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Patients' preferences for the management of non-metastatic prostate cancer: discrete choice experiment

Mark Sculpher, Stirling Bryan, Pat Fry, Patricia de Winter, Heather Payne and Mark Emberton

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Patients’ preferences for the management of non-metastatic prostate cancer: discrete choice experiment

Mark Sculpher, Stirling Bryan, Pat Fry, Patricia de Winter, Heather Payne, Mark Emberton

Abstract

Objective To establish which attributes of conservative treatments for prostate cancer are most important to men.

Setting Two London hospitals.

Participants 129 men with non-metastatic prostate cancer, mean age 70 years; 69 of 118 (58%) with T stage 1 or 2 cancer at diagnosis.

Main outcome measures Men’s preferences for, and trade-offs between, the attributes of diarrhoea, hot flushes, ability to maintain an erection, breast swelling or tenderness, physical energy, sex drive, life expectancy, and out of pocket expenses.

Results The men’s responses to changes in attributes were all statistically significant. When asked to assume a starting life expectancy of five years, the men were willing to make trade-offs between life expectancy and side effects. On average, they were most willing to give up life expectancy to avoid limitations in physical energy (mean three months) and least willing to trade life expectancy to avoid hot flushes (mean 0.6 months to move from a moderate to mild level or from mild to non).

Conclusions Men with prostate cancer are willing to participate in a relatively complex exercise that weighs up the advantages and disadvantages of various conservative treatments for their condition. They were willing to trade off some life expectancy to be relieved of the burden of troublesome side effects such as limitations in physical energy.

Introduction

Several situations exist where patients face trade-offs between the risks and benefits of alternative therapies. The conservative management of men with organ confined or locally advanced prostate cancer is such a situation. Men diagnosed at a stage when radical treatments such as prostatectomy or radiotherapy are inappropriate face several treatment options, including watchful waiting or oral steroidal or non-steroidal antiandrogen monotherapy. Many patients choose castration, performed medically rather than surgically. Alternatively, there is the option of antiandrogen treatment combined with medical or surgical castration.

To make an informed choice, men need to be able to weigh up the slight differences in effectiveness of treatment against a spectrum of side effects associated with alternative strategies. For example, non-steroidal antiandrogen monotherapy offers potential advantages over castration for impotence, loss of libido, and hot flushes, but these may be achieved at the cost of an increased risk of gynaecomastia and breast pain.

Individuals’ preferences for alternative treatments need to be considered in the light of the attributes of the treatments. Discrete choice experimentation, an approach for elicitation of preferences, is now being used widely in health care. This approach identifies the key characteristics of alternative treatments, such as hot flushes, and selects a series of levels for each (for example, absent, mild, moderate). Respondents choose from several options, each of which details a series of attributes at different levels. The relative importance of attributes to individuals and the trade-offs made between them, can be assessed by changing the levels of the attributes and asking participants to make their choice again. Findings on the reliability and validity of discrete choice experimentation in healthcare settings are encouraging. We used discrete choice experimentation to elicit treatment related preferences in a sample of men with non-metastatic prostate cancer.

Methods

Pilot study

Before the main study, we conducted a two phase pilot study in men with prostate cancer. Fourteen men were recruited into the first phase and were interviewed by a trained research nurse. On the basis of these interviews eight attributes were selected for the main study: diarrhoea, hot flushes, ability to maintain an erection, breast swelling or tenderness, physical energy, sex drive, life expectancy, and out of pocket expenses. In the second phase, nine men were asked to complete a questionnaire based discrete choice experiment with these attributes; there was also a brief unstructured interview with a research nurse. Several men did not understand the nature of the exercise and were only able to complete exercise with guidance from the research nurse. We therefore decided to use an interview format for the main study.

Study format

The attributes and levels used in the exercise are described on bmj.com. We chose mild and moderate levels only: it was explained to patients that therapy would be changed in a severe event. The mild level included symptoms that would not interfere with work, study, housework, family, or leisure activities and the moderate level included symptoms that would.

A trained research fellow conducted the interviews, during which personal data on the patients were collected (data were also taken from medical records). The men were presented with two treatment options, each containing a set of attributes at specific levels. The interviewer read out the pair wise options and
used show cards as prompts to help the men choose the options they preferred (table 1).

We divided the exercise into two parts to avoid overburdening patients with too many attributes for an option. The first part included three unique attributes—the ability to maintain an erection, physical energy, and libido. The second part included three unique attributes—diarrhoea, hot flushes, and breast tenderness. Both parts included two common attributes—life expectancy and a one off out of pocket expense.

The men had to assume a life expectancy of five years, estimated as the average for the sample considering the mean age (70 years) and clinical stage of disease. The clinical stage was typically not detected by screening but rather diagnosed on the basis of problems relating to progression of the cancer. The five year average was justified because the sample included men with T1 or T2 disease with an estimated seven year survival probability of 65% and men with T3 or T4 disease with a five year survival probability of 30%.

The two parts of the exercise each contained eight pair wise options. We prepared eight different versions of the questionnaire, each representing a new experimental design (orthogonal main effects). Each version of the questionnaire presented different levels of the cost attribute allowing a larger number of intervals between cost levels across the survey. Study patients were randomly allocated to one of the questionnaires.

Study sample

Our study sample was patients with non-metastatic prostate cancer who had or had never received antiandrogen therapy; there were no exclusion criteria. Potential participants were identified from records at the Middlesex Hospital, London. They were contacted in writing to obtain written informed consent. Respondents were asked to make an appointment for an interview at the Middlesex Hospital.

Analysis

We analysed the discrete choice exercise by taking each choice between pair wise options as a specific observation. Hence each respondent provided a maximum of 16 observations. Given the non-independence of the data provided by the same respondent, a random effects probit model was used. Two separate models were specified (one for each group of attributes), with the choice responses as the binary dependent variable and the difference in levels for each of the attributes as the independent variables (see bmj.com). The specification of the experiment precluded the testing for interactions between attributes, but we explored the interactions between attributes and patient characteristics (age, prostate specific antigen level, and T stage of cancer at diagnosis).

Results

Between 24 May and 8 September 2000, we invited 180 men to participate in our study. Of these, 129 were interviewed. Participants were similar to those who declined for mean age and T stage at diagnosis. Table 2 shows the characteristics of the participants.

Discrete choice experiment

Table 3 shows the results of the first part of the exercise. The coefficients for the unique attributes were all statistically significantly different from 0; negative values for libido, maintaining an erection, and physical energy indicate that the more severe the problems, the less likely the patient is to prefer that scenario; negative values for out of pocket expenses indicate that the higher the costs, the less likely the patient is to prefer that scenario. Positive values for life expectancy indicate that the greater the life expectancy the more likely the patient is to prefer that scenario. The only statistically significant interaction was between ability to maintain an erection and age; the positive value indicates that older men were less likely to be influenced by the ability to maintain an erection in choosing their preferred scenario.

Table 4 shows the results of the second part of the exercise, which also considered the unique attributes of diarrhoea, hot flushes, and breast tenderness. The coefficients for the attributes

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient (95% CI)</th>
<th>SE</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Libido</td>
<td>−0.3089 (−0.5719 to −0.0460)</td>
<td>0.1342</td>
<td>0.021</td>
</tr>
<tr>
<td>Ability to maintain erection</td>
<td>−0.4243 (−0.5221 to −0.3265)</td>
<td>0.0551</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Physical energy</td>
<td>−0.7032 (−0.8219 to −0.5845)</td>
<td>0.0608</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Out of pocket expenses</td>
<td>−0.0067 (−0.0014 to −0.0001)</td>
<td>0.0003</td>
<td>0.017</td>
</tr>
<tr>
<td>Life expectancy</td>
<td>0.2336 (0.1707 to 0.2966)</td>
<td>0.0321</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Interaction between ability to maintain erection and age</td>
<td>0.2184 (0.0934 to 0.3433)</td>
<td>0.0637</td>
<td>0.001</td>
</tr>
<tr>
<td>Constant</td>
<td>−0.0541 (−0.1459 to 0.0370)</td>
<td>0.0468</td>
<td>0.248</td>
</tr>
</tbody>
</table>

No of observations: 1000; 194.92; P<0.0001*;
*
χ² test.

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of six attributes), and the inclusion of a common core of two
This allowed the choices to be kept relatively simple (maximum
that this approach can be applied successfully in health care. A
first to elicit preferences from patients with prostate cancer using
treatments, irrespective of the stage of cancer or whether they
weigh up the benefits and risks of various conservative
Discussion

were all statistically significantly different from zero. Negative
values for diarrhoea, hot flushes, and breast tenderness indicate
that the more severe the problem the less likely the patient is to
prefer that scenario. None of the interaction terms were statisti-
cally significantly different from zero.
Table 5 shows the marginal rates of substitution between life
expectancy and other attributes—that is, how much life
expectancy the men were willing to trade off to achieve an
improvement by one level in one of the other attributes. For
example, men were willing to trade off 1.8 months of life expect-
ancy to change diarrhoea from a moderate to mild level or from
mild to absent. Because the levels of severity differed between
attributes, marginal rates of substitution between attributes
should be compared with caution. The least important marginal
rates of substitution were for hot flushes and the most important
were for physical energy.

Table 4 Results of second part of discrete choice exercise

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient (95% CI)</th>
<th>SE</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhoea</td>
<td>-0.4193 (-0.5452 to -0.2931)</td>
<td>0.0644</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hot flushes</td>
<td>-0.1225 (-0.2162 to -0.0287)</td>
<td>0.0479</td>
<td>0.010</td>
</tr>
<tr>
<td>Breast tenderness</td>
<td>-0.429 (-0.5147 to -0.3312)</td>
<td>0.0927</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Out of pocket expenses</td>
<td>-0.0016 (-0.0025 to -0.0007)</td>
<td>0.0009</td>
<td>0.001</td>
</tr>
<tr>
<td>Life expectancy</td>
<td>0.3329 (0.1827 to 0.2832)</td>
<td>0.0256</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Constant</td>
<td>0.1278 (0.0262 to 0.2294)</td>
<td>0.0518</td>
<td>0.014</td>
</tr>
<tr>
<td>No of observations</td>
<td>992; 164.35; P&lt;0.0001*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

“χ²” test.

The results are averaged across the sample and so there is
inevitable variation between the men. Our results are therefore
no substitute for careful assessment of individual patient prefer-
ences in a clinical setting but do provide some basis for clinicians
to prioritise issues they discuss with patients. The implications on
physical energy from conservative treatment, for example, may
be an important starting point for decisions on treatment.

Table 5 Patients' marginal rates of substitution between life expectancy and other attributes

<table>
<thead>
<tr>
<th>Attribute</th>
<th>Life expectancy willing to large (months)</th>
<th>Single level improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhoea</td>
<td>1.8</td>
<td>From moderate to mild or from mild to absent</td>
</tr>
<tr>
<td>Hot flushes</td>
<td>0.5</td>
<td>From moderate to mild or from mild to absent</td>
</tr>
<tr>
<td>Breast swelling</td>
<td>1.9</td>
<td>From present to absent</td>
</tr>
<tr>
<td>Loss of libido</td>
<td>1.3</td>
<td>From present to absent</td>
</tr>
<tr>
<td>Problems in maintaining an erection:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aged &gt;70 years</td>
<td>1.8</td>
<td>From moderate to mild or from mild to absent</td>
</tr>
<tr>
<td>Aged &lt;70 years</td>
<td>0.9</td>
<td>From moderate to mild or from mild to absent</td>
</tr>
<tr>
<td>Lack of energy or &quot;pep&quot;</td>
<td>3.0</td>
<td>From present to absent</td>
</tr>
</tbody>
</table>

Men are willing to contemplate trading off life expectancy to be relieved of the burden of side effects such as limitations in physical energy

The preferences of older men are not the same as those of younger men

attributes (cost and life expectancy) ensured trade-offs across all attributes.

The men were willing to trade off some life expectancy to be relieved of side effects. Men with metastatic cancer were not included in the study, so no patients faced imminent death, with life expectancy ranging from around 2 to 10 years. Given the diff-
iculty in estimating, and potential ethical problems in presenting, life expectancy for each patient, the men were asked to assume a life expectancy of five years (the average in the group) as a starting point. The size of the trade-offs between life expectancy and the other attributes should be treated with caution because men with a longer or shorter life expectancy than five years may have indicated different preferences if their actual life expectancy had been presented to them.

We looked at the application of discrete choice experiments in prostate cancer only. The ability and willingness of men to engage in this exercise is encouraging for future research. Perhaps the most common therapeutic dilemma that patients and clinicians face is the timing of androgen suppression. Should a patient start therapy early, once progression of prostate cancer has been identified? The potential benefits of this approach might include a slowing down of disease progression and possibly reducing the likelihood of death related to the cancer. Alternatively, the patient could defer treatment for an agreed time. This would avoid the immediate side effects of treatment and possibly reduce the medium to long term adverse effects. This type of trade-off is made by many patients with progression of disease everyday, and discrete choice experimentation could gain some insight into the way patients make this difficult choice.

We thank Rob Sheldon (Accent Marketing and Research) for help with the design and analysis of the study, Wendy Coucill for her work on the pilot study, and the patients.

Contributors: MS and ME initiated the research and designed the study with SB, HP, and PE. PF undertook the interviews, SB and MS undertook the
analyses, and MS produced the main drafts. MS and SB will act as guaran-
tors for the paper. They accept full responsibility for the conduct of the
study, had access to the data, and controlled the decision to publish.

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Ethical approval: Approval was obtained from the local research ethics
committee.

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