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The Estimated Economic Value of the Welfare Loss due to Prostate Cancer Pain in a Defined Population

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The aim of the study reported here was to estimate the economic value of the welfare loss due to prostate cancer pain by estimating the extent to which pain affects health-related quality of life among patients with prostate cancer. The material consisted of a point estimate of health status among men with prostate cancer in a well-defined population of 200 000 males. Clinical data concerning the disease at diagnosis (extracted from patients' records and the Regional Prostate Cancer Registry), and health utility ratings (using EuroQol) were obtained from 1 156 males with prostate cancer. A descriptive model showed that optimal treatment that would reduce pain to zero during the whole episode of disease would add on average 0.85 quality-adjusted life years (QALY) to every man with prostate cancer. Based on an estimate of the willingness to pay for a QALY the economic value of this welfare loss due to prostate cancer pain is in the magnitude of €86 600 000 per year (€19 800 000 per million men in Sweden).

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Prostate cancer is a growing health problem in most Western countries, with a significant, increasing incidence with advancing age (1). In 20 007 611 (173 per 100 000) men in Sweden received a diagnosis of prostate cancer (1). It is the most common male cancer and cause of cancer death in Sweden (2, 3). The prevalence in Sweden in 1999 was about 37 000 men (4), which corresponds to 845 per 100 000 men.

The main goal in prostate cancer care has long been to reduce mortality. With increased survival and a long life after diagnosis and treatment, interest in health-related quality of life, in addition to quantity of life, has increased. The literature showing that cancer affects patient-perceived health is growing rapidly (5–11). Knowledge about the disease and the risk of future health problems, and/or experiencing the actual symptoms of the disease, cause a reduction in quality of life. Pain is an important cause of ill health in patients with prostate cancer (8, 12, 13). We found that 62% of patients with prostate cancer experience pain, which causes a reduction in quality of life (14). Furthermore, the level of reduction in quality of life was partially explained by the accessibility of healthcare. How great this reduction in quality of life is in quantitative terms, and how great the economic value of the corresponding welfare loss is, constitute important information. This information forms an essential part of the socio-economic basis for decisions and as an indicator of the dignity of this health problem. Estimates of the burden of a disease for society indicate the potential benefits that can be gained with the help of new medical technology. Using data from a well-defined population on experiences of prostate cancer pain and perceived health, we have been able to simulate expected health utilities among a cohort of men with prostate cancer and to estimate the total expected survival and survival adjusted for reduced quality of life converted into quality adjusted life years (QALYs) for prostate cancer in Sweden. We have also estimated the economic value of the welfare loss due to prostate cancer pain.

MATERIAL AND METHODS

Subjects

Our basis for the calculation was a survey of pain and quality of life, where all men in the county of Östergötland, Sweden, who had received a diagnosis of prostate cancer from 1958 up to 31 December 1998, constituted the basis for selection (7 199 men) (14). They were identified through the National Tumour Register (1958–1986), and the Regional Prostate Cancer Register (RPCR) at the regional oncology centre at Linköping University Hospital

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(1987–1998) (15). All men who had died before the start of the study were excluded (5 679 men). Another 78 cases were excluded due to incomplete/mismatching registration numbers or having moved out of the county. The remaining 1 442 cases constituted our study population and they were asked to respond to a questionnaire. There were 1 243 (86%) responders. However, in 87 cases the questionnaire was filled in incompletely and was therefore not included in the analysis. Data on stage of prostate cancer at diagnosis and primary treatment on the remaining 1 156 men were used to populate the decision model. Details have been published elsewhere (14). Prostate cancer stages were defined as localized cancer (T0-2; N0, X; M0, X) in 866 (74.9%) cases and as advanced cancer (T3-4 and/or N1-4; M1) in 290 (25.1%) cases at time of diagnosis.

Questionnaire

The questionnaire and an explanatory letter were sent to the study population in September 1999. Differences in response rates between different geographical areas in the county were small, indicating that the risk of systematic dropouts due to local conditions is small.

The EuroQol

One part of the questionnaire was the commonly used global quality of life instrument, the EuroQol (16, 17). The EuroQol (EQ-5D) questionnaire consists of 5 questions with 3 response alternatives, where all combinations of responses form 243 different health states. Public preferences regarding a selection of these 243 health states, revealed by using a time-trade-off technique, have been obtained from a UK population (17). Full health has a value of 1, while values below 1 correspond to health states perceived as worse than full health. In our study we have used these health utility weights from the UK study, as equivalent weights for Sweden are lacking. However, a pilot study of a subset of the health utility weights show good agreement between Sweden and the UK (18).

The Brief Pain Inventory Form

Another part of the questionnaire comprised parts of the Brief Pain Inventory Form (BPI). The BPI is an instrument designed to assess the severity of pain and the impact of pain on daily functions among patients with cancer pain and pain due to chronic diseases. The ratings, ranging from 0 to 10, are classified as no pain (0), mild pain (1–4), moderate pain (5, 6) and severe pain (7–10). The question we used was, ‘Rate your pain by indicating the figure that best describes the severity of your pain right now’.

The results from these two parts of the survey were used to examine the relationship between patient-perceived pain, based on BPI severity question ratings, and patient-perceived health utility, based on the EQ-5D, for patients with prostate cancer. By comparing the answers on these two questions for each respondent we can show that the responses are relatively consistent. We used the Kruskal Wallis non-parametric test to investigate whether there were statistically significant differences between the patients rating their perceived pain as no pain, mild pain, moderate pain, or severe pain regarding their rating of perceived quality of life with the EQ-5D. In addition, we used the Spearman test to investigate whether there existed a correlation between the rating of the perceived pain measured by the BPI and the rating of the perceived quality of life measured by the EQ-5D.

DESCRIPTIVE MODEL

Patient categories

The starting point for us in the construction of the descriptive model of the course of the disease for different patient groups with prostate cancer was to define a number of relevant subgroups on the basis of background and prognostic factors. We chose stage of the prostate cancer and primary management as major variables. Primary management was identified as one of three treatment options: expectancy (wait-and-see and treatment when symptoms occur), curative (prostatectomy or treatment with internal or external radiation aiming at cure), or palliative treatment (any type of treatment to relieve symptoms, e.g. hormonal treatment (GnRH analogues) or surgical castration). From these main treatments we formed six stage and management groups (Table 3). Based on the distribution of the respondents regarding time since diagnosis we were able to calculate the probabilities of being alive in any one stage and management group for every year after diagnosis. The number of respondents in a certain stage and management group in any one year after diagnosis was divided by the total number of respondents in the same year after diagnosis and multiplied by the probability of being alive in that year. For example, the number of respondents in the group ‘Localized, expectancy’ two years after diagnosis was 70 and the total number of respondents in the same year after diagnosis was 186. The probability of being alive two years after diagnosis was 0.954. The probability of being alive in ‘Localized, expectancy’ two years after diagnosis was than calculated at 0.359 ((70/186) × 0.954). This was calculated for every stage and management group (Table 4). In the next step we distributed the patients in the six stage and management groups into three health states, according to the individuals’ experience of pain. The distribution was based on the individuals’ replies to question 4 in the EQ-5D concerning experience of pain. (The question from the EQ-5D actually uses the wording ‘Pain/discomfort’. For simplification, we use the word ‘pain’ to describe the scope of the question). This resulted in a total of 18 different patient categories—three for each of the six constructed patient groups based on stage

Table 1

Prostate cancer patient-perceived health utility based on EQ-5D regarding experienced pain

Stage and treatment group	n	Response to the 'pain question'[1]	Health utility
Localized, expectancy	200	1	0.850
	279	2	0.683
	21	3	− 0.050
Localized, palliative	67	1	0.838
	121	2	0.668
	10	3	0.011
Localized, curative	80	1	0.901
	79	2	0.683
	9	3	− 0.050
Advanced, expectancy	20	1	0.874
	31	2	0.665
	2	3	0.090
Advanced, palliative	64	1	0.828
	123	2	0.646
	10	3	− 0.004
Advanced, curative	17	1	0.910
	20	2	0.701
	3	3	0.173

[1] 1: I have no pain or discomfort, 2: I have moderate pain or discomfort, 3: I have severe pain or discomfort.

at diagnosis and primary management. Using the EQ-5D responses, we calculated a health utility weight for each of the 18 groups (Table 1).

Estimation of expected number of life years and quality adjusted life years

To estimate the potential number of life years the average prostate cancer patient will experience from time of diagnosis, the probability of being alive in any one stage and management group each year was multiplied by 1. This resulted in an expected survival each year after diagnosis. The expected survival each year was then added over the remaining life years. To estimate the potential number of QALYs the average prostate cancer patient will experience from time of diagnosis, the probability of being alive in any one stage and management group was multiplied by the corresponding utility of being in that health state. The expected quality adjusted survival each year was then added over the remaining life years. The results are presented in total for all individuals and separately for individuals with localized and advanced disease.

In the next step we carried out a simulation of a hypothetical treatment regime. We tested the effect on quality-adjusted survival if all pain could be adequately treated. All patients whose answers to question 4 of the EQ-5D were 2 or 3, i.e. moderate or severe pain or discomfort, were assumed to respond with a rating of 1 (no pain).

The model was constructed in Excel 2000 and allows an estimate to be made of the number of expected life years and quality-adjusted life years (QALYs) for different patient groups and different assumptions. A hypothetical cohort of patients was used to start the computer simulation in the stage and management group that matched their diagnosed type of cancer. They progressed according to the expected

Table 2

Relationship between patient-perceived pain, based on BPI severity question ratings, and patient-perceived health utility, based on EQ-5D, for patients with prostate cancer (%)

EQ-5D	BPI			
Response to the 'pain question'[1]	No pain (rating 0)	Mild pain (rating 1–4)	Moderate pain (rating 5–6)	Severe pain (rating 7–10)
1	52.0	15.4	8.1	3.6
2	48.0	81.5	82.3	61.0
3	0.0	3.1	9.6	35.4
Total	100.0	100.0	100.0	100.0
Average utility weight	0.82[2]	0.71†	0.58†	0.43†

[1] 1: I have no pain or discomfort. 2: I have moderate pain or discomfort. 3: I have severe pain or discomfort.

[2] Kruskal-Wallis test significant $p < 0.000$. Spearman test of correlation between responses to the BPI and responses to the EQ-5D = − 0.436, $p < 0.000$.

Table 3

Groups of prostate cancer patients based on tumour stage and primary management at diagnosis

Stage and management group	Number of individuals (%)
Localized, expectancy	500 (43.3)
Localized, palliative	198 (17.1)
Localized, curative	168 (14.5)
Advanced, expectancy	53 (4.6)
Advanced, palliative	197 (17.0)
Advanced, curative	40 (3.5)
Total	1156 (100)

distribution of patients over time. The simulation was carried out in annual cycles and continued until all patients were deceased.

RESULTS

Table 2 shows the relationship between patient-perceived pain, based on BPI severity question ratings, and patient-perceived health utility, based on the EQ-5D, for patients with prostate cancer. Of the patients who rated their pain as none (0) or mild (1–4) on the BPI rating scale, 98% gave a rating of 1 (I have no pain) or 2 (I have moderate pain) to the pain question in the EQ-5D. In addition, 95% of the patients who rated their pain as moderate (5, 6) or severe (7–10) on the BPI rating scale gave a rating of 2 (I have moderate pain) or 3 (I have severe pain) to the pain-question in the EQ-5D. Table 4 also shows that patient-perceived health utility decreases with increasing perceived pain and that there exists a statistically significant correlation between the two measures.

Our analysis estimates that a man with a diagnosis of prostate cancer can expect to live 5.87 years after time of diagnosis (Table 5). Expected number of life years for those patients classified at time of diagnosis as having localized cancer were 6.35 and for those with advanced cancer 5.39 years. Expressed in number of QALYs the figures were 4.66 and 3.69 for the two groups. Table 5 also shows that a treatment strategy by which all pain is being treated adequately would add on average 0.85 QALYs to the remaining life years after diagnosis. This corresponds to an annual average welfare loss of 0.14 (0.85/5.87) QALYs. The difference in utility corresponds to the patients' loss of quality-adjusted survival due to insufficient treatment of pain. The economic value of this welfare loss could be estimated if society's willingness to pay for a QALY were established. The question of what is an acceptable cost-effectiveness ratio, or what the willingness to pay for a QALY is for particular health conditions, has not yet been fully determined. Chapman et al. (19) constructed a league table of cost-utility ratios for 37 health interventions ranging from cost-savings up to a cost of €48 500 000 per QALY gained (median: €11 200 per QALY gained). Although league tables provide a useful reference, ratios may not be comparable in a fair way because of methodological variations. Earlier studies have, based on different assumptions, suggested a willingness to pay for a QALY of €30 000–80 000 (20–22) and a survey of health economists revealed a threshold value of €50 000 per QALY to be used in cost-effectiveness studies (23). However, recent

Table 4

Probabilities of being in any one stage and management group or being deceased every year after prostate cancer diagnosis

Year after diagnosis	n	LE[1]	LP[2]	LC[3]	AE[4]	AP[5]	AC[6]	Being deceased
1	53	0.340	0.113	0.264	0.094	0.151	0.038	0
2	186	0.359	0.185	0.082	0.041	0.256	0.031	0.046
3	148	0.254	0.205	0.070	0.043	0.200	0.022	0.206
4	126	0.275	0.148	0.037	0.037	0.143	0.026	0.334
5	110	0.253	0.101	0.030	0.030	0.126	0.015	0.445
6	117	0.254	0.067	0.043	0.039	0.055	0.004	0.538
7	63	0.211	0.057	0.029	0.001	0.051	0.011	0.640
8	88	0.198	0.028	0.035	0.010	0.024	0.010	0.695
9	51	0.112	0.045	0.036	0.009	0.022	0.004	0.772
10	47	0.087	0.039	0.047	0.001	0.012	0.001	0.813
11	36	0.052	0.004	0.060	0.004	0.020	0.004	0.856
12	60	0.034	0.008	0.045	0.004	0.009	0.013	0.887
13	35	0.023	0.009	0.025	0.001	0.001	0.005	0.936
14	20	0.008	0.003	0.014	0.002	0.002	0.003	0.968
15 or more	16	0.007	0.002	0.004	0.001	0.001	0.001	0.984
Total	1156							

[1] Localized expectancy.
[2] Localized palliative.
[3] Localized curative.
[4] Advanced expectancy.
[5] Advanced palliative.
[6] Advanced curative.

Table 5

Expected life years and total and incremental expected quality adjusted life years per case with regard to remaining life after diagnosis: comparison between the base case and a hypothetical treatment regime where all pain is being treated adequately

Tumour stage	Life years	Quality adjusted life years		
		Base case	All pain/discomfort being adequately treated	Incremental gain in QALYs
Localized	6.35	4.66	5.48	0.82
Advanced	5.39	3.69	4.57	0.88
All	5.87	4.17	5.02	0.85

data indicate lower willingness to pay for small incremental improvements, approximately €10 000 (24). In absence of an established value of the willingness to pay, assumptions of the economic value of a QALY must be used. One approach is to use the extra cost of treatment of moderate to severe pain with a painkiller (Duragesic®) versus morphine as an indicator of what society at least is willing to pay. It has in one study been estimated at approximately €19 600 per QALY (25). Although this pharmaceutical product is not always the first-line therapy it is still an accepted alternative. We think this could be a reasonable estimate, lower than the estimations based on risk of death and higher than the estimation based on small incremental improvements in quality of life. When we use this figure as an indicator of what society is willing to pay to gain quality-adjusted life expectancy and multiply it by 0.85 QALY, the economic value of the expected welfare loss per man with prostate cancer could be estimated at €16 600. A rough estimate for Sweden, using a prevalence approach and the local 1999 prevalence of prostate cancer in our study population (1 442 cases in a defined population of 200 000 males corresponds to 7 210 cases per million men and 31 580 totally in Sweden), is a total expected loss of 4 421 (31 580 × 0.14) QALYs per year at a value of €86 600 000 (€4421 × 19 600). This corresponds to a value of €19 800 000 per million men in Sweden (86 600 000/4.38).

DISCUSSION

We carried out a simulation of a hypothetical treatment regime in which all prostate cancer pain in a defined population was assumed to be adequately treated. Our estimation of the effect on quality-adjusted survival ignores any possible subtle interaction effects among the dimensions in the EQ-5D. It is likely that a total removal of pain would affect the responses on the other dimensions in the EQ-5D in a positive direction, i.e. the difference in valuation between baseline and the hypothetical treatment regime is probably greater than our estimation. This is also relevant to our estimation of the expected loss of QALYs per patient from time of diagnosis due to insufficient treatment of pain. A conservative valuation of the health utility would result in an underestimation of the expected loss of QALYs. However, if all prostate cancer pain is removed the patient may still experience pain and reduced health utility due to other conditions. This would probably reduce the underestimation of the difference in valuation between baseline and the hypothetical treatment regime.

Our analysis estimates that a man with a diagnosis of prostate cancer can expect to live 5.87 years after time of diagnosis. This estimation is slightly higher than actual survival data from a case-record study of men with prostate cancer in the county of Östergötland who died in 1997–1998 (26), where an average survival of 4.7 years after time of diagnosis was reported. The difference is probably partly due to different calculation techniques. We estimated survival based on the number of men who were alive at the beginning of each year and assumed that they survived until the end of the year. In the study on the 1997–1998 cohort data on survival were traced currently. Accordingly, our results are a conservative estimate of the number of life-years lost due to prostate cancer, although, we have no reason to believe that our calculation technique of expected survival significantly affects the estimation of the welfare loss due to pain.

In this study the expected survival of a patient with localized prostate cancer was on average 6.35 years after time of diagnosis, while a patient with advanced disease had an expected survival of 5.39 years after time of diagnosis. The small difference in expected survival between localized and advanced disease is probably due to the fact that prostate cancer mostly affects older men. Old age in addition to other comorbidities result in a low expected survival time even if the prostate cancer disease is localized. In addition patients with Nx disease (regional lymph nodes not assessed) or Mx disease (presence of distant metastasis not assessed) might have been mis-staged as localized.

Our results indicate that the quality-adjusted life expectancy for patients with prostate cancer could be increased with optimal pain treatment. However, for medical as well as other reasons achieving this is not always feasible in clinical practice. Nevertheless, many patients would probably benefit from a more individualized pain treatment programme. The reduction in quality-adjusted life expectancy for cancer patients is also affected by other circumstances, e.g. knowledge about the disease and the risk of future health problems, and/or having experienced other symptoms of the disease. These matters are probably more difficult to quantify and value in quality of life terms than the experience of pain. However, more knowledge concerning the substance of the reduction in quality of life increases the possibility for the healthcare system to offer appropriate measures to attain as good a quality of life as possible for the individual patient. In practice, however, it is probably not possible to remove all factors that decrease the quality of life in prostate cancer.

We used the question of ‘pain right now’ from the BPI questionnaire to examine the relationship between patient-perceived pain and patient-perceived health utility. We chose not to use the item ‘pain worst’ to avoid an extreme rating of the perceived pain, even though this item has been found to be a more sensitive and stable measure of pain (27).

Some argue that there should not be a particular trade-off in society because the willingness to pay for an extra quality adjusted life year is related to the patients’ or the populations’ need for health care (28). Society is willing to pay more for a QALY in patients with a severe health condition compared with those who have a less severe condition, where severe could mean degree of pain or discomfort, function reduction or risk of mortality. Patients with prostate cancer pain would probably be classified as having a relatively severe condition and be given high priority in terms of willingness to pay. Our estimate of the willingness to pay for an extra quality adjusted life year (€19 600) is uncertain. If we were to reason differently and choose an estimate of the willingness to pay for an extra QALY of €50 000 based on a survey of health economists (23) the value of the estimated annual welfare loss would be €221 050 000. Our value of the estimated annual welfare loss of €86 600 000 can be compared with the direct costs for prostate cancer in Sweden, which was €104 300 000 in 1998 (26). Using resources for optimal prostate cancer pain treatment means reducing the resources for treatment of some other state of ill health. Would it be more effective to use some of the resources allocated to early detection of prostate cancer for pain treatment? This can only be answered in well-designed health economic evaluations.

Limitations of our study design lie foremost in the fact that we estimated probabilities of being alive in any one health state at a defined point in time. An improvement would involve tracing a defined cohort over time. This would generate information on the course of events for individual patients and allow calculation of transition probabilities between different health states. However, such an approach takes at least 10 years of data collection and we have no reason to believe that our design incorporates bias into our results in any systematic way.

CONCLUSIONS

Perceived pain among men with prostate cancer is a common health problem, which leads to a substantial reduction in health-related quality of life. The reduction in health-related quality of life corresponds to on average 0.85 life years in full health (QALYs). Based on an estimate of the willingness to pay for a QALY the economic value of this welfare loss due to prostate cancer pain is in the magnitude of €86 600 000 per year (€19 800 000 per million men in Sweden).

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