)					
≤ 6	2,141 (36.0)	587 (13.9)	418 (20.6)	223 (5.5)	3,369 (20.8)
3 + 4	549 (9.2)	967 (23.0)	524 (25.8)	710 (17.6)	2,750 (17.0)
4 + 3	159 (2.7)	625 (14.9)	215 (10.6)	770 (19.1)	1,769 (10.9)
≥ 8	118 (2.0)	449 (10.7)	159 (7.8)	1,084 (26.9)	1,810 (11.2)
Unknown	2,976 (50.1)	1,580 (37.5)	715 (35.2)	1,243 (30.8)	6,514 (40.2)
Clinical risk score, n (%)					
cT1–2a	287 (4.8)	60 (1.4)	50 (2.5)	31 (0.8)	428 (2.6)
cT2b	49 (0.8)	79 (1.9)	140 (6.9)	197 (4.9)	465 (2.9)
cT2c, T3, T4	26 (0.4)	114 (2.7)	78 (3.8)	592 (14.7)	810 (5.0)
Unknown	5,581 (93.9)	3,955 (94.0)	1,763 (86.8)	3,210 (79.7)	14,509 (89.5)
CCI, n (%)					
0	4,410 (74.2)	3,734 (88.7)	1,496 (73.7)	2,872 (71.3)	12,512 (77.2)
1-2	1,270 (21.4)	438 (10.4)	440 (21.7)	972 (24.1)	3,120 (19.2)
3-4	210 (3.5)	31 (0.7)	76 (3.7)	158 (3.9)	475 (2.9)
≥ 5	53 (0.9)	5 (0.1)	19 (0.9)	28 (0.7)	105 (0.6)
Clinical outcomes 5-year OS	2,942 (80.1)	2,330 (95.6)	1,146 (85.9)	1,794 (79.7)	8,212 (84.7)
5-year MFS	2,766 (75.3)	2,179 (89.4)	1,057 (79.2)	1,643 (73.0)	7,645 (78.8)

Abbreviations: ADT = androgen deprivation therapy; CCI = charlson comorbidity index; MFS = metastasis-free survival; NIT = no immediate treatment; OS = overall survival; PSA = prostate-specific antigen; RP = radical prostatectomy; RT = radiotherapy; SD = standard deviation.

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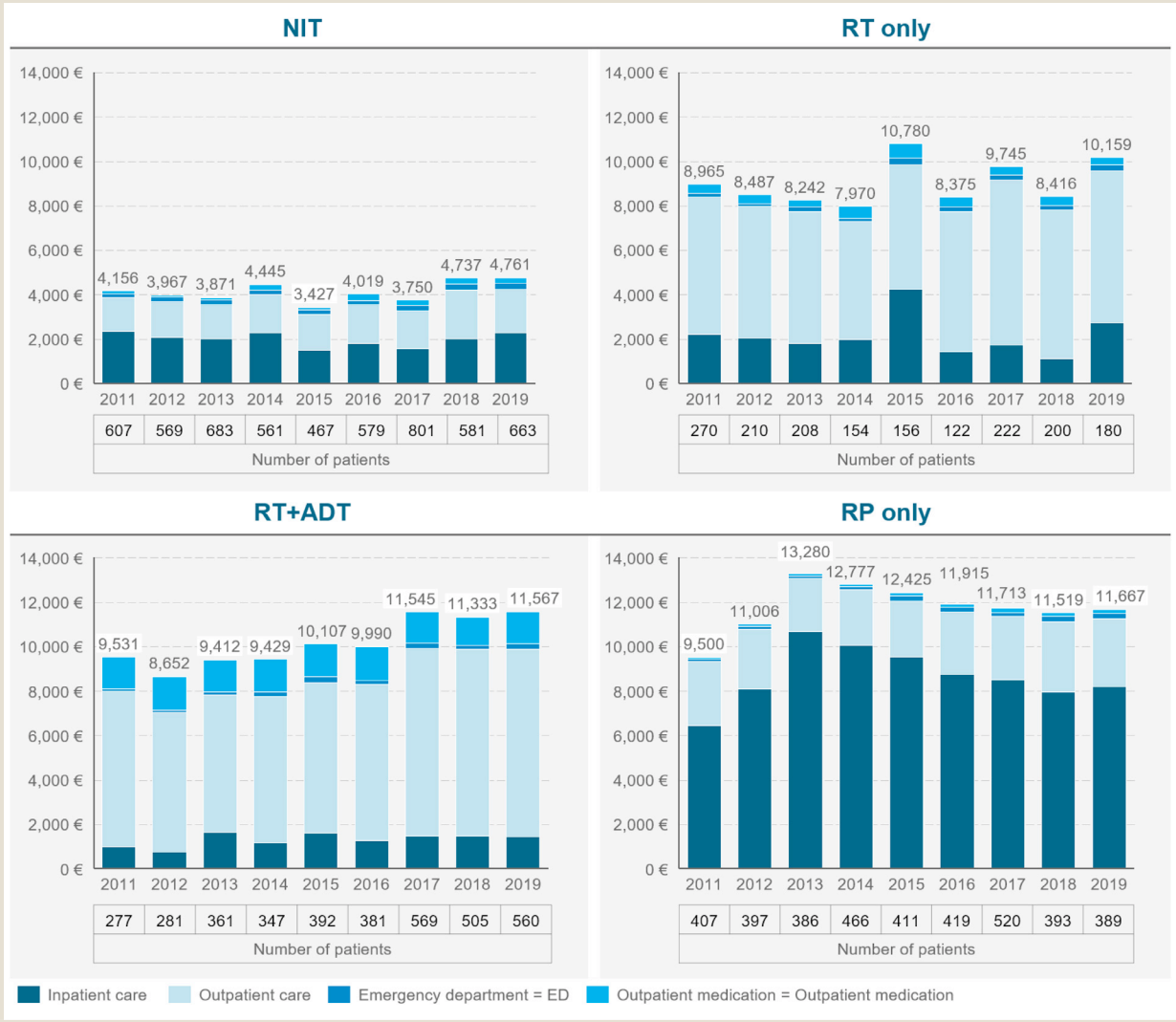
Figure 1 Average cost per patient for the first 12 months after diagnosis grouped by year of diagnosis. ADT = androgen deprivation therapy; NIT = no immediate treatment; RP = radical prostatectomy; RT = radiotherapy.



pathways fluctuated throughout the study period, beginning at €3,157 in 2011, peaking at €4,368 in 2014, and declining to €3,341 by 2019 (Appendix Table 3). The outpatient care costs remained relatively stable until 2015, after which they increased, reaching €4,717 in 2019. Outpatient medication costs steadily rose from €394 in 2011 to €617 in 2019. Emergency department costs also increased, from €136 in 2011 to €255 by 2019. The first-year costs in the different treatment groups show different trends over the years. Notably, all 3 groups receiving treatments (RT only, RT+ADT, and RP only) start at similar levels between €8,900 and 9,500 in 2011 and converge to approximately €11,500 in 2019, with RT only group slightly less costly at €10,150. In RP only group, most of the costs are from inpatient care, whereas the costs for RT+ADT and RT only groups arise mainly from outpatient care. The healthcare resource use in terms of visits and inpatient admissions is described in appendix Figures 4-6.

Mean direct healthcare costs per LPC patient stratified by years since diagnosis are depicted in Figure 2. The highest first-year costs were observed in the RP group (€11,766), followed by RT+ADT (€10,421) and RT only (€9,014). The NIT group incurred significantly lower first-year costs (€4,129) compared to other groups. The mean per-patient-year costs evened out between the groups after the first year. By the fifth year, the cost difference between the highest (RT+ADT €3,944) and lowest (RP €2,663) was €1,281. Within the first-year postdiagnosis, patients in the RP group incurred the highest inpatient care costs (€8,697), which decreased to €966 by the fifth year. The RT+ADT and RT only groups showed high initial outpatient costs (€7,438 and €6,284 respectively) that decreased to €1,166 and €1,003 respectively by the fifth year. The NIT group maintained lower and steadier costs over 5 years. RT+ADT group incurred the highest outpatient medication costs from the first year's €1,431 to the fifth year's €1,148.

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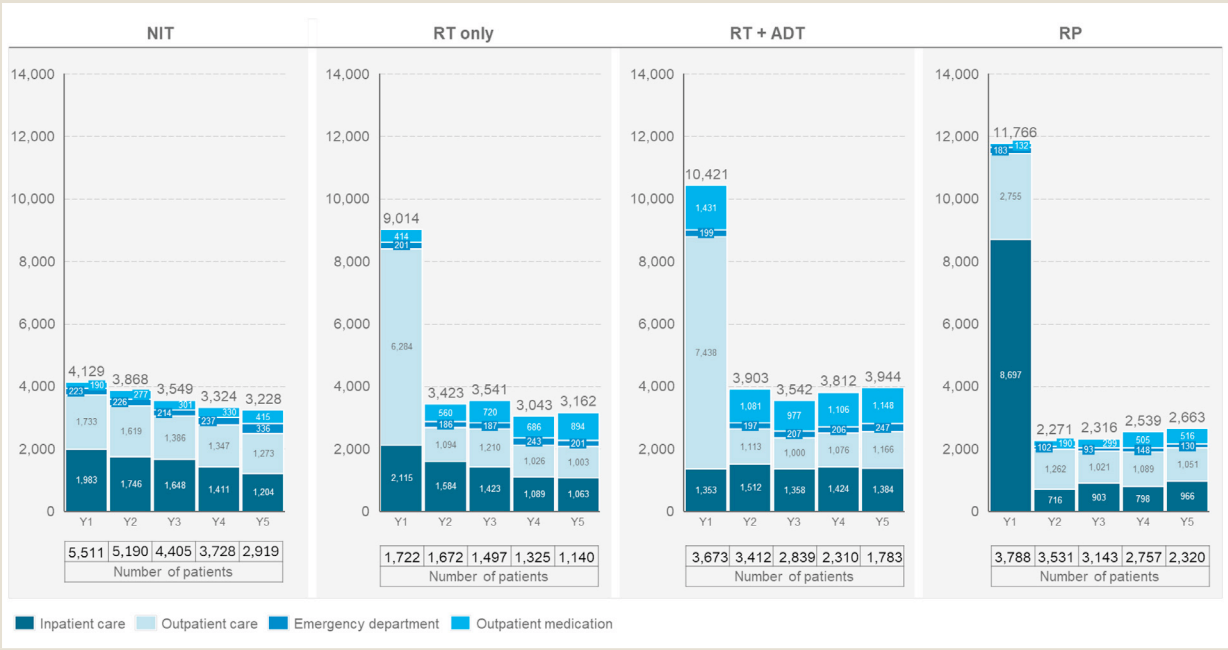
Figure 2 Average direct healthcare costs per patient-year grouped by years since diagnosis. ADT = androgen deprivation therapy; NIT = no immediate treatment; RP = radical prostatectomy; RT = radiotherapy.



Direct healthcare costs 3 years before and after prostate cancer metastasis are depicted in Figure 3. Costs showed an increasing trend postmetastasis, with inpatient care and outpatient medication constituting major expense components. For instance, in the RT only group, total costs increased from €2,291 three years prior to metastasis to €13,249 one year before metastasis, an increase of 478%. Increases were also observed in the RT+ADT, the RP, and the NIT groups, with increases of 86%, 67%, and 110% respectively. Postmetastasis, there was a significant increase in costs across all groups; the most substantial increase occurred in the RP group, where costs rose from €9,075 one year before metastasis to €37,767 (+316%) one year after metastasis. Across all groups, the increase in costs postmetastasis was mainly due to higher outpatient medication costs. Notably, in the RT only group, outpatient medication costs began to rise 1 year prior to metastasis. In most groups, inpatient care costs also increased after metastasis (Tables 4 and 5).

Discussion

This retrospective study analyzed healthcare resource utilization and costs for LPC patients in Finland based on their initial treatment. Using data from the 5 university hospitals and the Social Insurance Institution, it provides insights into the economic burden of prostate cancer in the Finnish healthcare system.

The findings highlight high direct healthcare costs in the first-year postdiagnosis, with the RP group having the highest costs. Costs across the active treatment groups, were driven by inpatient and outpatient care. Over time, inpatient care costs decreased, with outpatient medication costs, especially in the RT+ADT group, becoming a key differentiator, contributing around €1,000 annually. The NIT group had the lowest first-year costs, which remained steady over time. As this study includes all secondary healthcare costs, costs from the NIT group to some extent reflect the baseline costs for LPC patients.

The study highlights the significant increase in healthcare costs associated with metastasis, with yearly costs of up to €40,000 per patient postmetastasis. The surge in costs postmetastasis reflects the complex and resource-intensive interventions required to manage advanced-stage disease, including increased reliance on inpatient care and outpatient medications. Our findings are consistent with Trinh et al.,[12] who reported an increase in costs ranging from 2 to 7 fold as prostate cancer progressed from nonmetastatic to metastatic stages. A pre-emptive increase in healthcare costs was observed 1 to 2 years prior to the confirmed metastasis date, suggesting difficulties in pinpointing the precise onset of metastasis from the structured medical records and potential deterioration in patient health preceding formal diagnosis. This aligns with findings from both Trinh et al.[12] and Kaye et al.,[13] who also observed rising costs prior to advanced-stage or first-line therapy initiation. These findings emphasize the need for early detection and prevention of metastases to not only prevent mortality from PC but also to manage costs associated with advanced stage disease.

The mean first-year cost across all treatment groups was €8,220. With 5,000 new prostate cancer cases annually in Finland, this translates to €41 million in direct healthcare costs for incident cases in the first year alone. To fully understand the economic burden of prostate cancer, it's also important to consider the costs associated

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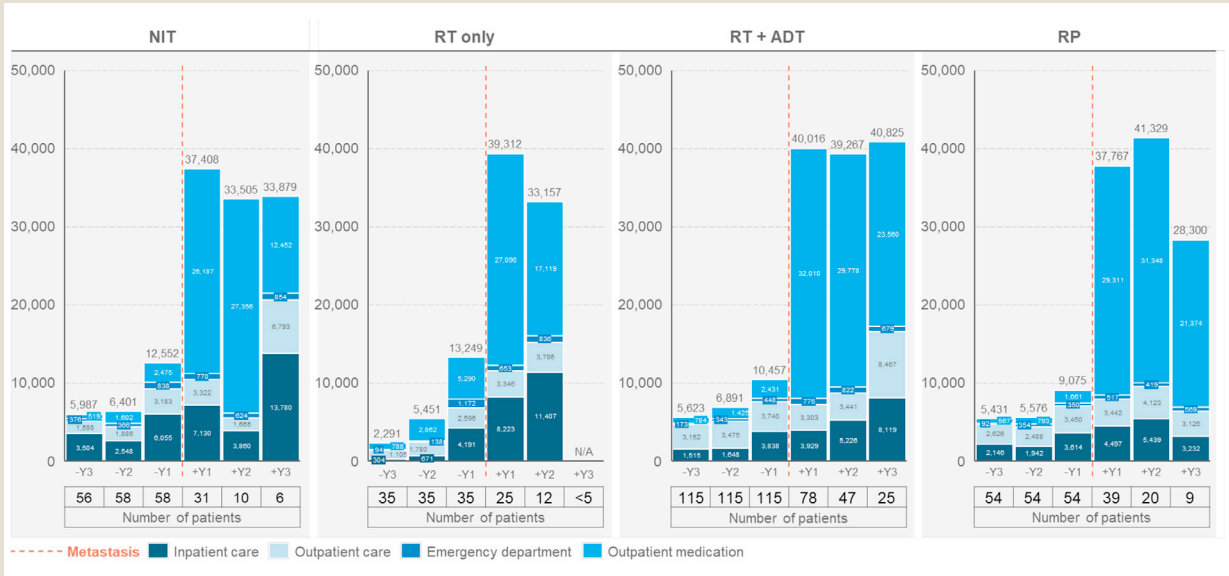
Figure 3 Average direct healthcare costs per patient-year 3 years before and after metastasis. ADT = androgen deprivation therapy; NIT = no immediate treatment; RP = radical prostatectomy; RT = radiotherapy.



with prevalent cases, which significantly impact long-term healthcare utilization. The Cancer Foundation Finland estimated total costs for malignant neoplasms of male genital organs (C60-C63) at €162 million, which includes costs for both incident and prevalent prostate cancer cases, as well as other related conditions.

Hamdy et al.[4] found that although the active monitoring group had a higher incidence of metastases than those treated with radical prostatectomy or radiotherapy, prostate cancer-related deaths remained low. In this study, we were unable to reliably identify active surveillance patients, resulting in the NIT group including both patients under active surveillance and those who did not initiate treatment due to other factors, such as poor health. However, our findings suggest that active surveillance incurs lower costs compared to active treatments, warranting further investigation into resource utilization in this group.

Limitations of this study include its retrospective design and the reliance on register data, which may not capture all nuances of patient care and outcomes. In addition, as in any register study, there may be limitations associated with completeness and accuracy of data reporting. For example, the identification of metastatic disease solely using ICD-10 codes was not accurate due to inconsistent reporting in patient records. Consequently, proxy variables were incorporated to improve the identification of metastasis timing, although this method does not fully remove the potential misclassification bias. However, the registers used in this study are assumed to be of high quality and cover the entire population of Finland. Lastly, our effort to avoid bias due to end-of-life costs by excluding patients who died during the follow-up may slightly underestimate costs, but given the low annual mortality rate (n = 318-419, 2.3%-5.1 %), the impact is likely minimal. Future studies would benefit from incorporating patient-reported outcomes and quality of life measures to provide a more comprehensive assessment of treatment impact.

Conclusions

This study provided a detailed description of the economic dimensions of prostate cancer treatment in Finland, highlighting significant cost variations among different treatment pathways. Treatment of prostate cancer, especially the metastatic disease, incurs significant direct healthcare costs and therefore effective patient management is essential for cost containment.

Clinical Practice Points

- What is already known about this subject?
  Treatment decisions for localized prostate cancer impact long-term outcomes and healthcare costs, but real-world cost data comparing different treatment pathways remain limited.
- What are the new findings?
  First-year costs are highest for radical prostatectomy (€11,766) and radiotherapy with androgen deprivation therapy (€10,421), while metastatic disease significantly increases costs, particularly due to outpatient medication.
- How might it impact clinical practice?
  Understanding cost variations between treatment options can support evidence-based decision-making and healthcare resource planning for localized prostate cancer.

Disclosure

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Tuukka Hakkarainen, Paula Pennanen, Mari Lahelma and Riikka-Leena Leskelä have received consulting fees paid directly to

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CRediT authorship contribution statement

Teemu J. Murtola: Writing – review & editing, Validation. **Tuukka Hakkarainen:** Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Conceptualization. **Mari Lahelma:** Writing – original draft, Software, Formal analysis, Data curation. **Paula Pennanen:** Writing – original draft, Validation, Supervision, Methodology. **Riikka-Leena Leskelä:** Project administration, Conceptualization. **Mika Pietilä:** Writing – review & editing, Validation, Funding acquisition, Conceptualization. **Petteri Hervonen:** Writing – review & editing, Validation, Funding acquisition, Conceptualization. **Okko-Sakari Kääriäinen:** Writing – review & editing, Validation. **Heikki Minn:** Writing – review & editing, Validation. **Timo K. Nykopp:** Writing – review & editing, Validation. **Hanna Ronkainen:** Writing – review & editing, Validation. **Otto Ettala:** Writing – review & editing, Validation. **Antti Rannikko:** Writing – review & editing, Validation.

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Supplementary Materials

Figure 4 Outpatient visits per 1,000 LPC patients for the first 12 months after diagnosis grouped by year of diagnosis. ADT = androgen deprivation therapy; NIT = no immediate treatment; RP = radical prostatectomy; RT = radiotherapy.

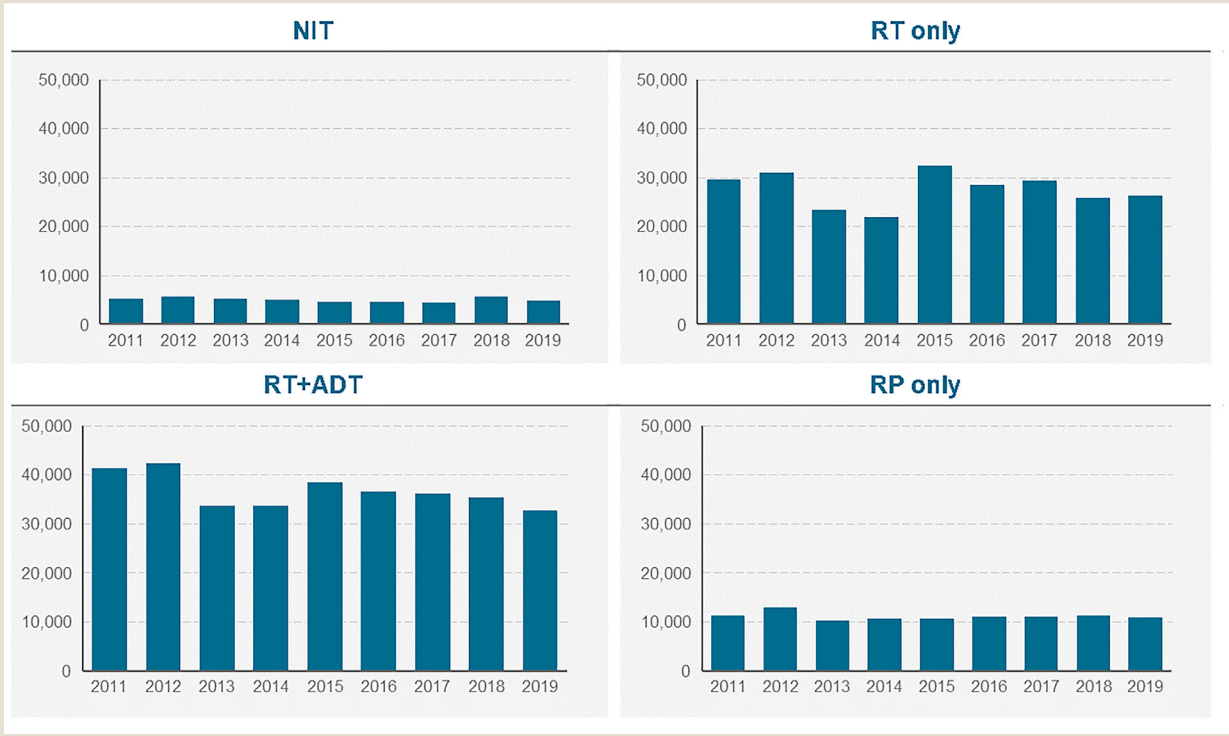

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Figure 5 Inpatient admissions per 1,000 LPC patients for the first 12 months after diagnosis grouped by year of diagnosis. NIT: No immediate treatment, RT: Radiotherapy, ADT: Androgen deprivation therapy, RP: Radical prostatectomy.

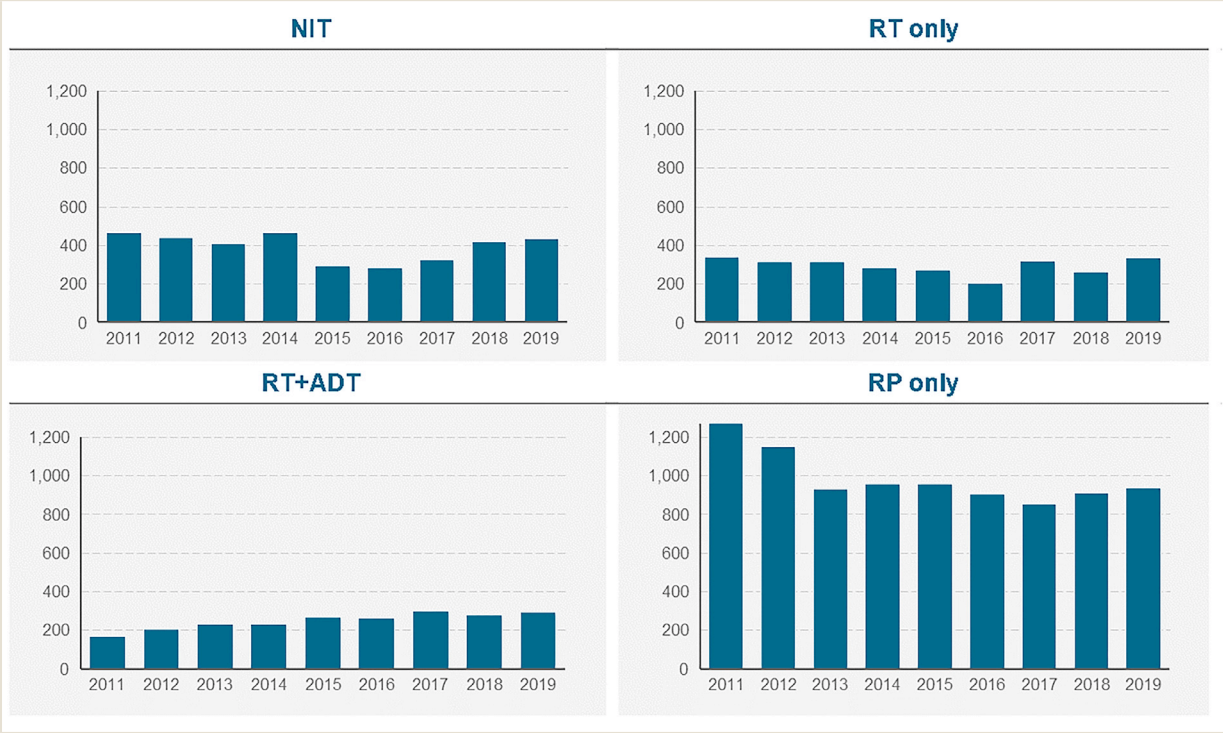

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Figure 6 Emergency department visits per 1,000 LPC patients for the first 12 months after diagnosis grouped by year of diagnosis. NIT: No immediate treatment, RT: Radiotherapy, ADT: Androgen deprivation therapy, RP: Radical prostatectomy.

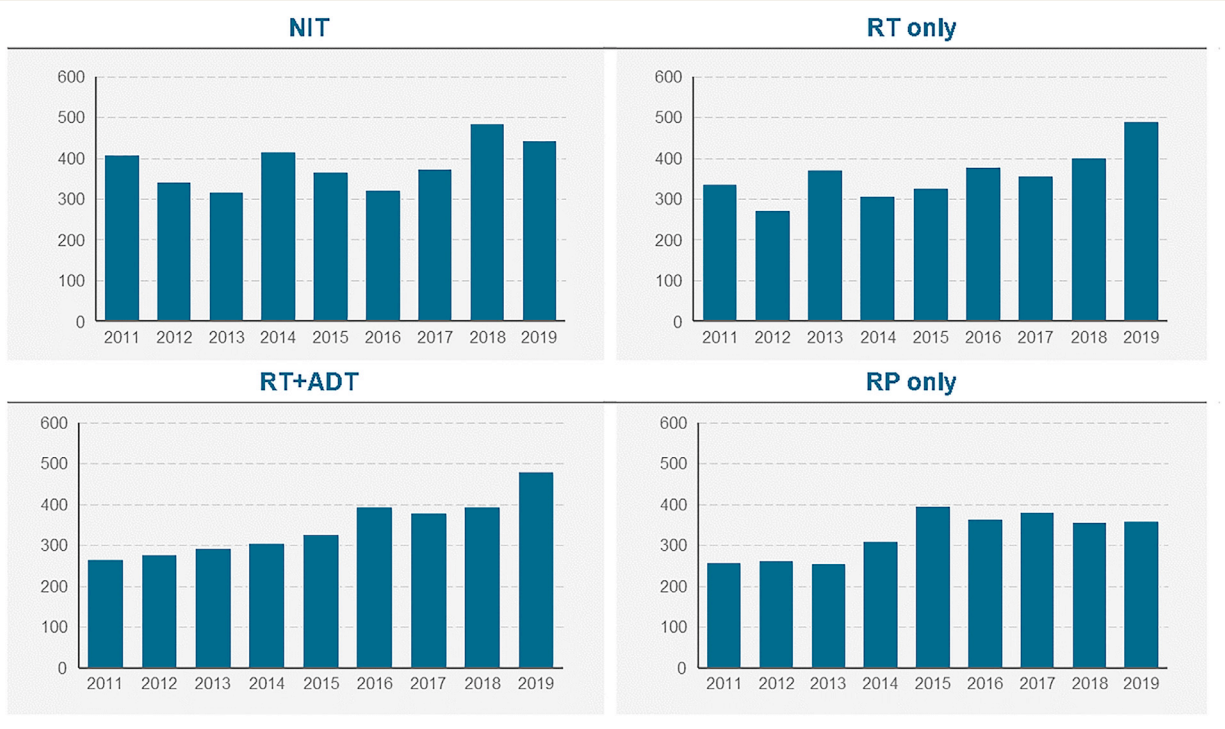

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Table 2 Patient Characteristics by Diagnosis Year

	2011	2012	2013	2014	2015	2016	2017	2018	2019	Total
Patients, n (%)	1,561 (9.6)	1,457 (9.0)	1,957 (12.1)	1,873 (11.6)	1,764 (10.9)	2,017 (12.4)	2,112 (13.0)	1,679 (10.4)	1,792 (11.1)	16,212
Age (year), mean (SD)	68.7 (8.7)	69.3 (8.9)	69.1 (8.3)	68.7 (8.5)	69.5 (8.1)	69.8 (8.3)	69.9 (8.4)	70.0 (8.4)	70.5 (8.5)	69.5 (8.5)
Treatment pathway, n (%)										
NIT	607 (38.9)	569 (39.1)	761 (38.9)	654 (34.9)	548 (31.1)	759 (37.6)	801 (37.9)	581 (34.6)	663 (37.0)	5,943 (36.7)
RP	270 (17.3)	210 (14.4)	286 (14.6)	232 (12.4)	212 (12.0)	219 (10.9)	222 (10.5)	200 (11.9)	180 (10.0)	2,031 (12.5)
RT	277 (17.7)	281 (19.3)	425 (21.7)	429 (22.9)	491 (27.8)	493 (24.4)	569 (26.9)	505 (30.1)	560 (31.2)	4,030 (24.9)
RT+ADT	407 (26.1)	397 (27.2)	485 (24.8)	558 (29.8)	513 (29.1)	546 (27.1)	520 (24.6)	393 (23.4)	389 (21.7)	4,208 (26.0)
Risk group, n (%)										
Low or intermediate risk	763 (48.9)	631 (43.3)	1,081 (55.2)	999 (53.3)	985 (55.8)	1,162 (57.6)	1,212 (57.4)	930 (55.4)	873 (48.7)	8,636 (53.3)
High risk	347 (22.2)	359 (24.6)	499 (25.5)	544 (29.0)	589 (33.4)	631 (31.3)	646 (30.6)	557 (33.2)	588 (32.8)	4,760 (29.4)
Unknown	451 (28.9)	467 (32.1)	377 (19.3)	330 (17.6)	190 (10.8)	224 (11.1)	254 (12.0)	192 (11.4)	331 (18.5)	2,816 (17.4)
PSA (ng/mL), mean (SD)	11.1 (11.6)	11.0 (11.0)	10.2 (10.2)	10.8 (10.5)	11.1 (11.3)	10.7 (10.8)	10.4 (10.3)	11.3 (11.4)	11.7 (12.5)	10.9 (11.0)
Gleason Score, n (%)										
≤6	287 (18.4)	252 (17.3)	451 (23.0)	383 (20.4)	378 (21.4)	495 (24.5)	488 (23.1)	353 (21.0)	282 (15.7)	3,369 (20.8)
3 + 4	207 (13.3)	136 (9.3)	295 (15.1)	311 (16.6)	383 (21.7)	415 (20.6)	412 (19.5)	321 (19.1)	270 (15.1)	2,750 (17.0)
4 + 3	135 (8.6)	143 (9.8)	184 (9.4)	202 (10.8)	218 (12.4)	237 (11.8)	249 (11.8)	215 (12.8)	186 (10.4)	1,769 (10.9)
≥8	108 (6.9)	127 (8.7)	166 (8.5)	213 (11.4)	252 (14.3)	270 (13.4)	235 (11.1)	206 (12.3)	233 (13.0)	1,810 (11.2)
Unknown	824 (52.8)	799 (54.8)	861 (44.0)	764 (40.8)	533 (30.2)	600 (29.7)	728 (34.5)	584 (34.8)	821 (45.8)	6,514 (40.2)
Clinical risk score, n (%)										
cT1–2a	19 (1.2)	22 (1.5)	44 (2.2)	37 (2.0)	61 (3.5)	51 (2.5)	66 (3.1)	77 (4.6)	51 (2.8)	428 (2.6)
cT2b	25 (1.6)	18 (1.2)	50 (2.6)	42 (2.2)	58 (3.3)	66 (3.3)	89 (4.2)	62 (3.7)	55 (3.1)	465 (2.9)
cT2c, T3, T4	51 (3.3)	56 (3.8)	65 (3.3)	76 (4.1)	102 (5.8)	104 (5.2)	109 (5.2)	103 (6.1)	144 (8.0)	810 (5.0)
Unknown	1,466 (93.9)	1,361 (93.4)	1,798 (91.9)	1,718 (91.7)	1,543 (87.5)	1,796 (89.0)	1,848 (87.5)	1,437 (85.6)	1,542 (86.0)	14,509 (89.5)
CCI, n (%)										
0	1,326 (84.9)	1,189 (81.6)	1,556 (79.5)	1,448 (77.3)	1,373 (77.8)	1,517 (75.2)	1,590 (75.3)	1,248 (74.3)	1,265 (70.6)	12,512 (77.2)
1-2	198 (12.7)	222 (15.2)	340 (17.4)	353 (18.8)	333 (18.9)	431 (21.4)	437 (20.7)	370 (22.0)	436 (24.3)	3,120 (19.2)
3-4	32 (2.0)	36 (2.5)	53 (2.7)	60 (3.2)	48 (2.7)	51 (2.5)	69 (3.3)	49 (2.9)	77 (4.3)	475 (2.9)
≥5	5 (0.3)	10 (0.7)	8 (0.4)	12 (0.6)	10 (0.6)	18 (0.9)	16 (0.8)	12 (0.7)	14 (0.8)	105 (0.6)

Abbreviations: ADT = androgen deprivation therapy; CCI = charlson comorbidity index; NIT = no immediate treatment; PSA = prostate-specific antigen; RP = radical prostatectomy; RT = radiotherapy; SD = standard deviation.

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Table 3 Average Cost (€) Per Patient for the First 12 Months After Diagnosis Grouped by Year of Diagnosis

Calendar year	2011	2012	2013	2014	2015	2016	2017	2018	2019
NIT									
Inpatient care	2,366	2,068	2,016	2,292	1,497	1,792	1,561	1,998	2,272
Outpatient care	1,509	1,611	1,528	1,710	1,622	1,760	1,704	2,192	1,963
Emergency department	174	209	229	197	199	182	240	284	278
Outpatient medication	108	79	98	247	108	286	245	263	247
Total costs	4,156	3,967	3,871	4,445	3,427	4,019	3,750	4,737	4,761
RT only									
Inpatient care	2,208	2,058	1,814	1,959	4,252	1,429	1,723	1,119	2,723
Outpatient care	6,182	5,917	5,914	5,337	5,567	6,319	7,431	6,693	6,838
Emergency department	155	121	210	138	321	209	230	199	264
Outpatient medication	420	391	305	536	640	418	361	406	334
Total costs	8,965	8,487	8,242	7,970	10,780	8,375	9,745	8,416	10,159
RT + ADT									
Inpatient care	977	742	1,648	1,154	1,603	1,256	1,485	1,464	1,438
Outpatient care	6,997	6,274	6,156	6,598	6,762	7,044	8,441	8,396	8,449
Emergency department	105	122	162	187	291	187	238	195	222
Outpatient medication	1,453	1,513	1,446	1,489	1,452	1,503	1,381	1,278	1,459
Total costs	9,531	8,652	9,412	9,429	10,107	9,990	11,545	11,333	11,567
RP only									
Inpatient care	6,453	8,088	10,652	10,055	9,522	8,735	8,511	7,955	8,186
Outpatient care	2,876	2,681	2,399	2,496	2,504	2,811	2,839	3,156	3,057
Emergency department	91	124	131	149	259	221	169	248	261
Outpatient medication	80	113	98	78	140	149	195	159	164
Total costs	9,500	11,006	13,280	12,777	12,425	11,915	11,713	11,519	11,667

Abbreviations: ADT = androgen deprivation therapy; NIT = no immediate treatment; RP = radical prostatectomy; RT = radiotherapy.

Table 4 Average Direct Healthcare Costs Per Patient-Year Grouped by Years Since Diagnosis

Group	Years Since Diagnosis	Inpatient Care	Outpatient Care	Emergency Department	Outpatient Medication	Total Costs
NIT	1Y	1,983	1,733	223	190	4,129
	2Y	1,746	1,619	226	277	3,868
	3Y	1,648	1,386	214	301	3,549
	4Y	1,411	1,347	237	330	3,324
	5Y	1,204	1,273	336	415	3,228
RT only	1Y	2,115	6,284	201	414	9,014
	2Y	1,584	1,094	186	560	3,423
	3Y	1,423	1,210	187	720	3,541
	4Y	1,089	1,026	243	686	3,043
	5Y	1,063	1,003	201	894	3,162
RT + ADT	1Y	1,353	7,438	199	1,431	10,421
	2Y	1,512	1,113	197	1,081	3,903
	3Y	1,358	1,000	207	977	3,542
	4Y	1,424	1,076	206	1,106	3,812
	5Y	1,384	1,166	247	1,148	3,944
RP (+ADT)	1Y	8,697	2,755	183	132	11,766
	2Y	716	1,262	102	190	2,271
	3Y	903	1,021	93	299	2,316
	4Y	798	1,089	148	505	2,539
	5Y	966	1,051	130	516	2,663

Abbreviations: ADT = androgen deprivation therapy; NIT = no immediate treatment; RP = radical prostatectomy; RT = radiotherapy.

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Table 5 Average Direct Healthcare Costs Per Patient-Year Three Years Before and After Metastasis

All Patients	Years Before/After Metastasis	Inpatient Care	Outpatient Care	Emergency Department	Outpatient Medication	Total Costs
NIT	−3Y	3,504	1,588	376	519	5,987
	−2Y	2,548	1,886	366	1,602	6,401
	−1Y	6,055	3,183	838	2,475	12,552
	1Y	7,130	3,322	770	26,187	37,408
	2Y	3,860	1,665	624	27,356	33,505
	3Y	13,780	6,793	854	12,452	33,879
RT only	−3Y	304	1,105	94	788	2,291
	−2Y	671	1,780	138	2,862	5,451
	−1Y	4,191	2,596	1,172	5,290	13,249
	1Y	8,223	3,346	653	27,090	39,312
	2Y	11,407	3,795	836	17,119	33,157
	3Y	N/A	N/A	N/A	N/A	N/A
RT + ADT	−3Y	1,515	3,152	173	784	5,623
	−2Y	1,648	3,475	343	1,425	6,891
	−1Y	3,838	3,740	448	2,431	10,457
	1Y	3,929	3,303	775	32,010	40,016
	2Y	5,226	3,441	822	29,778	39,267
	3Y	8,119	8,467	679	23,560	40,825
RP (+ADT)	−3Y	2,146	2,626	92	567	5,431
	−2Y	1,942	2,488	354	793	5,576
	−1Y	3,614	3,450	350	1,661	9,075
	1Y	4,497	3,442	517	29,311	37,767
	2Y	5,439	4,123	419	31,348	41,329
	3Y	3,232	3,126	569	21,374	28,300

Abbreviations: ADT = androgen deprivation therapy; NIT = no immediate treatment; RP = radical prostatectomy; RT = radiotherapy.

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