Survival gains needed to offset persistent adverse treatment effects in localised prostate cancer

Men diagnosed with localised prostate cancer (LPC) face difficult treatment decisions. Although the eradication of cancer is a major issue for most men (Zeliadt et al, 2006), controlled trial evidence about the survival benefits of the full range of treatment alternatives is limited and patients’ views on the survival gains that might justify these problems have not been quantified.

**Background:** Men diagnosed with localised prostate cancer (LPC) face difficult choices between treatment options that can cause persistent problems with sexual, urinary and bowel function. Controlled trial evidence about the survival benefits of the full range of treatment alternatives is limited, and patients’ views on the survival gains that might justify these problems have not been quantified.

**Methods:** A discrete choice experiment (DCE) was administered in a random subsample (n = 357, stratified by treatment) of a population-based sample (n = 1381) of men, recurrence-free 3 years after diagnosis of LPC, and 65 age-matched controls (without prostate cancer). Survival gains needed to justify persistent problems were estimated by substituting side effect and survival parameters from the DCE into an equation for compensating variation (adapted from welfare economics).

**Results:** Median (2.5, 97.5 centiles) survival benefits needed to justify severe erectile dysfunction and severe loss of libido were 4.0 (3.4, 4.6) and 5.0 (4.9, 5.2) months. These problems were common, particularly after androgen deprivation therapy (ADT): 40 and 41% overall (n = 1381) and 88 and 78% in the ADT group (n = 33). Urinary leakage (most prevalent after radical prostatectomy (n = 839, mild 41%, severe 18%)) needed 4.2 (4.1, 4.3) and 27.7 (26.9, 28.5) months survival benefit, respectively. Mild bowel problems (most prevalent (30%) after external beam radiotherapy (n = 106)) needed 6.2 (6.1, 6.4) months survival benefit.

**Conclusion:** Emerging evidence about survival benefits can be assessed against these patient-based benchmarks. Considerable variation in trade-offs among individuals underlines the need to inform patients of long-term consequences and incorporate patient preferences into treatment decisions.

**Keywords:** prostate cancer; preferences; trade-off; utility; survival benefit; quality of life
preferences in terms of utility decrements caused by specific adverse effects (Lubeck et al., 2002; Bremner et al., 2007). Utility has traditionally been estimated with time trade off and standard gamble methods, and more recently with discrete choice experiments (DCE) (Ryan, 2004). When hypothetical health states are included in these ‘stated preference’ methods, they yield more accurate and valid results than those based on personalised health states because the description of health states is standardised (Chapman et al., 1998).

To date, no studies have explicitly expressed patient preferences for treatment of LPC in terms of the relative tolerability of adverse treatment-related effects or the survival gains needed to make persistent adverse effects worthwhile. Each of these is relevant to clinicians counselling patients on treatment decisions, and the latter perspective provides a benchmark against which emerging evidence about actual survival benefits of alternative treatments can be assessed. The aim of this study was to quantify these issues using a DCE.

MATERIALS AND METHODS

Study design and sample

Data were obtained from the New South Wales (NSW) Prostate Cancer Care and Outcomes Study (PCOS). PCOS is a population-based (NSW, Australia) cohort study of men aged <70 when diagnosed with prostate cancer and recruited from the NSW Central Cancer Registry, and age and postcode matched controls (without prostate cancer) recruited via the White Pages telephone directory. Details of recruitment to PCOS and detailed demographic and clinical profiles of each treatment group and the controls are reported elsewhere (Smith et al., 2009). Flow diagrams for PCOS case and control recruitment and follow-up are given in Supplementary Figures A and B. Sample flow relevant to this paper is depicted in Figure 1. The study was approved by the ethics committees of the Cancer Council NSW, Cancer Institute NSW and NSW Department of Health. Informed consent was obtained from each participant.

Figure 1  Flow diagram showing derivation of HRQOL and preference survey samples of the PCOS.
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et al (Louviere respondents per treatment group per version were needed 2005), arranged into 54 pairs ('choice sets') (Supplementary Figure optimal subsample of 108 health states was selected (Street ± expectancy and its uncertainty, with levels 4, 8 or 12 years and assigned three levels (Table 1). We also included average life seven common treatment-related adverse effects; each was consulted with clinicians and a consumer representative to identify related adverse effects and survival. We reviewed the literature and British Journal of Cancer (2012)

Analysis of the preference data

Prevalence of urinary, sexual and bowel problems, fatigue and other hormonal effects were estimated from the 3-year post-diagnosis HRQOL data. Seven questions from the long-form University of California Los Angeles Prostate Cancer Index (Litwin et al, 1998) that most closely corresponded to the seven attributes in the preference survey were used to classify each individual (n = 1381) into one of the three categories (none, mild and severe) for each treatment-related adverse effect (see technical Supplementary Appendix for details).

Data collection

The preference survey was piloted (see technical Supplementary Appendix for details). Preference survey participants were randomly assigned to questionnaire version within treatment strata. Preference surveys were posted to subjects, who were then contacted by telephone and the data collected by telephone interview. Collection of the health-related quality of life (HRQOL) data is described elsewhere (Smith et al, 2009).

Relative tolerability of treatment-related adverse effects was addressed by ranking the fixed effects coefficients: those with the largest negative coefficients (greatest negative impact on utility) were interpreted as least tolerable, and those with the smallest negative coefficients or positive coefficients were interpreted as the most tolerable. Confidence intervals on coefficients were taken into account in interpreting the relative rankings.

The degree of variation among men in preferences was quantified by the distribution of the random effect coefficients. These are assumed to be normally distributed, so the majority (60%) lie within one s.d. of the fixed effect coefficients. As this

Table 1 Treatment-related adverse effects included as attributes in the preference survey and their prevalence at 3-year follow-up in 1381 PCOS participants who had localised prostate cancer at diagnosis and no recurrence at 3 years, and in the subset of 357 men (PCOS cases) who participated in the DCE

| Attribute          | Level | Wording                                           | PCOS case participants (n = 1381) (%) | DCE case participants (n = 357) (%) |
|--------------------|-------|---------------------------------------------------|--------------------------------------|------------------------------------|
| Erectile dysfunction | Base  | No problems achieving an erection when you want one | 27                                   | 27                                 |
|                    | Mild   | Some problems achieving an erection when you want one | 33                                   | 29                                 |
|                    | Severe | Never able to achieve an erection when you want one | 40                                   | 44                                 |
| Loss of libido     | Base   | No change in sexual desire                        | 8                                    | 7                                  |
|                    | Mild   | Less sexual desire                                | 50                                   | 43                                 |
|                    | Severe | Complete loss of sexual desire                    | 41                                   | 51                                 |
| Urinary leakage    | Base   | No problems with leaking urine                    | 53                                   | 64                                 |
|                    | Mild   | Occasional problems with leaking urine            | 33                                   | 23                                 |
|                    | Severe | Severe problems with leaking urine (no urinary control whatsoever) | 14                                   | 12                                 |
| Urinary blockage   | Base   | No problems with urine blockage                   | 74                                   | 67                                 |
|                    | Mild   | Some problems with urine blockage (have a weak urine stream but get some relief or comfort afterwards) | 19                                   | 23                                 |
|                    | Severe | Severe problems with urine blockage (continually feeling the need to urinate but passing very little with no relief afterwards) | 7                                    | 10                                 |
| Bowel symptoms     | Base   | No bowel problems                                | 79                                   | 75                                 |
|                    | Mild   | Occasional loose bowel movements with discomfort/pain | 20                                   | 25                                 |
|                    | Severe | Very frequent loose bowel movements with discomfort/pain and leakage | 1                                    | 1                                  |
| Fatigue            | Base   | No change in your energy level                    | 47                                   | 44                                 |
|                    | Mild   | Some tiredness and loss of energy                 | 49                                   | 51                                 |
|                    | Severe | Severe tiredness and loss of energy               | 4                                    | 5                                  |
| Hormonal effects   | Base   | No hot flushes or moodiness                       | 88                                   | 85                                 |
|                    | Mild   | Mild hot flushes and moodiness                    | 7                                    | 7                                  |
|                    | Severe | Severe hot flushes and moodiness                  | 5                                    | 8                                  |

Abbreviation: PCOS = Prostate Cancer Outcomes Study.

Preference elicitation method

A DCE was used to determine the utility of hypothetical health states that might result from treatment for LPC (Louviere et al, 2003). Each state was described in terms of ‘attributes’: treatment-related adverse effects and survival. We reviewed the literature and consulted with clinicians and a consumer representative to identify seven common treatment-related adverse effects; each was assigned three levels (Table 1). We also included average life expectancy and its uncertainty, with levels 4, 8 or 12 years and ±25%, 50% or 75%, respectively.

Experimental design and sample size

Health states were constructed according to an experimental design. The ‘full factorial’ design contains all possible combinations of attributes and levels (3^9 = 19,683 states). A statistically optimal subsample of 108 health states was selected (Street et al, 2005), arranged into 54 pairs (‘choice sets’) (Supplementary Figure C), then split into three versions (18 choice sets each). Twenty respondents per treatment group per version were needed (Louviere et al, 2000), thus 420 participants were required for the preference survey.

Analysis of the HRQOL data

Prevalence of urinary, sexual and bowel problems, fatigue and other hormonal effects were estimated from the 3-year post-diagnosis HRQOL data. Seven questions from the long-form University of California Los Angeles Prostate Cancer Index (Litwin et al, 1998) that most closely corresponded to the seven attributes in the preference survey were used to classify each individual (n = 1381) into one of the three categories (none, mild and severe) for each treatment-related adverse effect (see technical Supplementary Appendix for details).

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represents the typical range of individual utility coefficients, it is a clinically relevant expression of preference heterogeneity.

The effect of treatment group on preferences was evaluated by estimating separate fixed effects models for each treatment group. As parameter estimates in discrete outcome models are confounded by error variance (Swait and Louviere, 1993), parameter estimates were not directly comparable across treatment groups. Rank ordering of parameter estimates was used to assess the similarity of preferences across the treatment groups, again taking confidence intervals into consideration. The effect of age on preferences for sexual function was addressed with a likelihood ratio test for the interaction of age (dichotomised at 65) with severe erectile dysfunction and severe loss of libido (see technical Supplementary Appendix for details).

Estimation of survival gains needed

To estimate the survival gains needed to justify persistent treatment-related adverse effects, the value of changes in health utility associated with each level of each side effect was expressed in terms of survival time (see technical Supplementary Appendix for details). In summary, the survival gain needed to justify a chronic treatment-related adverse effect(s) was such that the value of this health state for this extended time (T + survival gain needed) was equivalent to the value of the base case (health state without treatment) for a survival time of 12 years (T). The base case was determined from the 3-year post-diagnosis HRQOL data of men initially managed with active surveillance; in the absence of a randomised design, this group was deemed the most valid comparator. The survival gains needed for the additional burden of each persistent treatment-related adverse effect level singly and for each commonly occurring combination of effects were calculated, and their distributions were simulated. We report medians and 2.5 and 97.5 centiles, analogous to 95% confidence intervals estimated by bootstrap methods.

RESULTS

Study participants

Table 2 shows the characteristics of the 1381 PCOS cases with complete 3-year HRQOL data (the ‘HRQOL sample’) and the 422 men, who participated in the preference survey (the ‘preference sample’). Supplementary Figures A and B and Figure 1 show the derivation of these samples.

Prevalence of adverse effects (Table 1) is given by treatment group in Figure 2. Only 1.2% of the HRQOL sample (including 1.2% of the active surveillance group) reported none of the seven side-effects/symptoms 3 years after diagnosis. Prevalence of adverse effects for the 357 cases in the preference sample in also given Table 1. Severe erectile dysfunction and severe loss of libido (see technical Supplementary Appendix for details).

Survival gains needed for localised prostate cancer

| Numbers per treatment strata                                      | HRQOL sample n (% of 1381) | Preference sample n (% of 422) |
|-------------------------------------------------------------------|------------------------------|--------------------------------|
| Cases (localised prostate cancer)                                 |                              |                                |
| Radical prostatectomy                                            | 839 (46.3)                   | 64 (15.2)                      |
| External beam radiotherapy (EBRT) only                          | 106 (5.8)                    | 66 (15.6)                      |
| Androgen deprivation therapy (ADT) only                         | 37 (2.0)                     | 37 (8.8)                       |
| Combined EBRT and ADT                                           | 136 (7.5)                    | 64 (15.2)                      |
| Low-dose rate brachytherapy                                     | 56 (3.1)                     | 31 (7.3)                       |
| High-dose rate brachytherapy                                    | 41 (2.3)                     | 29 (6.9)                       |
| Controls (without prostate cancer)                              | 166 (9.2)                    | 66 (15.6)                      |

Age-group at 3-year follow-up or preference survey

| Highest level of education                                       | HRQOL sample n (% of 1381) | Preference sample n (% of 422) |
|-----------------------------------------------------------------|------------------------------|--------------------------------|
| Less than high school certificate                               | 57 (4.1)                     | 20 (4.7)                       |
| Completed high school                                          | 953 (69.0)                   | 290 (68.7)                     |
| University or college degree                                   | 364 (26.4)                   | 110 (26.1)                     |
| Unknown                                                         | 7 (0.5)                      | 2 (0.5)                        |

Marital status at diagnosis

| Married or living as married                                    | 1160 (84.0)                  | 350 (82.9)                     |
| Never married, divorced, separated or widowed                  | 217 (15.7)                   | 72 (17.1)                      |
| Missing                                                         | 4 (0.3)                      | 0 (0.0)                        |

Self reported health 3 year after diagnosis

| Poor                                                             | 66 (48)                      | 11 (3.1)                       |
| Fair                                                            | 176 (12.7)                   | 55 (13.4)                      |
| Good                                                            | 338 (24.5)                   | 98 (23.5)                      |
| Very good                                                       | 519 (37.6)                   | 126 (33.5)                     |
| Excellent                                                       | 275 (19.9)                   | 64 (17.9)                      |
| Missing                                                         | 7 (0.5)                      | 3 (0.8)                        |

PSA level at diagnosis (ng ml⁻¹)

| <4.0                                                            | 140 (10.1)                   | 35 (9.8)                       |
| 4.0–9.9                                                        | 799 (57.9)                   | 163 (45.7)                     |
| 10.0–19.9                                                     | 282 (20.4)                   | 87 (24.4)                      |
| 20+                                                            | 129 (9.3)                    | 65 (18.2)                      |
| Missing                                                        | 31 (2.2)                     | 7 (2.0)                        |

Gleason score at diagnosis

| 2–5                                                            | 135 (9.8)                    | 36 (10.1)                      |
| 6                                                              | 651 (47.1)                   | 151 (42.3)                     |
| 7                                                              | 465 (33.7)                   | 120 (33.6)                     |
| 8–9                                                            | 114 (8.3)                    | 47 (13.2)                      |
| Missing                                                        | 16 (1.2)                     | 3 (0.8)                        |

Median months between diagnosis and preferences survey (cases)

| Median months between diagnosis and preferences survey (cases) | 46 (32–60)                   |
|----------------------------------------------------------------|----------------------------|
| Median months between recruitment and preferences survey (controls) | 30 (27–50)                   |

| Abbreviations: HRQOL = health-related quality of life; PCOS = Prostate Cancer Outcomes Study; PSA = prostate specific antigen. |

years for the severe levels of the three least tolerable treatment-related adverse effects (both aspects of urinary function and bowel problems), through to about 1 year for severe fatigue and other
hormonal effects, about 10 months for mild other hormonal effects and 3–6 months for the remainder (Figure 3).

Many men reported more than one adverse effect at 3 years. There were $3^3 = 2187$ unique health states described by the three levels of the seven adverse effects. It was not practicable to estimate survival gains for each one. As the function used to calculate survival gains needed (expression 4 in the technical Supplementary Appendix) is not linear, the cumulative effect of multiple adverse effects cannot be derived simply by summing over component effects. We therefore simulated the survival gains needed for the three most common treatment-related adverse effect profiles for each treatment group (Supplementary Table B). Approximations based on the simple sum of the component adverse effects in most cases fell within the 2.5 and 97.5 centiles of the simulated distributions. For example, severe erectile dysfunction alone would be compensated by a 4-month survival benefit and severe libido loss with 5.02 months (Figure 3), giving a sum of 9.02, which is a reasonable approximation of the simulated estimate of 9.14 months, well within the 95% confidence interval (8.46–9.80, Supplementary Table B).

**DISCUSSION**

Severe urinary dysfunction and bowel symptoms were least tolerable, severe hormonal effects and fatigue were somewhat more tolerable, and severe sexual dysfunction was relatively benign, having about the same negative impact as mild urinary dysfunction and bowel symptoms. Other hormonal effects were the least tolerable of the mild treatment-related adverse effects. These patterns were consistent across treatment groups and unaffected by age. Overlaid on these aggregate results was substantial variation in individual preferences, consistent with the decision analysis of Sommers et al (2007) and two preference studies (Singer et al, 1991; Stewart et al, 2005). Ours is the first study to quantify this variation. This leads to two important observations. First, virtually all men were averse to severe urinary leakage (predominantly negative individual coefficients), although some men’s aversion was much greater than others’. The same was true for all severe adverse effects except severe loss of libido (where the impact on utility of each attribute on average across respondents). Second, the lower end of the range of individual utility decrements for

**Figure 2** Prevalence of urinary, sexual and bowel problems, fatigue and other hormonal effects 3 years after diagnosis by treatment group (HRQOL sample, $n = 1381$): active surveillance (AS, $n = 166$), radical prostatectomy (RP, $n = 839$), external beam radiotherapy (EBRT, $n = 106$), ADT ($n = 37$), combined therapy (EBRT + ADT, $n = 136$), low-dose rate brachytherapy (LDRBT, $n = 56$), high-dose rate brachytherapy (HDRBT, $n = 41$). White = none, grey = mild, black = severe.

**Table 3** Relative tolerability of treatment-related adverse effects (mean utility impact) and preference variability (range of individual utility coefficients) based on estimates from the random parameter logit model

| Preference survey attributes, ranked by impact in utility | Mean utility impact (MUI)* coefficient (95% CI) | $P^*$ | MUI ± 1 s.d. | $P^{**}$ |
|----------------------------------------------------------|-----------------------------------------------|------|--------------|---------|
| Severe urinary leakage | $-1.33\,(\pm 1.49, \pm 1.16)$ | $<0.001$ | $-2.21$ | $0.001$ |
| Severe bowel symptoms | $-1.23\,(\pm 1.40, \pm 1.07)$ | $<0.001$ | $-2.13$ | $<0.001$ |
| Severe urinary blockage | $-1.08\,(\pm 1.22, \pm 0.93)$ | $<0.001$ | $-1.73$ | $<0.001$ |
| Severe hormonal effects | $-0.63\,(\pm 0.77, \pm 0.49)$ | $<0.001$ | $-1.20$ | $<0.001$ |
| Severe fatigue | $-0.62\,(\pm 0.73, \pm 0.50)$ | $<0.001$ | $-0.95$ | $<0.001$ |
| Mild hormonal effects | $-0.43\,(\pm 0.54, \pm 0.31)$ | $<0.001$ | $-0.57$ | $<0.001$ |
| Severe erectile dysfunction | $-0.30\,(\pm 0.43, \pm 0.16)$ | $<0.001$ | $-1.17$ | $<0.001$ |
| Mild urinary blockage | $-0.23\,(\pm 0.35, \pm 0.12)$ | $<0.001$ | $-0.37$ | $0.40$ |
| Mild bowel symptoms | $-0.27\,(\pm 0.38, \pm 0.15)$ | $<0.001$ | $-0.32$ | $<0.001$ |
| Severe libido loss | $-0.21\,(\pm 0.32, \pm 0.10)$ | $<0.001$ | $-0.27$ | $0.87$ |
| Mild urinary leakage | $-0.20\,(\pm 0.31, \pm 0.09)$ | $<0.001$ | $-0.30$ | $0.56$ |
| Mild fatigue | $-0.14\,(\pm 0.25, \pm 0.03)$ | $0.01$ | $-0.18$ | $<0.001$ |
| Mild erectile dysfunction | $0.14\,(0.02, 0.25)$ | $0.025$ | $0.08$ | $<0.001$ |
| Mild libido loss | $0.04\,(\pm 0.08, 0.15)$ | $0.55$ | $-0.15$ | $0.13$ |

* **p-value for test of null hypothesis that fixed (*) and random (**) parameter estimates are equal to zero.  
  ** The mean ($\bar{\beta}$, in Expression 2 in Supplementary Appendix) reflects the impact on utility of each attribute on average across respondents.  
  *** The degree of variation among men in preferences (preference heterogeneity) was quantified with the s.d. of the distribution of the $\alpha_k$ (see Equation 2 in technical Supplementary Appendix). Since the $\alpha_k$ are normally distributed, the majority (68%) lie within one s.d. of the mean. This range therefore represents the typical range of individual utility coefficients.
severe urinary leakage, severe bowel symptoms and severe urinary blockage was typically more negative than the upper end of the range of decrements for most of the mild side effects (MUI ± s.d. in Table 3). Together, these two observations have an important clinical implication: patients are likely to make decisions about treatment based on severe adverse effects, not mild ones.

Men managed with active surveillance commonly experienced mild loss of libido 3 years after diagnosis; this formed the base case for estimating survival benefit. Severe erectile dysfunction and severe loss of libido were prevalent, particularly in men who had androgen deprivation therapy (ADT); 4 and 5 months additional survival, respectively, were needed to justify these singly and about 9 months if experienced together. Urinary leakage was most prevalent in the radical prostatectomy group; 4 months additional survival was needed for mild levels and about 28 months for severe levels. Mild bowel problems were most prevalent in men who had external beam radiotherapy; about 6 months was needed to justify these. Of the 18 most common health states 3-years post-diagnosis, 10 required <6 months of additional survival; the 4 health states most common after radical prostatectomy were among these. For 6 of the 18 most common health states, survival benefits needed ranged from 1–3 years; of these, 5 were relatively common in the ADT group, accounting for 33.5% of that group in total. All involved severe libido loss and severe erectile dysfunction, accounting for about 9 months of the survival benefit needed.

Thus we found that relatively modest survival benefits were sufficient to offset the most common side effects of treatments for prostate cancer for about two-thirds of the most common health states 3-years post-diagnosis. These are similar to those judged by women with early breast cancer as sufficient to make adjuvant chemotherapy or endocrine therapy worthwhile (Duric and Stockler, 2001; Thewes et al, 2005). However, even substantial survival benefits were insufficient to offset severe urinary dysfunction, which is not rare (reported by 14% of our HRQOL sample at 3 years, with similar prevalence estimates in other population-based studies (Potosky et al, 2000, 2004; Sanda et al, 2008; Gore et al, 2009; Mols et al, 2009; Smith et al, 2009)). Men considering their options should be counselled about the risks of treatment-related adverse effects, their likely effects on quality of life, and possible remedial measures.

The results of our study corroborate the findings of many utility studies in LPC: mild symptoms have higher utility than severe, and urinary and bowel symptoms have much lower utility than sexual dysfunction and loss of libido (Bremner et al, 2007). Our study adds to this literature by providing estimates of survival gains required for each common adverse treatment effect, thereby translating utilities into something practical for clinicians and patients—survival gains needed to justify persistent problems. By incorporating the HRQOL data from the our larger PCOS study, the current paper uniquely reveals the potential overall impact of the trade-offs and survival gains required for adverse treatment side effects.

Although there are numerous studies of patient preferences in LPC prostate cancer, ours provides the most comprehensive set of treatment-related adverse effects. Our population-based sample is a major strength, containing experiences of all treatment options and controls. Like many previous studies, ours was retrospective, with men bringing personal experience to their hypothetical choices. We avoided bias arising from patient’s preconceptions by not associating health states with treatments (Zeliadt et al, 2006). Although real choices made before treatment may differ from hypothetical choices made with the benefit of hindsight, arguably the latter are more informative than the former for future men facing similar decisions. Our controls were men of similar age and demographic profile to our cases, and therefore most like men facing a primary treatment decision. It is noteworthy that their results were similar to those of each of the treatment groups (as shown in Supplementary Table A), suggesting that men’s preferences are in fact not markedly affected by experience of treatment. We limited our sample of cases for the DCE to men with localised disease as we felt their opinions were most informative for men facing future choices about curative treatments for LPC. The attitudes of patients whose disease progressed, particularly those who died early because of very aggressive disease, have not been captured in our study, and so our results may not generalise to this group. Whether such patients would have preferred to be alive even with severe adverse effects is a question that is beyond the scope of this study.

Previous studies have various limitations: considering only one/some adverse effects (Singer et al, 1991; Saigal et al, 2001; Bruner et al, 2004); assigning different severity levels to adverse effects (Saigal et al, 2001; Sculpher et al, 2004); assessing only one or two treatment options (Singer et al, 1991; Bruner et al, 2004; Sculpher et al, 2004; Jenkins et al, 2005); sampling respondents from only one treatment type (Smith et al, 2002; Bruner et al, 2004); combining bladder and bowel problems into one attribute (Chapman et al, 1999; Knight et al, 2004); investigating just a few hypothetical health states (Chapman et al, 1999; Saigal et al, 2001; Bruner et al, 2004; Knight et al, 2004; Jenkins et al, 2005); using patients’ rating of their own health states (Smith et al, 2002; Krahn et al, 2003). These factors limit the comparability of our results for relative tolerability of adverse effects with those from other studies.

![Figure 3](image-url)
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Chapman GB, Elstein AS, Kuzel TM, Nadler RB, Sharifi R, Bennett CL (Sculpher et al., 2004) versus 0.34 (ours). Our survival benefit time scale was realistic in terms of life expectancy of participants. Our CV approach has several advantages: it allows for combinations of adverse effects (more clinically relevant than single side effects); it takes into account an empirically based base case and it quantifies additional survival required to compensate for loss in quality of life because of treatment (again with empirically based health states).

We found that mild erectile dysfunction had a significant positive utility value (0.14, Table 3). This was probably because of the high prevalence of severe erectile dysfunction in the DCE sample (44%, Table 1). Although the positive utility impact of mild erectile dysfunction can be explained, it can become problematic when added to other negative utility effects. For example, our results paradoxically suggest that severe libido loss requires 5.02 months survival gain, whereas severe libido loss plus mild erectile dysfunction requires only 1.82 months. This empirical quirk should be kept in mind when interpreting results in Supplementary Table B for heath states including mild erectile dysfunction. It also highlights the potential gains in utility of remedial measures for erectile dysfunction.

Increasing uptake of prostate-specific antigen testing and attendant risks of overdiagnosis and overtreatment present clinical and ethical dilemmas (Barry, 2009). If treated, men are at risk of adverse treatment-related effects and a contestable survival benefit (Potosky et al., 2004; Sanda et al., 2008; Gore et al., 2009; Mols et al., 2009; Smith et al., 2009). The most fruitful avenues for future research are therefore those that increase our understanding of variation in individual preferences, the relationship of preferences to treatment decisions and the effectiveness of different ways of presenting complex choice information to men before treatment decisions are made, of treatment innovations to minimise treatment-related adverse effects and of early interventions to ameliorate them. The ultimate goal is evidence-based shared decision making that matches management and outcomes to patients’ preferences, thereby maximising patient utility after diagnosis of LPC.

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