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Economic Burden of Prostate Cancer in Iran: Measuring Costs and Quality of Life

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Abstract

Background: Prostate cancer (PCa) is the third most diagnosed cancer among men in Iran with approximately 4200 new cases in 2015. Considering the rapid growth of cancer diagnosis, this study aims to investigate the economic burden of PCa patients and their health-related quality of life (HRQoL)

Methods: A retrospective survey was conducted on 500 registered patients to discover the pattern of care and distribution of patients in the main treatment categories. In the next step, a multi-center survey of the patients under treatment was conducted. The objective of this survey was to estimate direct medical costs (DMC), non-medical costs, and productivity losses for patients and family members. HRQoL was measured by the Functional Assessment of Cancer Therapy–Prostate questionnaire.

Results: Despite high age of patients (72±9.25 years), only 53.3% of them were retired or disabled. The largest proportion of patients (54.3%) received medicinal or surgical hormone therapy. Radical prostatectomy was the main treatment for 31.7% of patients, 10.2% received radiation therapy, and 3.8% underwent chemotherapy. DMC for incident population was approximately 12.5 million US dollars/year, and the highest average cost per capita belonged to chemotherapy patients. Unpredictably, productivity loss was nearly as much as direct cost. The mean score for HRQoL was 0.62±0.16 for all patients. Orchiectomy group had the lowest HRQoL score (0.55±0.16). Chemotherapy patients suffered the worst scores in the physical well-being subscale (0.47±0.24). Hormone therapy patients had the least scores in the prostate-specific subscale (0.50±0.18).

Conclusion: The economic burden of PCa is estimated approximately 25.8 million US dollars per year for incident population. When we refer to the high proportion of patients diagnosed in advanced state of the disease and higher per capita cost for these patients, policy makers should promote screening strategies to control health care costs and to increase both life expectancy and HRQoL.

Keywords: Cost of illness, Societal perspective, Productivity loss, Health-related quality of life, FACT-P

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Introduction

Prostate cancer (PCa) is the second most common cancer in men. Worldwide, approximately one million cases of PCa were diagnosed during 2012, which accounted for 15% of the cancers diagnosed in men. Prostate cancer is the fifth leading cause of cancer related deaths in men with more than 300,000 deaths in 2012 (6.6% of the total deaths in men).[1] In 2013, PCa caused 4.8 million disability adjusted life years (DALYs) globally, from which 57% occurred in developed countries and 43% in developing countries. The aging of the world's population and population growth have led to an increase in PCa incidence where the number of reported PCa cases has more than tripled – from less than 500,000 new cases in 1990 to 1.4 million in 2013. Although age-standardized DALY rates decreased by 3% at the global level and by 9% in developed countries, there has been a 28% increase in DALY rate in developing countries.[2] In 2015, Iran had an estimated incidence of PCa of 4268 with a 5-year prevalence of more than 10000 patients.[3]

There is a rapid increase in the costs of all cancers, including PCa, as the result of a volatile mixture of demographic factors (ageing and growing populations), rapid development of new medicines and technologies, and early diagnosis. Along with the increasing incidence and prevalence of cancers, there are significant economic losses due to premature morbidity and mortality.[4]

All cancers impose a substantial economic burden on societies. Considerable health-care costs are associated with prevention and management of cancer. Moreover, some patients will be disabled and unable to work and many will need their family or friends' support for the remainder of their lives. Therefore, quantification of the economic burden of cancer should estimate the direct costs of cancer care and the productivity lost due to disability or premature death. In addition, the costs associated with unpaid care provided by family and friends or, in other words, the informal care cost should be considered.[5]

Along with cost considerations, healthcare policy-makers and managed care organizations are paying increasing attention to the assessment of quality of life (QOL) benefits apart from clinical outcome, as a measure of patient satisfaction with treatment guidelines.[6] Health-related QOL (HRQOL) is an important and considerable parameter in healthcare decision-making and health economics. Guideline development is one of the main applications of patient-level data that mainly includes HRQOL.[7]

Table 1. Distribution of the patients in the treatment categories.

Treatment	Frequency	%
Radical prostatectomy	158	31.7
Radiation therapy	51	10.2
Hormone therapy	98	19.6
Orchiectomy	173	34.7
Chemotherapy	19	3.8
Total	499	100

The provision of affordable care for cancer patients requires a comprehensive estimation of the costs of cancer care. A systematic cost of illness (COI) study will provide useful data on the relative economic burden of diseases. These data could be considered a valuable infrastructure by health policy-makers for the main objectives of resource allocation, allocation of research funds, decisions about screening programs, and prioritization policies.[5]

Researchers admit that there is a radical shift in the global cancer burden from developed countries to low-income and middle-income countries.[4] In Iran, because of the rapidly increasing prevalence and incidence of PCa, it is reasonable to expect considerable morbidity, mortality, and social costs from this disease. The health care costs of PCa are likely to rapidly increase in the future because of new cancer screening strategies, in addition to new and more expensive technologies for diagnosis and treatment. These expenditures will become increasingly important as healthcare budget holders continue to be forced to limit or reduce costs and increase efficiency in healthcare provision. The purpose of this study is to estimate the economic burden of PCa from a societal perspective and estimate the HRQOL of Iranian

Table 2. Relationship between age and treatment type.

Age	group (years)	RP	RT	HT	Orchi.	Chemo.	Total
<70	N	86	25	27	39	16	193
	%	57.3	50.0	29.0	23.4	84.2	40.3
70-80	N	52	17	37	63	2	171
	%	34.7	34.0	39.8	37.7	10.5	35.7
>80	N	12	8	29	65	1	115
	%	8.0	16.0	31.2	38.9	5.3	24.0

Pearson chi-square: *P*=0.000; Linear-by-linear association: *P*=0.012; RP: Radical prostatectomy; RT: Radiation therapy; HT: Hormone therapy; Orchi.: Orchiectomy; Chemo.: Chemotherapy; The difference between total numbers of patients in this table with the original sample is attributed to missing data.

patients from different PCa treatment categories. These results will provide basic data for the abovementioned health-policy objectives or future cost-effectiveness studies if necessary.

Materials and Methods

Study design

This study was performed in two main parts. The purpose of the first part was to find the distribution of treatment categories among patients in Iran. Exploration of the main diagnostic strategies and current medicines used by patients was the outcome of this part. A retrospective questionnaire-based survey was performed by urology students through phone interviews with patients. The target population included registered patients who had a pathological diagnosis of PCa. These patients were registered in Urology Research Center of Sina Hospital, one of the referral centers for research and treatment of PCa.

The second part of the study was a cross-sectional questionnaire-based survey that targeted newly diagnosed patients who were under treatment at the time of the survey. We invited a sample of PCa patients from different treatment groups to participate in this study. The objective was to estimate direct medical and non-medical costs, and productivity losses of patients and their family members due to PCa.

Sample size

The first part of the study was a descriptive epidemiological study that sought to determine the proportion of various treatment groups. By considering the least prevalent treatment group (chemotherapy) that had an estimated proportion of about 5%, the following sample size formula would best fit the study objective:

$$n = \frac{Z^2_{\frac{a}{2}} p(1-p)}{d^2}$$

Where $Z_{a/2}$ is 1.96, p stands for the estimated proportion of chemotherapy patients, and d stands for the maximum marginal error of 0.02 in this study.[8] Based on the above formula, a sample size of 456 would be enough for this study. Therefore, the researchers selected 500 patients for this part of the study considering non-responding patients. In the second part, we used a quota sampling technique to select a proportion of new incident cases. Since the number of patients with PCa is very low in Iran, we have recruited approximately all patients under treatment in the cooperative medical centers during the study period. An estimated 1400 new cases are diagnosed with PCa in Tehran each year; therefore, 10% of this population could be a good representative. However, in this part, 200 patients were targeted.

Data collection

As previously mentioned, we used questionnaire-based surveys as the data collection method in both parts of this study. In part one, we prepared a complete questionnaire that covered all available and routinely practiced therapeutic options and diagnostic methods. Development of this questionnaire was based on a guideline review and expert opinions; major diagnostic and therapeutic protocols and approved medicines were derived from globally available guidelines. These guidelines included the European Association of Urology guidelines on PCa and

Table 3. Number and percentage of recruited patients in each treatment category.

Treatment category	Frequency	Percentage
Radical prostatectomy	17	11.4
Hormone therapy	24	16.1
Orchiectomy	31	20.8
Radiation therapy	70	47.0
Chemotherapy	7	4.7
Total	149	100.0

Table 4. Employment status of patients.

Employment status	Frequency	%
Retired	33	22.1
Working	83	55.7
Disabled	15	10.1
Unemployed	18	12.1
Total	149	100.0

NICE clinical guidelines on diagnosis and treatment of PCa.[9,10,11] Available and routinely practiced options in Iran were subsequently scrutinized based on the opinions of an expert panel.

The questionnaire, which was applied in the second part, was developed based on the opinions of urology and oncology specialists and experts in the field of economics. This questionnaire covered nearly all possible sources of medical, nonmedical, and indirect costs. Respondents were asked about the type of treatments, brand name of medicines, and other sources of costs, but not the amount of money that patients were paying during the course of the treatment. Costs were calculated based on medical tariffs in public and private sectors, as defined by the Ministry of Health, and is updated yearly.[12] Cost of prescription medicines was calculated by applying the unit price of the medicines and daily and monthly dosage of medicines taken by patients. The official prices of medicines is released by the Iran Food and Drug Administration (Iran FDA).[13]

We measured productivity loss by calculating the total working hours and/or days lost by patients and their families. We also assessed total time spent on care (number of days per month) in PCa patients who needed their families to care for them. The average income of patients and families was also considered in calculating productivity loss. If the income was not declared by the respondent, we took into consideration the average wage of the Iranian society according to the patients and/or his family's education level. The minimum wage was taken into account when calculating informal care cost, particularly for housewives. Numbers were changed to United States dollars (USD) based on the current year's exchange rate listed on the Central Bank of Iran's website. Of note, purchasing power parity rate was not included in the calculations.

The second section of the questionnaire assessed respondent's general and disease-specific QOL. This was a standard QOL questionnaire developed by the Functional Assessment of Chronic Illness Therapy (FACIT) organization. We used the Functional Assessment of Cancer Therapy–Prostate (FACT-P) tool to measure the HRQOL of patients in general and disease-specific aspects of life. The FACT-P consists of physical, social, emotional, functional, and PCa specific subscales. The FACT-G (general) total score is the sum score of the physical, social, emotional, and functional subscales and shows the general well-being of patients. The FACT-P total score is the sum score of the FACT-G and prostate cancer subscale (PCS), whereas the FACT-P Trial Outcome Index (TOI) is the sum of physical, functional, and cancer-specific subscales, which would be the most likely to change in clinical trials.[14]

Patients signed an informed consent form before responding to the questions. The informed consent form contained an explanation about the purpose of the study, contact information of the researchers, and a statement that assured the participants about the confidentiality of their responses.

Statistical analysis

We used SPSS version 16 and MS Excel 2013 for data analyses. Mean, standard deviation, median and harmonic mean (H. mean) were used as descriptive statistics. The Pearson's chi-square test was used for categorical variables such as

Table 5. Average yearly productivity loss in US dollars (USD).

		Productivity loss of patients	Informal care cost	Total indirect cost
N	**Valid**	47	96	110
	Missing	102	53	39
Mean		6393.2	2454.7	4873.9
Median		3127.8a	3223.9[a]	3307.3a
Std. deviation		8924.1	1571.1	6790.9

a: Calculated from grouped data.

treatment categories and age groups. Continuous variables that included cost were analyzed by one-way analysis of variance (ANOVA). For analyzing the difference between therapeutic groups in terms of the different subscales of HRQOL, Analysis of Variances Test (ANOVA) was either performed. For in depth analysis and between-group differences of productivity loss, and direct non-medical costs (DNMC), we used Mood's median and Kruskal-Wallis tests because of the dispersity among data (large standard deviation). In these cases, we used the median values instead of means.

Ethics Committee Approval

This study was approved in the meeting number 121 of the Ethics Committee on Medical Researches of Shahid Beheshti University of Medical Sciences (SBMU). The ethics code of this approval is 121/30.

Results

Results of the first part of the study

At the end of the first part of the study, we collected 499 completed questionnaires. Patients' ages ranged between 48 to 100 years, but most (more than 68%) were between 60 to 80 years of age. The mean age of the patients was 72±9.25 years, with a median age of 72 years. Patients had a normal age distribution.

Descriptive analysis showed that 53.3% of patients were retired or disabled and 46.7% were of working status and might be considered productive. The results showed that 67.2% of patients were managed in public medical centers and 32.8% received treatment in private hospitals or physician offices.

The main objective of this part of the study was to determine the distribution of Iranian patients according to the primary PCa treatment groups. Descriptive analysis indicated that orchiectomy was the most prevalent treatment with the largest percentage of patients (34.7%). Next, approximately 31.7% of patients underwent surgery, specifically radical prostatectomy, as their first treatment option. Medicinal hormone therapy (19.6%), radiation therapy (10.2%), and chemotherapy (3.8%) comprised the next treatments. The most common medicines for hormone therapy included triptorelin and flutamide. Of note, nearly half of the patients in the chemotherapy group also received hormonal medicines and/or radiation therapy. A combination of second-line hormone therapies plus chemotherapeutic medicines was used for these patients. The only cytotoxic medicine was docetaxel; none of the surveyed patients reported any other chemotherapeutic medicines, including mitoxatrone or estramustine phosphate. In addition, zoledronic acid was used by approximately 50% of patients (Table 1).

Treatment groups by age

Table 2 lists the distribution of treatment groups according to age. As can be seen, radical prostatectomy and radiation therapy were performed for the largest proportion of patients under age 70. Orchiectomy was the most frequent treatment with increasing age.

Results of the second part of the study

At the end of the second part of the study, we collected 149 completed, valid questionnaires. Approximately the same number of patients were targeted in each treatment category; however, there was an unequal distribution of patients

Table 6. Kruskal-Wallis test for productivity loss among the treatment groups.

	N	Mean	SD	Minimum	Maximum
Total indirect cost	110	4873.93	6790.91	31.58	45473.68
Type of treatment	110	3.40	0.98	Radical prostatectomy	Chemotherapy

Asymp. sig.= 0.000

because of the different response rates and limited number of patients in some treatment categories in the cooperative medical centers. Table 3 lists the percentage of patients in each treatment group. Of note, a substantial proportion of patients in the radiation therapy group also used hormonal medicines and could be considered as part of the major combination therapy category.

Approximately half of the patients (48.3%) were recruited from public medical centers and 52.7% were under treatment in private medical centers or physician offices.

The working status of patients in this part of the study followed the same model as the first part. Approximately half of the patients were working and had a productive status. The remaining patients were retired, unemployed, or disabled (Table 4). An in-depth interview with patients showed that almost 20% of the total population lost their jobs because of PCa and disability. This item, along with other items such as the number of working days lost due to PCa were the basis for calculating the productivity loss.

Productivity loss

Table 5 shows the mean, median, and total amount of productivity lost by patients and their families. Productivity loss of patients' families also could be considered an informal care cost due to PCa. As seen in table 5, there was tremendous diversity in the values such that the standard deviation was higher than mean for some of the variables. Therefore, the most useful statistic would be the median value, which accounted for 3300 USD per year for each patient as the total indirect cost. Median indirect cost was used for calculation of this cost category for the entire incident population of PCa patients. This could prevent overestimation of costs because mean cost was much higher than median cost. Missing cases were those that had no productivity loss so that they were retired and/or did not need family care (Table 5). Accordingly, the calculated values were representative of the productive patients. If we substituted zeros for the missing values, there would be greater diversity in the data and, consequently, the mean and median would be underestimated. For measuring the total productivity loss, these central statistics would be applied only to the working patients to avoid overestimation of the costs.

The results indicated a significant difference between treatment categories in the total productivity loss ($P<0.05$; Tables 6, 7). Table 8 shows the mean and median amount of productivity loss in various treatment groups. We used these amounts and multiplied them by the number of productive patients to estimate the total productivity loss due to PCa in Iran. The highest value was observed in the orchiectomy group, whereas the lowest value belonged to the chemotherapy group.

We calculated the productivity loss of the incident population of PCa in each year by multiplying the median productivity loss by the number of patients with productivity loss in each treatment category. Chi-square results showed a significant difference between the groups (Table 9).

We considered the incidence of PCa, which was estimated to be 4268 in 2015,[3] the percentage of each treatment category, and the percentage of patients who had productivity loss in each treatment group. We determined that the total productivity loss of patients and their family would be approximately 10 million USD for the first year after diagnosis. This number was calculated from median data and the formal currency exchange rate of Iranian rials to USD. Table 10 lists the productivity loss in each treatment group for the total population of PCa patients in Iran.

The total productivity loss due to PCa was

Table 7. Mood's median test for productivity loss among the treatment groups.

		RP	RT	HT	Orchi.	Chemo.
Total Indirect cost	>Median	3	12	1	17	3
	≤Median	4	43	10	13	4

Median= 3368 US dollars (USD); RP: Radical prostatectomy; RT: Radiation therapy; HT: Hormone therapy; Orchi*:; Orchiectomy, Chemo*: Chemotherapy.; Asymp. sig.= 0.007

estimated to be about 12.5 million USD per year for the total population of PCa patients who were diagnosed in Iran in 2015. The orchiectomy group had the greatest value because of the higher number of patients in this category, percentage of patients with productivity loss, and amount of average indirect cost for each patient.

Direct medical costs (DMC)

Table 11 shows the detailed information on direct medical costs (DMC) for each category of treatment in the public and private sector. The DMC were categorized into three main categories: total DMC, drug acquisition costs, and diagnostic costs. Total DMC included physician fees, hospitalization and nursing costs. Drug acquisition costs included the price of medicines plus cost of administration (i.e., injection fee).

The highest total DMC belonged to the chemotherapy group with a yearly mean cost of approximately 14200 USD in which the greatest amount was attributed to drug acquisition (10900 US dollars per year). The difference between sum of the diagnostic and pharmaceutical costs to total DMC was related to physician visits, drug administration, and other costs that included occasional hospitalizations. The lowest total DMC of approximately 2950 USD per year was for hormone therapy (triptorelin, flutamide, cyproterone acetate, finasteride). These patients must continue to take medications for the duration of their lives, unlike patients in the orchiectomy, radiation therapy, and prostatectomy groups. The ANOVA results showed a significant difference between the treatment groups. Mean total DMC, drug acquisition cost, and diagnostic costs differed between the therapeutic groups (P<0.05).

We calculated the total DMC for PCa in Iran in the same way as the indirect cost for PCa. The harmonic mean (H. mean) was multiplied by the number of patients in each treatment category based on the distribution determined in the first part of the study and by considering the PCa incidence in Iran. There was a large spread in the cost data in all treatment categories; thus, we used the H. mean instead of the mean and standard deviation. We considered the distribution of patients in the public (67.2%) and private (32.8%) sectors from the first part of the study, with the exception of the chemotherapy group. The evidence from specialists employed in the public and private sectors indicated that a great proportion of chemotherapy patients underwent treatment in the private sector. Since the major proportion of costs in this category was due to drug acquisition, which was the same in all sectors of the health system in Iran, it appeared to the authors that the inaccuracy which resulted from this estimation would be negligible (Table 12).

The highest amount of DMC (3.6 million USD) was related to radical prostatectomy and the least amount of DMC was for patients treated with hormonal medicines (1.8 million USD). Chemotherapy for PCa, despite the smallest number of patients, was approximately 2.1 million USD per year, which was higher than hormone therapy or orchiectomy despite the substantially higher number of patients in these two treatment groups.

Direct non-medical costs (DNMC)

The total DNMC of patients in this study included disease-related transfer, travel, and

Table 8. Total productivity loss/year (median).

Treatment category	Total indirect cost (USD)
Radical prostatectomy	3157.9
Hormone therapy	2694.7
Orchiectomy	5894.7
Radiation therapy	3157.9
Chemotherapy	842.1

USD: US dollars

Table 9. Percentage of patients with and without productivity loss in each treatment category.

Treatment category		Without productivity loss	With productivity loss
Radical prostatectomy	N	10	7
	%	58.8	41.2
Hormone therapy	N	13	11
	%	54.2	45.8
Orchiectomy	N	1	30
	%	3.2	96.8
Radiation therapy	N	15	55
	%	21.4	78.6
Chemotherapy	N	0	7
	%	0.0	100.0

accommodation costs of patients. Some patients travel from small cities to a metropolis like Tehran to receive their treatment. Travel and accommodations for these patients impose a tremendous cost. We have also considered the transfer cost of patients who were being treated in their home city.

There was notable dispersion between these data; accordingly, we used the median statistic to calculate DNMC for the total population of patients. We observed no significant difference between groups. A rough estimate of the total DNMC of PCa for all incident cases in the first year after diagnosis was approximately 900,000 USD per year (4268 patients × 210.5 USD).

Table 13 contains information about the DNMC for each treatment category. The values were calculated based on distribution of patients in the incident population, which was estimated to be 4268 in 2015.

Total costs

We calculated the sum of all types of costs for the different treatment categories in order to summarize the results of the economic burden of PCa and to obtain a perspective of the cost burden of this disease. The highest cost burden was estimated for orchiectomy group. The highest number of patients in this group and concomitant use of hormonal medicines was the reason for the highest cost.

Another important finding was total economic burden of PCa in Iran, which we estimated to be approximately 25.6 million dollars for the incident population of patients in the first year after diagnosis. About half of this burden was due to direct costs of the disease. The remaining was the result of the productivity loss of patients and their families (Table 14).

Health-related quality of life (HRQOL)

The standard validated FACT-P questionnaire was completed by patients or through interviews conducted by an expert. The scoring process was performed according to the scoring guideline of the FACIT organization. Table 15 lists the standard score range of various PCa subscales. Of note, all answers were changed to the positive mode in the scoring process; consequently, higher scores indicated a higher QOL. All scores were changed to percentages (i.e., 0-100 scores) for ease of comprehension and comparability with the results of other studies. The mean QOL of all patients was approximately between 60% and 70%. The lower values were related to functional well-being, the PCa subscale, and PCa TOI.

The statistical tests revealed significant differences between groups in all subscales except EWB and PCS ($P<0.05$). In the physical subscale, the lowest scores were observed in chemotherapy patients (47.7%) and orchiectomy patients (approximately 47.5%). The FACT-P TOI was lowest for hormone-therapy and orchiectomy patients (53.7%). The FACT-G and FACT-P scores were lowest for orchiectomy patients (approximately 55%; Table 16). Thus, patients in the orchiectomy and hormone-therapy categories had the lowest QOL scores.

Table 10. Total productivity loss in each treatment category.

Treatment category	Proportion of patients	Number of incident cases	Percent with productivity loss	Number with productivity loss	Total productivity loss[a]
Radical prostatectomy	31.7%	1353	41.2%	557	$1,760,326
Hormone therapy	19.6%	837	45.8%	383	$1,032,535
Orchiectomy	34.7%	1481	96.8%	1434	$8,451,096
Radiation therapy	10.2%	435	78.6%	342	$1,080,586
Chemotherapy	3.8%	162	100.0%	162	$136,559
Total	100%	4268		2879	$12,461,102

a: Percentage of patients × total incidence × proportion with productivity loss × median productivity loss in each group.

Discussion

Prostate cancer is one of the major causes of cancer-related morbidity and mortality in men. In addition to tremendous costs to patients, their families and the health care system, decreased QOL is another consequence of this disease. Patients' mean age and working status are factors which influence the economic and health burden of a disease on the society. The current study patients had a mean age of 72 years with a range between 48 to 100 years. Approximately half of the patients were still employed, which showed that this group might lose productivity because of PCa.

The main treatment groups and their prevalence were other important outcomes of this study. The distribution of treatment categories might be useful for health decision makers as well as businesses. Health policy makers and other stakeholders could forecast the infrastructures necessary for radiation therapy and pharmaceutical products needed for these groups of patients.

The description of DMC, DNMC, and indirect costs as well as pharmaceutical and diagnostic costs were other valuable results of this study. These data might be helpful for priority setting, health care budgeting, and for decision-making about preventive or screening programs.

Finally, global HRQOL and its subscales including physical, social, emotional, and functional were the other important results of this study. Prostate cancer substantially decreased patients' QOL. This would predict a great burden of PCa in terms of years of life adjusted for disability.

Alemayehu et al., in 2010, identified the average per patient per month PCa-related costs for castration resistant patients in the United States. Their cost categories included 1152 dollars (SD: 2073 dollars) for ambulatory visits, 559 dollars (SD: 2383 dollars) for inpatient stays, 72: dollars (SD: 229 dollars) for pharmacy costs, and one dollar (SD: 14 dollars) for emergency room visits. Total monthly per patient PCa-related costs averaged 1799 dollars (SD: 3505 dollars).[15] In the current study, the average DMC for chemotherapy patients was approximately 14181 dollars (SD: 4304 dollars) for the first year, which could be an estimated 1181 US dollars per month. Unlike the study of Alemayehu et al., the major expense was drug acquisition (about 77%). Furthermore, their data was very disperse and could not give an accurate estimation for costs.

Brandeis et al. reported that of 10107 men treated for early stage PCa in the United States, 58% received external beam radiation therapy, 35% underwent radical prostatectomy, and 7% received brachytherapy. They also found that men aged 65-69 years were more likely to have radical prostatectomy and after age 70, radiation therapy was the preferred option. Per patient cost of radical prostatectomy (19019 dollars) was more than radiation therapy (15937 dollars; $P<0.05$) or brachytherapy (15301 dollars; $P<0.05$). They concluded that mean charges for the treatment and 6-month follow-up of patients treated for early-stage PCa ranged between 15301 and 31329 dollars, with significant differences between groups and without any clear survival benefit.[16] In the current study, the average cost of patients with radical prostatectomy for their treatment and one year follow-up was approximately 3709

Table 11. DMC in the first year after diagnosis (USD).

Treatment group	Medical center		Total DMC/Y	DAC/Y	DC/Y
Radical Prostatectomy	Public	Mean	1719.6	21.9	641
		SD	355.7	46.2	238.2
		H. mean	1652	.a	555.4
	Private	Mean	6552.2	323	913.4
		SD	4222	721.2	166.3
		H. mean	4695.8	.a	886.8
	Total	Mean	3709.5	145.9	753.2
		SD	3572.9	468.6	247.7
		H. mean	2253.5	.a	656.4
Radiation therapy	Public	Mean	6283.1	903.3	571.2
		SD	2383.6	1070.5	168.3
		H. mean	5325	.a	537.1
	Private	Mean	10707.9	884.2	791.2
		SD	2199.8	1261.6	59.6
		H. mean	10400.1	.a	787.2
	Total	Mean	8242.6	894.9	668.6
		SD	3183.4	1150.3	171
		H. mean	6793	.a	625
Hormone therapy	Public	Mean	3121.8	694.2	495.6
		SD	2738.9	401	174.7
		H. mean	1933.3	.a	448.2
	Private	Mean	2849.8	1482.9	721.7
		SD	1096.9	934.3	143
		H. mean	2547.1	1212.1	700.6
	Total	Mean	2940.4	1220	646.3
		SD	1756.4	873.2	185.7
		H. mean	2303.3	.a	589.9
Orchiectomy	Public	Mean	1340.6	509.8	423.8
		SD	1166.9	1073	117.4
		H. mean	934.1	.a	404.8
	Private	Mean	5082.2	1601.2	842
		SD	7473.8	4864.5	164
		H. mean	2246	.a	815.3
	Total	Mean	3392.5	1108.3	653.1
		SD	5827.8	3663.9	255.1
		H. mean	1374.3	.a	559.2
Chemotherap	Private	Mean	14181.3	10898	882.5
		SD	4304.5	4925.6	119.5
		H. mean	12895.1	6812.5	869.5
	Total	Mean	14181.3	10898	882.5
		SD	4304.5	4925.6	119.5
		H. mean	12895.1	6812.5	869.5

Table 11. DMC in the first year after diagnosis (USD) (continued).

Treatment group	Medical center		Total DMC/Y	DAC/Y	DC/Y
Total	Public	Mean	4309.6	678	543.4
		SD	3025.9	973.5	182.2
		H. mean	2184.4	.a	496.3
	Private	Mean	7808.6	2011.6	807.1
		SD	5525.4	3960.2	132.9
		H. mean	4134.7	.a	787.8
	Total	Mean	6141.3	1376.1	681.5
		SD	4825.9	3009.1	205.8
		H. mean	2900.6	.a	615.5

USD: US dollars; DMC: Direct medical cost; DAC: Drug acquisition cost; DC: Diagnostic cost; SD: Standard deviation; H. Mean: Harmonic mean; a: The data possibly contains

dollars (SD: 3573 dollars). These patients had significantly lower costs than radiation therapy patients, whose treatment cost an average of 8243 US dollars (SD 3183). The odds ratio that an early-stage PCa patient would undergo a prostatectomy relative to radiation therapy was 3:1, which meant there was a three-fold chance that patients would undergo a radical prostatectomy. Unlike the study by Brandeis et al., treatment choice did not differ significantly by age in the present study.

Chon et al. estimated the discounted medical cost of hormonal therapy with orchiectomy. Based on their results, the total cost of a bilateral orchiectomy was 2022 dollars, whereas 30 months of hormonal therapy cost 13620 dollars in the year 2000. Adjusting the costs for one year, medical hormone therapy might be estimated at approximately 6000 dollars (considering the diagnostic cost at the beginning of treatment) which was three times higher than an orchiectomy. They reported that patients preferred to pay the higher cost to avoid dissatisfaction with the orchiectomy compared to medical hormone therapy.[17] The present study indicated nearly the same cost and QOL, with no significant difference between these two groups of patients. This result could be explained by the high percentage of orchiectomy patients who received concomitant medicinal treatment.

Crawford et al. conducted a study to determine treatment patterns, resource utilization, and economic consequences of different PCa treatments. The mean age of patients in their study was 61.4 years; patients aged 50-59 years comprised the highest proportion at 51%. The biggest proportion of patients (30%) were in the watchful waiting category with an average 2-year cost of 24809 dollars. The estimated cost for active treatment in the mentioned time frame was 59286 dollars. Surgery was the most common therapeutic option among younger patients. They concluded that PCa was a substantial economic burden to society regardless of whether patients received treatment or watchful waiting that means just following with no treatment application.[18] In comparison to the study by Crawford et al., patients in the current study had an average age of 72 years and the highest proportion of patients were between 60 to 80 years. There was only one case of watchful waiting in the first part of the study, which might be interpreted as a different management approach in Iran and would be the result of cultural differences or the lack of official guidelines.

De Oliveira et al., who analyzed 585 PCa patients in Canada, reported a comparable mean age (73 years) with the current study; however, they reported a higher percentage of retired patients (77%) compared to the current study (53%). Vice versa, their estimated overall productivity loss was 838 Canadian dollars compared to the current study of 3598 dollars per patient.[19]

According to Broder et al. and Félix et al., a significant part of PCa health care costs were due to skeletal-related events (SREs), particularly

Table 12. Total DMC for each treatment category.

Treatment category	Proportion of patients (%)	Number of new cases	Medical center	Number of patients	DMC[a]	Total DMC
Radical prostatectomy	31.7	1353	Public	909	$1,501,976	$3,585,918
			Private	444	$2,083,942	
Hormone therapy	19.6	837	Public	562	$1,086,630	$1,785,479
			Private	274	$698,849	
Orchiectomy	34.7	1481	Public	995	$929,544	$2,020,576
			Private	486	$1,091,032	
Radiation therapy	10.2	435	Public	293	$1,557,806	$3,042,825
			Private	143	$1,485,018	
Chemotherapy	3.8	162	Private	162	$2,088,990	$2,088,990
Total	100	4268				$12,523,787

a: Number of patients × H. mean of total DMC of the related treatment category. ; H. mean: Harmonic mean; DMC: Direct medical cost.

among metastatic patients, which highlighted the necessity of early diagnosis and treatment. These events, including fractures and spinal cord compression, have been associated with severe outcomes, increased pain, worsening QOL, morbidity, and decreased survival.[20,21] Unfortunately, we could not determine these costs because of the smaller numbers of patients and the cross-sectional study type. The authors only noted the costs related to calcium metabolite modifiers, specifically zoledronic acid, which was used by approximately 12% of patients. Chemotherapy patients had a significantly higher use of zoledronic acid (P=0.000).

Fourcade et al. assessed the primary treatment options for patients in five European countries – the UK, Germany, France, Italy, and Spain. Their results indicated very low percentages of patients who received chemotherapy in the first year after diagnosis. Because they reported the results for various stages of PCa, we could not directly compare our results with theirs. However, some differences and similarities were seen, which could be interpreted as different treatment strategies in different countries. In contrast with Crawford et al., they found a lower percentage of patients in the watchful waiting or active surveillance groups. In each country, they noted that very few patients had orchiectomy as the initial treatment. We found the biggest proportion of patients in the orchiectomy category, which might imply that Iranian patients have been diagnosed in more advanced disease stages or it might be due to cost implications that resulted in different treatment algorithms.[17,22]

Groot et al., in 2003, quantified the health care costs associated with metastatic PCa in the Netherlands. The cost of treatment and two year follow-up was determined to be approximately 13000 Euros, which consisted of the costs for treatment of SREs.[23] We added a 5% inflation rate to these costs in order to be comparable to the costs for 2015 (the year for the current study) and made adjustments for a one year follow-up period. The resultant costs after these adjustments were comparable to those reported in the present study. However, considering the average income of the Iranian society, the Iranian health care system has been paying a much higher proportion of its Gross Domestic Product (GDP) for PCa

Table 13. DNMC for each treatment category.

Treatment category	Proportion of patients (%)	No. of new cases	Total DNMC[a]
Radical prostatectomy	31.7	1353	$284,797
Radiation therapy	10.2	435	$91638
Hormone therapy	19.6	837	$176,089
Orchiectomy	34.7	1481	$311,750
Chemotherapy	3.8	162	$34140
Total	100	4268	$898,414

DNMC: Direct non-medical cost; a: Number of patients × median DNMC

treatment. The Iranian GDP per capita for the year 2015 was 5090 dollars compared to 55190 dollars for the Netherlands.[24]

Hanly et al. estimated the patient productivity loss in Ireland using both the human capital approach and friction cost method. When compared to the current study, the results of the human capital method indicated a much higher productivity loss (109,154 Euro) than our study (6393 USD).[25] Adjustment with the GDP per capital, which was approximately 10 times higher in Ireland compared to Iran, would minimize this difference; however, the productivity loss in Ireland remained higher.

Most of the comorbidities related to PCa could not be assessed because of the short time span of the study. These comorbidities included musculoskeletal events as well as depressive disorder that was estimated by Jayadevappa et al. to happen in about 8.54 percent of PCa patients. They reported that depression during treatment was associated with a higher chance of emergency room visits, hospitalizations, outpatient visits, and increased risk of death over the course of the follow-up. Depression during the treatment was associated with significant health resource utilization, costs, and mortality among PCa patients.[26]

Krahn et al. estimated the DMC of PCa in Canada during different phases of the disease. They estimated total costs from initial treatment to one year after diagnosis as 3289 Canadian dollars.[27] This cost for the total patients in the current study accounted for 6141±4826 US dollars. After considering the 5% inflation rate (2009-2015) and adjustment for the currency exchange rate, it seemed that health care costs for PCa in the first year after diagnosis was much higher in Iran (6141 USD) compared to Canada (3376 USD).

In a study by Li et al., the mean annual informal care cost among partner caregivers of localized PCa patients was 6063 USD (range: 571-47105 USD) adjusted for the year 2009 for the first year after diagnosis. The annual time lost followed a mean of 276.2 hours (range: 26-2146) in the study population.[28] In our study, the patients in the radical prostatectomy and radiation therapy groups, which we considered to be locally advanced cases, had average informal care costs of 1375 dollars (SD: 1588 dollars). The annual lost time for family members was 123.8 h (SD: 153.1 h), nearly half of that reported by Li et al.

We compared productivity costs with direct costs and compared their ratio. Our results indicated that despite the lower cost for PCa in Iran, the ratio between direct costs and indirect

Table 14. Total economic burden of PCa in the incident population.

Treatment category	Proportion of patients (%)	Number of new cases	Productivity loss	DMC	DNMC	Total COI
Prostatectomy	31.7	1353	$1,760,326	$3,585,918	$284,797	$5,631,041
Radiation therapy	10.2	435	$1,080,586	$3,042,825	$91638	$4,215,049
Hormone therapy	19.6	837	$1,032,535	$1,785,479	$176,089	$2,994,103
Orchiectomy	34.7	1481	$8,451,096	$2,020,576	$311,750	$10,783,422
Chemotherapy	3.8	162	$136,559	$2,088,990	$34140	$2,259,689
Total	100	4268	$12,461,102	$12,523,787	$898,414	$25,883,303

PCa: Prostate cancer; DMC: Direct medical cost; DNMC: Direct non-medical cost; COI: Cost of illness

Table 15. HRQOL for the total study population.

Subscale	N	Min.	Max.	Mean	SD	Score Range	Mean (%)	SD (%)
PWB	142	0	28	18.64	6.79	0-28	67.04	23.71
SWB	144	1	28	17.78	5.15	0-28	63.50	18.40
EWB	144	1	24	17.76	4.54	0-24	74.10	18.92
FWB	146	0	28	16.64	6.77	0-28	59.88	23.76
PSC	142	2	48	28.73	9.43	0-48	59.92	19.62
FACT-P TOI	147	8	101	62.29	20.39	0-104	59.95	19.59
FACT-G	147	25	103	69.35	18.74	0-108	64.25	17.32
FACT-P	147	34	148	97.10	26.02	0-156	62.20	16.68

HRQOL: Health-related quality of life; PWB: Physical well-being; SWB: Social/family well-being; EWB: Emotional well-being; FWB: Functional well-being; PCS: Prostate cancer subscale; FACT-P TOI: Functional Assessment of Cancer Therapy–Prostate Trial Outcome Index; FACTG: Functional Assessment of Cancer Therapy-General total score; FACTP: FACT-P total score.

costs were in line with those reported by Max et al. who estimated the economic burden of PCa in California in 1998. They calculated 180 million dollars for health care costs and 180 million dollars for productivity loss.[29]

Mehra et al. estimated the health care costs of metastatic castration-resistant prostate cancer (mCRPC) patients in the United States for the first 6-month follow-up period. The cost categories in their study were all-cause hospitalizations, emergency room visits, physician visits, ambulatory visits, and PCa-related prescription treatments. Their results showed that the health care cost of patients who were treated with a docetaxel regimen followed a mean of 5847 USD (SD: 6990 USD), which seemed lower than the results of our study, where we reported 14381 USD (SD: 4304 USD).[30]

Sullivan et al. assessed the HRQOL of hormone refractory PCa patients in a multi-center multinational study. They used the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ C30), the FACT-P, and the EQ-5D index health assessment questionnaires. In their study, the mean score in PCS according to FACT-P was approximately 29.8 (0-48). We converted their score to a 0-100 scale and compared the results with the current study results. Our comparison showed a negligible difference between the results. They suggested effective palliative therapy for men with metastatic hormone refractory prostate cancer (HRPC) considering the substantial worsening in HRQoL.[31]

A study by Choi et al. compared the HRQOL of Chinese patients with PCa against the general population and patients with other types of cancer. The results showed better scores in the physical well-being (PWB), social/family well-being (SWB), emotional well-being (EWB), functional well-being (FWB), and prostate cancer subscale (PCS) domains in comparison with patients of the current study. Participants in their study underwent the following treatments: radical prostatectomy (35.05%), androgen deprivation therapy/androgen blockade (40.21%), radical and adjuvant radiation therapy (18.21%), and chemotherapy (1.37%).[32] The difference between HRQOL scores could be interpreted by the different distributions of patients in various treatment categories.

Bourke et al. assessed the effect of life-style intervention on disease-specific QOL in PCa patients who were under androgen deprivation therapy (ADT). They reported a score of about 120 (0-156) as the total FACT-P score.[33] This score was approximately 20% higher than our findings for hormone therapy patients. The difference in scores could be explained by sociocultural differences, different treatments, and available medicines in various countries.

Stone et al. evaluated the QOL of patients from localized to metastatic advanced PCa according to FACT-P, Schedule for the Evaluation of Individual Quality of Life-Direct Weighting (SEIQoL-DW), and a visual analogue scale (VAS). They transformed the FACT-P results to a 0-100 linear scale. Their results were higher than the present study; however, a similar pattern was observed, which means that patients had better scores in the emotional, physical, and social

Table 16. Mean score for each subscale of HRQOL within the treatment categories.

Therapeutic category		PWB	SWB	EWB	FWB	PCS	TOI	FACT-G	FACT-P
Radical prostatectomy	Mean	70.33	65.56	70.06	61.88	66.50	61.35	62.71	62.65
	SD	13.46	15.22	13.78	16.62	13.47	15.29	13.15	13.16
Radiation therapy	Mean	71.97	71.87	75.47	70.54	61.71	64.78	70.52	66.97
	SD	23.78	15.38	20.99	23.48	20.92	20.51	17.98	17.51
Hormone therapy	Mean	66.96	56.18	70.61	49.48	50.82	53.74	59.83	56.26
	SD	21.31	16.99	19.34	17.60	18.45	16.53	13.62	14.06
Orchiectomy	Mean	59.10	47.48	74.84	44.57	57.87	53.74	55.00	55.61
	SD	26.04	15.47	17.05	20.77	19.90	20.36	16.04	16.14
Chemotherapy	Mean	47.71	71.43	79.29	50.14	65.57	56.86	61.71	62.71
	SD	24.22	15.64	16.76	19.48	12.93	15.57	14.93	13.62
Total	Mean	67.04	63.50	74.10	59.88	59.92	59.95	64.25	62.20
	SD	23.71	18.40	18.92	23.76	19.62	19.59	17.32	16.68

HRQOL: Health-related quality of life; PWB: Physical well-being; SWB: Social/family well-being; EWB: Emotional well-being; FWB: Functional well-being; PCS: Prostate cancer subscale; TOL: Trial Outcome Index; FACT-G: Functional Assessment of Cancer Therapy-General; FACT-P: Functional Assessment of Cancer Therapy-Prostate

domains as well as lower scores in the functional and prostate specific domains. It is presumed that patients with localized disease would have significantly better QOL than those with metastatic disease.[34]

Future studies in this field may focus on cost-effectiveness of screening programs as well as preventive programs for PCa. Screening programs may increase the incidence of PCa because of an increase in the number of diagnosed patients. It should be justified if earlier diagnosis would decrease the burden of disease or not. However, early diagnosis may result in a lower number of patients that have more advanced stages of PCa.

Conclusion

As previously mentioned, approximately 50% of the patients were in working status which was a substantial number for patients who had a mean age of greater than 70 years. This indicated a noticeable amount of productivity loss due to PCa. Direct medical costs and indirect costs of PCa were almost the same and should be emphasized by high level policy makers in Iran. Unfortunately, most often the productivity losses due to diseases that particularly occur in the elderly population are overlooked. Both patients and their families lose their actual productivity in these situations.

We compared the results of this study with the results from other countries, most of which were performed in developed countries that had greater revenues (GDP per capita). We concluded that the Iranian society was paying a greater proportion of its revenue for PCa treatment. This would make it necessary for the policy makers to perform cost containment policies regarding diagnostic and therapeutic procedures for PCa.

Another important conclusion of this study was the different cost pattern in terms of pharmaceutical, technological, and human cost resources compared to other countries. In comparison to developed countries, the costs related to human resources such as physician visits and surgeries constituted a lower proportion of the total costs. On the other hand, the costs

related to pharmaceutical and other technological resources such as radiation therapy brought about a greater proportion of costs. This finding could be another essential initiative for policy makers and reimbursement organizations to perform an economic evaluation of the related technologies and implement cost-effectiveness as well as health-technology assessment strategies.

Limitations

One of the limitations for this study was the inability of the investigators to evaluate the adverse effects from androgen deprivation therapy, which included myocardial infarction, acute coronary syndrome, congestive heart failure, stroke, deep vein thrombosis or pulmonary embolism, diabetes, and fractures or osteoporosis .[35]

Another limitation was the prospective nature of the study which decreased the accuracy of the results. In addition, the time span of this study was short and limited to the first year after diagnosis. Since PCa is an end-of-life disease with variable economic burdens in its different stages, we suggest that a lifetime time horizon be applied for this disease considering all end-of-life costs.

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Conflict of Interest

None declared.

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