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Real-world treatment patterns and medical costs of prostate cancer patients in Switzerland – A claims data analysis

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ABSTRACT

Background: Prostate cancer (PC) is the most prevalent cancer in men in Switzerland. However, evidence on the real-world health care use of PC patients is scarce. The aim of this study is to describe health care utilization, treatment patterns, and medical costs in PC patients over a period of five years (2014–2018).

Method: We used routinely collected longitudinal individual-level claims data from a major provider of mandatory health insurance in Switzerland. Due to the lack of diagnostic coding in the claims data, we identified treated PC patients based on the treatments received. We described health care utilization and treatment pathways for patients with localized and metastatic PC. Costs were calculated from a health care system perspective.

Results: A total of 5591 PC patients met the inclusion criteria. Between 2014 and 2018, 1741 patients had outpatient radiotherapy for localized or metastatic PC and 1579 patients underwent radical prostatectomy. 3502 patients had an androgen deprivation therapy (ADT). 9.5% of these patients had a combination therapy with docetaxel, and 11.0% had a combination with abiraterone acetate. Docetaxel was the most commonly used chemotherapy (first-line; n = 413, 78.4% of all patients in chemotherapy). Total medical costs of PC in Switzerland were estimated at CHF 347 m (95% CI 323–372) in 2018.

Conclusion: Most PC patients in this study were identified based on the use of ADT. Medical costs of PC in Switzerland amounted to 0.45% of total health care spending in 2018. Treatment of metastatic PC accounted for about two thirds of spending.

1. Introduction

Prostate cancer (PC) is the most common cancer in men worldwide and a frequent cause of death in high income countries [1,2]. The number of incident cases in Switzerland has stabilized recently, in spite of a growing and aging population, while age-adjusted incidence and mortality rates have decreased [3,4]. The Swiss National Agency for Cancer Registration estimates an average annual 6649 incident cases for

Abbreviations: ADT, Androgen Deprivation Therapy; AL, Swiss List of Analyses (holds laboratory analyses covered by mandatory health insurance); ATC, Anatomical therapeutic chemical; CHF, Swiss francs; mCRPC, (Metastatic) Castration-resistant prostate cancer; CT, Computed Tomography; DRG, Diagnosis-related group; EUR, Euro; mHSPC, (Metastatic) Hormone-sensitive prostate cancer; locPC, Localized prostate cancer; m, Million; metPC, Metastatic prostate cancer; MHI, Mandatory health insurance; mpMRI, Multiparametric Magnetic Resonance Imaging; OS, Overall survival; PC, Prostate cancer; PSA, Prostate-specific antigen; RPE, Radical prostatectomy; RT, Radiotherapy; TARMED, Tarif médical (outpatient tariff system for physician services).

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the period 2014–2018 [4] and a 10-year-prevalence of 48,412 cases in 2018 [5]. There were on average 1352 deaths per year due to PC between 2014 and 2018 [6].

The past decade has seen important changes in the screening for PC and in its treatment. A large European trial showed that routine screening for prostate-specific antigen (PSA) could reduce cancer mortality [7]. However, screening is controversial as it could lead to substantial harm due to over-diagnosis, unnecessary prostate biopsies and over-treatment [8,9]. These findings led to a recommendation against routine PSA-screening in many populations [10–12]. Currently, there are no screening recommendations in Switzerland. After publication of the US preventive services task force recommendation against PSA based prostate cancer screening 2012 the Swiss Society of Urology (SGU/SSU) published a statement on PSA-based PC case finding [13]. In the light of current efforts of the European Community to establish a sound PC screening program, an update of these recommendations is forthcoming. One study investigated the time trends in PC screening in Swiss primary care from 2010 to 2017 and reported the decline in PSA screening practices based on updated recommendations [14]. There is also a consensus that active surveillance should be the preferred management option in patients with low risk PC [11,15,16].

Several new drugs improving the overall survival (OS) of patients with metastatic PC (metPC) have been introduced in the last decade [17]. Androgen deprivation therapy (ADT) is still the basis for treatment of metPC. The CHAARTED study showed that ADT combined with docetaxel increases the median OS significantly [18]. The STAMPEDE trial confirmed these results [19]. Several studies documented benefits in terms of OS when ADT was combined with abiraterone or enzalutamide [20–24]. Additional studies were published after 2017, but they are not relevant for our 2014–2018 study period. Five substances were demonstrated to improve OS for patients with metastatic castration-resistant PC (mCRPC): The two chemotherapeutic agents docetaxel and cabazitaxel, the alpha emitter radium-223 and the inhibitors of the androgen receptor pathway abiraterone and enzalutamide. The optimal sequence of therapies has been investigated in recent studies [25,26].

The prices of these treatments are substantial. Evidence on the real-world utilization and costs of PC patients in Switzerland is scarce. This study aims at describing the real-world utilization and direct medical costs of treated PC patients between 2014 and 2018 based on health insurance claims data.

2. Data and methods

2.1. Data

We used anonymized and de-identified mandatory health insurance (MHI) claims data from Helsana, a major health insurer with a market share of about 14% in 2018. Claims data hold detailed patient level information on all treatments, diagnostic procedures and drugs covered by MHI. Although claims data contain no diagnostic coding, they contain diagnostic clues identifying many diseases [27]. These clues include the type of drugs and health services used. Claims data also hold information on the time of treatments and on the age (in 5-years bins), sex and date of death of the insured. Random noise was added to the dates of service provision and of death to preclude the identification of individuals.

2.2. Identification of treated PC patients and PC treatments

We selected individuals from the insurance claims data base who met the following three criteria: 1) male and at least 40 years old on January 1st 2014, 2) insured continuously until December 31st 2018 or deceased within the five years, 3) at least one billed PSA test and at least one diagnostic clue for a PC-specific treatment (e.g., hormonal therapy).

We identified PC-specific procedures and treatments based on their billing codes in national tariff catalogs. The TARMED catalog [28] was used for physician services such as prostate biopsies, and the Swiss List of Analyses [29] for laboratory tests such as PSA tests. Drugs were identified based on the Anatomical Therapeutic Chemical (ATC) substance classification.

Table A2 in the supplementary information lists the billing codes used to identify treated PC patients. Table A3 in the supplementary information lists treatments and diagnostic procedures identified as additional PC-related services in patients previously identified as treated PC patients.

We distinguished between patients with localized (locPC) and metastatic PC (metPC), based on the type of treatment received (Table 1). The treatment regimen was determined at the end of each half-year of the 5-year period. When a patient showed only unspecific diagnostic procedures (e.g., PSA test), we assigned the regimen of the preceding half-year. Patients who underwent a treatment for locPC before 2014 (e.g., RPE) may not be identified as prevalent PC patients at the start of the study period, but only when they used PC-specific treatments at a later stage (e.g., ADT). A distinction of patients with ADT in locPC and in metastatic hormone-sensitive PC (mHSPC) was not possible. When ADT was taken before or at the same time as the patient underwent RPE or RT for locPC, the patient was classified as a locPC.

We analyzed the number of patients using PC-related services and the number of services / prescriptions per patient (and year).

2.3. Estimation of medical costs

We estimated the medical costs of PC with a prevalence-based bottom-up approach taking a health care system perspective. Costs are reported in Swiss francs (CHF). Average annual exchange rates were 1.215 CHF/EUR in 2014 and 1.155 CHF/EUR in 2018 [30].

The costs were calculated multiplying the tariff points/cost weights according to the national tariff catalogues by average tax point values (for physician services in TARMED, laboratory tests in the AL catalogue, and hospital inpatient treatments) or using the prices from the list of medications (Spezialitätenliste) for drugs. Details on the cost estimation methodology can be found in the supplementary material (Section 2.3).

We estimated total costs for PC by year as well as by stage (locPC and metPC). In addition, we reported mean costs per patient and calendar year for four groups of patients: 1) metPC patients who used one of five substances (docetaxel, cabazitaxel, abiraterone, enzalutamide, and radium-223), and locPC with 2) RPE without RT in the same year, 3) RPE and RT in the same year, 4) RT and no RPE in the same year.

Table 1
Classification by treatment regimen by type of treatment.

Service category	Treatment regimen
Radical prostatectomy (RPE)	locPC
Brachytherapy	locPC
Radiotherapy (RT), external beam (>=20 applications)	locPC
Radiotherapy (RT), external beam (<20 applications) *	metPC
Radiotherapy (RT), stereotactic	metPC
Hormonal therapy: androgen-deprivation and anti-androgen therapy * *	metPC
Hormonal therapy: abiraterone, enzalutamide	metPC
Bone metastases treatment: denosumab, zoledronic acid, radium-223	metPC
Chemotherapy	metPC
Unspecific diagnostic procedures after active treatment	locPC/metPC

* We assumed that hypofractionation in locPC was not used frequently in the study period.

* * When hormonal therapy was taken before or at the same time as the patient underwent the RPE or RT for locPC, the patient was still classified as a locPC. Patients were classified as metPC if hormonal therapy was the sole treatment. Substances included: bicalutamide (anti-androgen), degarelix, goserelin, leuprorelin, triptorelin (androgen-deprivation)

Total medical costs according to claims data were extrapolated to the national level.

3. Results

We identified 5591 treated PC patients in the 5-year period from 2014 to 2018. 40.7% of all PC patients in 2018 were classified as locPC patients. 20.3% of locPC patients and 5.8% of metPC patients were younger than 65 years. 1385 patients (24.8%) died in the 5-year period (cause of death unknown).

3.1. Health care use and pathways

Table 2 shows the use of PC-related services and drugs in the sample (n = 5591). Patients used PC-related services for a period ranging from one to five years. The table shows (1) the number of patients who had at least one use of a service or drug, (2) the median, first and third quartile of the number of services/prescriptions per patient during time in sample and (3) the same figures for the years with any PC service use.

3.1.1. Prostatectomy and radiotherapy

Between 2014 and 2018, 1579 patients (28.2% of study population, Table 2) underwent RPE. Most patients (56.4%) were between 65 and 74 years old. 9.4% of surgeries were performed in patients above age 75, and 14.3% in patients below age 60.

In the same period, 1741 patients (31.1%) had at least one outpatient RT (external beam or stereotactic, see Table 2). 42.8% of the patients were between 65 and 74 years old at the time of their first RT. The proportion was 40.2% for those aged 75 or older.

The median number of RT per patient stayed constant over time at around 33–35 treatment sessions, depending on the year the treatment started. We observed peaks at 5, 10, 20, 33–35, and 39 applications. The median RT duration was 48–53 days.

We defined RPE or RT as index treatments and investigated how many patients had any subsequent PC treatment and the time between the index and the subsequent treatments (Table 3). For RT, only patients with at least 20 consecutive RT sessions were included (n = 1169). After RPE, 348 patients (22.0%) had another PC treatment within the study period. The most common subsequent treatment after RPE was RT with 291 patients. For 170 patients, it was the first treatment after surgery (most likely adjuvant or salvage radiotherapy). On average, 447 days (median: 304) passed before postoperative RT after RPE. After RT, 582 patients (49.8%) had another PC treatment within the study period. Most patients (n = 545) had a hormonal therapy after RT. Few patients underwent chemotherapy after RT (n = 59).

3.1.2. Medication for PC

3.1.2.1. Androgen deprivation therapy. 3502 patients (62.6%) had an ADT. 37.1% of them had the first ADT in the first half of 2014, and thus the start of the therapy was possibly unobserved. After mid-2014, there were about 200–300 patients starting an ADT each half year. The mean (median) ADT duration was 657 (531) days for all ADT patients, and 495

Table 2
Overview of PC-specific service and drug use.

	(1) number of patients with at least one use	(2) use per patient for years in sample			(3) use per patient and year for years with positive use		
	N (share of total in %)	**Median**	**Q1**	**Q3**	**Median**	**Q1**	**Q3**
Laboratory test							
PSA	5591 (100)	9.00	5.00	14.00	2.20	1.50	3.50
Outpatient procedures							
Biopsy	2210 (40)	1.00	1.00	1.00	0.25	0.20	0.40
CT abdomen	2597 (46)	1.00	1.00	3.00	0.40	0.20	1.00
CT planning	1698 (30)	1.00	1.00	2.00	0.33	0.20	0.80
CT thorax	2232 (40)	2.00	1.00	4.00	0.50	0.20	1.00
Implantation of gold markers	156 (3)	1.00	1.00	1.50	-	-	-
MRI full	73 (1)	1.00	1.00	1.00	0.25	0.20	0.40
MRI MP	2464 (44)	1.00	1.00	2.00	0.25	0.20	0.50
PET-CT	1018 (18)	2.00	1.00	3.00	0.50	0.25	1.00
Radiotherapy (external beam)	1602 (29)	33.00	14.00	38.00	7.20	4.00	9.25
Radiotherapy (stereotactic)	316 (6)	1.00	1.00	1.50	0.25	0.20	0.40
SPECT	1376 (25)	1.00	1.00	2.00	0.25	0.20	0.40
Drugs							
Abiraterone	481 (9)	8.00	4.00	13.00	2.33	1.20	4.50
Bicalutamide	2562 (46)	1.00	1.00	3.00	0.40	0.20	1.00
Cabazitaxel	140 (3)	5.00	3.00	10.00	2.00	1.00	3.20
Carboplatin	102 (2)	7.00	4.00	12.00	2.13	1.00	5.00
Cyproterone	195 (3)	2.00	1.00	3.00	0.50	0.20	1.00
Degarelix	157 (3)	7.00	3.00	18.00	2.00	0.80	5.50
Denosumab	1220 (22)	8.00	3.00	17.00	2.00	1.00	5.55
Dexamethasone	1173 (21)	5.00	2.00	14.00	1.50	0.40	4.50
Docetaxel	413 (7)	12.00	8.00	18.00	3.60	2.00	6.00
Enzalutamide	518 (9)	6.00	3.00	11.00	1.80	1.00	3.00
Goserelin	1578 (28)	6.00	2.00	11.00	1.80	0.80	3.20
Leuprorelin	2109 (38)	5.00	2.00	10.00	1.60	0.75	2.75
Mitoxantrone	19 (0)	2.00	2.00	6.00	1.00	0.50	2.00
Paclitaxel	35 (1)	13.00	4.00	23.00	4.40	1.20	9.25
Prednisone	1131 (20)	3.00	1.00	8.00	1.00	0.33	2.40
Radium-223	114 (2)	6.00	3.00	8.00	1.25	0.80	2.00
Triptorelin	51 (1)	3.00	1.00	5.00	0.80	0.40	1.40
Zoledronic Acid	157 (3)	5.00	2.00	15.00	2.00	0.50	4.60
Inpatient treatments							
Brachytherapy	60 (1)	1.00	1.00	1.00	0.20	0.20	0.25
Rad. Prostatectomy	1579 (28)	1.00	1.00	1.00	-	-	-
Number of patients	**5591 (100)**						

Table shows the utilization of PC-related services by PC patients (n = 5591). It includes all patients identified as PC patients at one point in the study period. For medication, the number refers to prescriptions, which may differ from applications (e.g., for chemotherapy). "-": not applicable because service is performed only once.

Table 3
Treatments after prostatectomy/radiotherapy and time of first treatment after prostatectomy/radiotherapy in locPC patients.

Index treatment	PC treatment after index treatment	Number of patients with treatment after index treatment (% of all patients with index treatment)	Number of patients with treatment as first treatment after index treatment (% of alle patients with index treatment)	Mean (median) time (days) after index treatment
Radical prostatectomy	Radiotherapy	291 (18.4%)	170 (10.8%)	447 (304)
	Hormone therapy (androgen-deprivation, anti-androgen)	206 (13.0%)	174 (11.0%)	273 (121)
	Chemotherapy (Docetaxel)	23 (1.5%)	1 (0.1%)	93 (93)
	Chemotherapy (Cabazitaxel)	3 (0.2%)	0 (0.0%)	-
	Chemotherapy (Carboplatin or Paclitaxel)	3 (0.2%)	2 (0.1%)	682 (682)
	Radium 223	3 (0.2%)	0 (0.0%)	-
	Abiraterone	9 (0.6%)	1 (0.1%)	58 (58)
	Enzalutamide	11 (0.7%)	0 (0.0%)	-
	Total	-	**348 (22.0%)**	-
Radiotherapy	Other radiotherapy	43 (3.7%)	35 (3.0%)	429 (340)
	Hormone therapy (androgen-deprivation, anti-androgen)	545 (46.6%)	524 (44.8%)	101 (40)
	Chemotherapy (Carboplatin or Paclitaxel)	16 (1.4%)	8 (0.7%)	416 (266)
	Enzalutamide	26 (2.2%)	2 (0.2%)	67 (67)
	Chemotherapy (Docetaxel)	32 (2.7%)	3 (0.3%)	321 (20)
	Abiraterone	24 (2.1%)	5 (0.4%)	8 (9)
	Chemotherapy (Cabazitaxel)	11 (0.9%)	0 (0.0%)	-
	Radium-223	4 (0.3%)	0 (0.0%)	-
	Total		**582 (49.8%)**	

Table shows the number of patients with a subsequent PC-related treatment after the index treatment (RT or RPE; for RT, only patients with at least 20 consecutive RT sessions were included). The third column reports the number of patients with the treatments listed in the second column after the index treatment (first column). The fourth column reports the number of patients who had the treatment as first PC treatment after the index treatment. The last column reports the mean (median) time in days from RPE to the subsequent PC treatment.

(376) days for the 1895 patients with therapy start after mid-2014 and therapy end before mid-2017 (no truncation). At the time of their first ADT prescription, 8.1% of the patients were younger than 65, 57.5% were younger than 80, and 93.6% were younger than 90 years old.

3.1.2.2. Medication for metastatic PC. 959 patients (17.1%) had at least one of the five drugs docetaxel, cabazitaxel, abiraterone, enzalutamide, or radium-223. Table 4 shows the number of metPC patients who consumed at least one of these substances (columns) as well as other drugs (rows). The numbers in the rows show the average number of prescriptions for patients who received the drug in the column at any point. For instance, among the 481 patients who took abiraterone, 278 had also bicalutamide, 344 had also denosumab, 288 had also leuprorelin.

Fig. 1 shows the sequences of the first prescriptions of all 765 patients who had at least one of the substances and who had their first treatment with any of these substances after mid-2014. Most patients had only one substance: enzalutamide (n = 186, 66 of whom died), abiraterone (n = 142, 76 died), docetaxel (n = 105, 38 died), radium-223 (n = 16, 6 died) and cabazitaxel (n = 2, 2 died). Many patients (n = 159) received enzalutamide after any of the other substances (e.g., 49 patients after abiraterone, 45 patients after docetaxel). In total, 369 (48.2%) patients with any of these drugs died within 4.5 years after their first treatment with one of the drugs.

803 patients (14.4%) were prescribed abiraterone or enzalutamide. The mean (median) number of packages per patient was 10.7 (7.0) for abiraterone and 10.7 (8.0) for enzalutamide. 188 patients starting abiraterone therapy and 210 starting enzalutamide therapy after mid-2014 died by the end of 2018 (78.6% and 69.5%, respectively, of those starting therapy).

196 patients received both abiraterone and enzalutamide. The number of first uses of enzalutamide which were not followed by abiraterone increased substantially between 2014 (n = 39) and 2018 (n = 98).

334 patients (i.e., 9.5% of all 3502 patients with an ADT during the study period) had docetaxel prescriptions at the same time. The corresponding share was 11.0% for the combination ADT+abiraterone.

Details of the sequences and substance combinations are provided in the supplementary material (Table A6).

527 patients (9.4%) had chemotherapy. Table 5 summarizes the number of patients and the number of prescriptions per patient for different substances. Of note, both carboplatin and paclitaxel are not approved for treatment of patients with PC. Docetaxel (n = 413) was used most frequently.

370 (70.2%) patients had only one substance, 134 (25.4%) had two, 21 (4.0%) had three, and 2 (0.4%) patients had four substances. Figure A1 in the supplementary material shows the sequences of the chemotherapy drugs in PC patients.

3.2. Medical costs

Total direct medical costs of PC were estimated to be CHF 347 m (323–372) in 2018 (extrapolated to national level from claims data). They amounted to CHF 127 m (118–136) for locPC (36.4% of costs) and CHF 221 m (205–236) for metPC (63.6%). The share of inpatient care costs in total costs amounted to 65–70% in locPC patients and about 15% in metPC patients. The share of medication costs in metPC patients was 59–63%. Table A8 in the supplementary material shows the details for each year.

The mean costs per patient by four treatment options are shown in Table 6. They were CHF 38,971 (36,830–41,111) in metPC patients receiving one of five OS-improving substances in 2018. All of the five substances were approved in Switzerland for metastatic castration-resistant PC (mCRPC) throughout the whole study period. However, Table A7 in the supplementary material shows that e.g. the approval of enzalutamide for patients with mCRPC before docetaxel based on the PREVAIL trial data has led to an increased use of enzalutamide and in parallel to a decrease in use of abiraterone. The prices per package were constant or decreasing over time (see Table A1 in the supplementary material). For locPC, the costs per patient were lowest in patients with RT only (CHF 16,799 (15,791–17,806)) and highest in patients with both RPE and RT in the same year (CHF 43,802 (41,224–46,379)).

Table 4
Use of five main survival-improving drugs and other drugs consumed by patients using these drugs (prescriptions per patient; 2014–2018).

	Docetaxel			**Cabazitaxel**			**Abiraterone**			**Enzalutamide**			**Radium-223**		
	Number of patients (% of patients in column)[1]	Mean	Median	Number of patients (% of patients in column)[1]	Mean	Median	Number of patients (% of patients in column)[1]	Mean	Median	Number of patients (% of patients in column)[1]	Mean	Median	Number of patients (% of patients in column)[1]	Mean	Median
Abiraterone	186 (45%)	10.5	7.5	81 (58%)	12.2	9.0	481 (100%)	10.5	8.0	196 (38%)	10.8	8.0	55 (48%)	13.7	11.0
Bicalutamide	279 (68%)	2.8	2.0	63 (45%)	3.4	2.0	278 (58%)	3.4	2.0	342 (66%)	3.8	3.0	70 (61%)	3.1	2.0
Cabazitaxel	105 (25%)	7.5	5.0	140 (100%)	7.5	5.0	81 (17%)	7.1	6.0	82 (16%)	8.9	6.5	24 (21%)	9.3	5.5
Carboplatin	32 (8%)	8.4	6.0	19 (14%)	11	4.0	23 (5%)	14.4	7.0	19 (4%)	9.1	7.0	2 (2%)	3	3.0
Cyproterone	28 (7%)	3.5	2.0	4 (3%)	2.8	2.0	23 (5%)	4.7	3.0	30 (6%)	4.1	2.0	10 (9%)	5.10	2.50
Degarelix	28 (7%)	18.6	8.0	7 (5%)	11.1	6.0	25 (5%)	11.1	6.0	41 (8%)	21.0	10.0	13 (11%)	25.5	18.0
Denosumab	305 (74%)	16.7	12.0	109 (78%)	20.4	16.0	344 (72%)	17.3	14.0	395 (76%)	17.6	14.0	97 (85%)	24.5	21.0
Dexamethasone	407 (99%)	18.3	13.0	137 (98%)	22.8	18.0	277 (58%)	16.0	11.0	283 (55%)	16.0	11.0	73 (64%)	20.1	14.0
Docetaxel	413 (100%)	13.8	12.0	105 (75%)	14.8	13.0	186 (39%)	15.6	14.0	196 (38%)	14.7	12.0	58 (51%)	15.3	12.0
Enzalutamide	196 (47%)	8.2	6.0	82 (59%)	7.1	6.0	196 (41%)	7.0	5.0	518 (100%)	9.2	6.0	70 (61%)	10.0	8.0
Goserelin	193 (47%)	10.3	9.0	70 (50%)	10.4	9.0	191 (40%)	10.7	10.0	237 (46%)	11.3	10.0	55 (48%)	15.3	15.0
Leuprorelin	226 (55%)	9.4	8.5	66 (47%)	10.8	10.0	288 (60%)	9.9	8.0	288 (56%)	10.4	9.0	59 (52%)	13.1	12.0
Mitoxantron	9 (2%)	2.2	2.0	9 6%)	3.1	2.0	8 (2%)	2.9	2.0	9 (2%)	3.7	3.0	0 (0%)	-	-
Paclitaxel	8 (2%)	12.8	7.5	4 (3%)	19.8	7.5	9 (2%)	15.9	10.0	3 (1%)	11.0	10.0	0 (0%)	-	-
Prednisone	254 (62%)	9.9	7.0	87 (62%)	13.9	9.0	366 (76%)	10.1	7.0	241 (47%)	9.0	6.0	72 (63%)	9.8	7.0
Radium-223	58 (14%)	6.1	6.0	24 (17%)	7.1	6.0	55 (11%)	6.0	6.0	70 (14%)	6.3	6.0	114 (100%)	5.8	6.0
Triptorelin	3 (1%)	6.7	3.0	1 (1%)	16.0	16.0	5 (1%)	6.6	3.0	5 (1%)	6.4	5.0	1 (1%)	16	16.0
Zoledronic Acid	42 (10%)	15.8	8.0	22 (16%)	18.0	6.5	67 (14%)	12.5	8.0	49 (9%)	14.3	8.0	13 (11%)	22.9	20.0
Number of patients (% of patients in column)	**413 (100%)**			**140 (100%)**			**481 (100%)**			**518 (100%)**			**114 (100%)**		

[1]patients with positive utilization

Table shows the number of patients by combination of substances in the columns and rows for five survival-improving drugs used in PC patients, as well as the mean and median number of prescriptions of the patients with positive utilization. The last row refers to the total number of patients who were given the substance in that column. Example: among the 481 patients who took abiraterone, 278 had also bicalutamide, 344 had also denosumab, 288 had also leuprorelin. The average number of prescriptions was 3.4, 17.3, and 9.9, respectively.

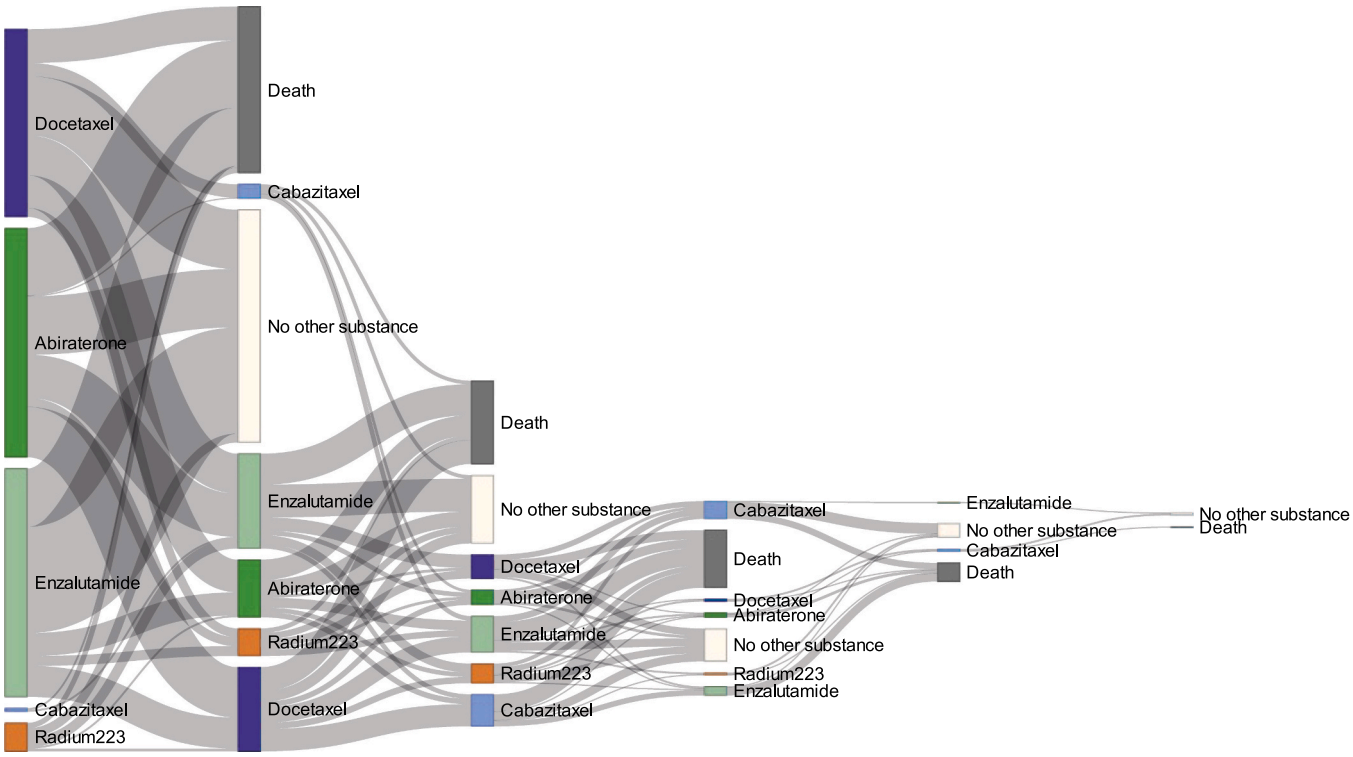

Fig. 1. Sequences of treatment with survival-improving substances (2014–2018). Figure shows sequences of drug treatment with five survival-improving drugs in PC patients; only patients starting the therapy with the first drug after mid-2014 and before mid-2017 (n = 765) are shown (to avoid truncation). The width of the lines refers to the number of patients switching from one substance to the other. Only the chronological order of the first use of each drug is shown. The time between each event in the sequence is not accounted for.

Table 5
Chemotherapy utilization in PC patients.

	Docetaxel	Cabazitaxel	Mitoxantrone	Carboplatin	Paclitaxel
Number of patients (% of all patients with chemotherapy)	413 (78.4%)	140 (26.6%)	19 (3.6%)	102 (19.4%)	35 (6.6%)
Mean (median) number of prescriptions, among patients with at least 2 prescriptions	13.9 (12)	7.8 (5.5)	4.3 (3)	11.4 (7)	17.4 (13.5)
Mean (median) duration of therapy in days	129 (109)	112 (83)	101 (41)	142 (71)	111 (73)

Table shows the number of patients by chemotherapy substance. The table also shows the mean (median) number of prescriptions as well as the mean (median) therapy duration of patients with at least two applications. The duration was calculated as the time between the first and the last application of this substance.

Table 6
Mean costs per calendar year and treatment option in PC patients.

	metPC patients with OS-improving drugs in that year		locPC patients with RPE (without RT) in that year		locPC patients with RPE and RT in that year		locPC patients with RT (without RPE) in that year	
Year	n	Mean costs per patient in CHF (95% CI)	n	Mean costs per patient in CHF (95% CI)	n	Mean costs per patient in CHF (95% CI)	n	Mean costs per patient in CHF (95% CI)
2014	293	40,345 (37,771-42,919)	279	24,900 (24,493-25,308)	21	37,670 (34,966-40,373)	122	19,060 (17,424-20,695)
2015	336	41,589 (39,150-44,028)	280	26,392 (25,994-26,789)	21	41,543 (38,682-44,404)	168	17,146 (15,772-18,520)
2016	398	38,298 (36,126-40,468)	275	26,228 (25,830-26,627)	15	45,746 (41,460-50,033)	185	17,343 (16,164-18,523)
2017	410	38,926 (36,807-41,045)	325	28,296 (27,833-28,759)	22	46,796 (43,413-50,178)	173	17,728 (16,622-18,834)
2018	411	38,971 (36,830-41,111)	315	28,023 (27,541-28,506)	15	43,802 (41,224-46,379)	198	16,799 (15,791-17,806)

Table shows the mean PC-related costs per calendar year for patients classified by treatment option for metPC (one of the five substances docetaxel, cabazitaxel, abiraterone, enzalutamide, or radium-223 in given year) and locPC (RPE without RT, RPE and RT, RT without RPE in given year). For the options including RT, only patients with at least 20 applications were included. Note that patients were not necessarily treated for a full year with one of the four treatment options.

Patients with an RPE had PC-related costs of CHF 28,023 (27,541−28,506).

4. Discussion and limitations

In this claims-based study, we identified 5591 patients actively treated for PC between 2014 and 2018. More than half of the 1579 patients undergoing RPE were between 65 and 74 years old, and less than 10% were older than 75. In contrast, RT was used more frequently in older patients (40.2% older than 75 years). This may be due to the presence of comorbidities. RT is also used in the treatment of metPC.

ADT was the most frequently used treatment in PC patients (n = 3502, 62.6% of sample). 9.5% of these patients had an ADT+docetaxel combination, and 11.0% of patients had an

ADT+abiraterone combination for at least some time. This might indicate that the clinical evidence of a potential survival benefit of combinations for metPC are taken up in practice [31,32]. The ADT+docetaxel combination was increasingly used over the five years period. Note that the data for ADT+abiraterone were only published in summer 2017, i.e., towards the end of the study period. The frequent use of abiraterone and enzalutamide after their approval has been documented previously [33]. We found that the number of patients treated exclusively with enzalutamide and without abiraterone increased between 2014 and 2018. The relatively frequent use of carboplatin and paclitaxel is a reflection of the lack of active treatment options, once approved therapies have been exhausted.

The study by Wen et al. (2019) for the United States reported mean treatment duration of 7.3 (abiraterone) and 5.4 months (enzalutamide) [34], which seems to be slightly shorter than our results for the mean (median) number of packages (dose of 28 days) per patient suggest (10.7 (7) for abiraterone and 10.7 (8) for enzalutamide).

Overall PC spending was estimated at CHF 347 m in 2018, approximately 0.45% of total health care spending [35]. We consider this as a conservative estimate as we only included patients with an active PC-specific treatment, but no patients in watchful waiting or active surveillance, and because we were not able to identify all PC-related costs (e.g., for unspecific primary care visits or complications after surgery). PC-related health care costs were estimated at EUR 5.43 billion in the European Union in 2009 [36] and at EUR 1.85 billion in Germany in 2015 [37]. The latter amounted to about 0.5% of total health are spending, similar to our estimate. A recent study for Switzerland estimated total spending for four types of cancer in 2017 [38]. The spending estimate for PC was higher (CHF 458 m) than in our study and lower than the spending for breast cancer (CHF 742 m), trachea, bronchus, and lung cancer (CHF 734 m), and colon and rectum cancer (CHF 549 m).

While the survival prolonging treatments for advanced prostate cancer were primarily established and approved in the mCRPC setting, in recent years a considerable number of large clinical trials have proven a benefit for the earlier use (e.g., in non-metastatic HSPC, mHSPC and non-metastatic CRPC) in particular of the androgen receptor pathway inhibitors. This trend is likely to increase the burden on health care expenditures, but it will also lead to benefits for patients in terms of quality of life and longer survival.

The mean PC-related yearly costs per metPC patient who was prescribed one of the five substances docetaxel, cabazitaxel, abiraterone, enzalutamide or radium223 decreased slightly over time, from CHF 40,345 (37,771−42,919) in 2014 to CHF 38,971 (36,830−41,111) in 2018. This may be partly explained by a decrease in the price per package for some of the substances. In addition, the publication of the CHAARTED (2015) and subsequently the STAMPEDE trial data (2016) showing a statistically and clinically large benefit of docetaxel in the mHSPC situation resulted in many patients with mHSPC receiving ADT plus docetaxel for mHSPC, and the subsequent use of more expensive medications (abiraterone, enzalutamide, cabazitaxel, radium-223) was significantly delayed. This may be an explanation for the slight decrease in mean PC-related yearly costs in the observed period. It remains unclear if this trend towards lower costs per patient persists after 2018. Moreover, mean costs refer to all patients with at least one prescription in that year, even if they were not treated for a full year.

This study has several limitations. *First*, the 5-years study period was too short to discover relevant changes in treatment patterns. *Second*, we identified PC patients only based on treatments and drugs. Claims data contain health care utilization and costs data, but include no direct clinical or diagnostic information, a limitation previously noted also for PC research in Germany [39]. *Third*, we were not able to distinguish between more granular disease stages beyond the simple distinction of locPC and metPC treatment regimens. A further differentiation between high-risk locPC and metPC would be of interest for the use of drug therapies in earlier disease stages. The recent use of abiraterone in locally advanced PC based on the STAMPEDE M0 data published 2022 could not yet be observed in our data. However, this may have an effect on the number of patients treated and the mean costs per patient. *Fourth*, the spending estimation was based on several assumptions regarding the prices of services (e.g., for drugs).

5. Conclusion

This study is the first to describe health care use and costs of patients with PC in Switzerland. Using individual-level insurance claims data, we showed that metPC patients accounted for about two thirds of total PC-related health care spending. The total yearly spending for PC was estimated at 0.45% of total health care spending in Switzerland.

Ethics approval and consent to participate

Ethics committee approval was not required in accordance with the Swiss law on human research because all data sources were retrospective, routinely collected, and anonymized.

Consent for publication

Not applicable.

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CRediT authorship contribution statement

Michael Stucki: Writing – review & editing, Writing – original draft, Visualization, Project administration, Methodology, Formal analysis, Data curation, Conceptualization. **Stephanie Dosch:** Writing – review & editing, Formal analysis. **Markus Gnädinger:** Writing – review & editing, Supervision. **Sereina M. Graber:** Writing – review & editing, Resources, Data curation. **Carola A. Huber:** Writing – review & editing, Resources. **Golda Lenzin:** Writing – review & editing, Formal analysis. **Räto T. Strebel:** Writing – review & editing, Supervision. **Daniel R. Zwahlen:** Writing – review & editing, Supervision. **Aurelius Omlin:** Writing – review & editing, Supervision. **Simon Wieser:** Writing – review & editing, Writing – original draft, Project administration, Methodology, Funding acquisition, Conceptualization.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ejca.2024.114072.

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