

The best of both worlds: An example mixed method approach to understand men's preferences for the treatment of lower urinary tract symptoms.

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Compliance with ethical standards

DI, SH, VW and MR are employed by the University of Aberdeen and performed the research. CM and JN are employees of Astellas Pharma EMEA, which funded the study in an unrestricted contract. All authors were involved in writing or reviewing the manuscript. Ethical approval was obtained from the College Ethics Research Board of the College of Life Science and Medicine, University of Aberdeen (CERB/2013/8/942). HERU is supported by the Chief Scientist Office (CSO) at the Scottish Government Health and Social Care Directorate. We also thank two anonymous reviewers and the journal editor for their comments.

Abstract

Background

Discrete choice experiments (DCEs) are widely used to quantify individuals' preferences for healthcare. Guidelines recommend the design of DCEs should be informed by qualitative research. However, only few studies go beyond guidelines by fully presenting qualitative and quantitative research jointly together in a mixed methods approach (MMA).

Objectives

Using an example study about men's preferences for medical treatment of lower urinary tract symptoms (LUTS), we demonstrate how qualitative research can complement DCEs to gain a rich understanding of individuals' preferences.

Methods

We were the first to combine online discussion groups (ODGs) with an online DCE. A thematic analysis of the ODGs and a conceptual map provided insights into men's quality of life (QoL) with LUTS and relevant treatment attitudes. This was used to design the DCE. Men's willingness to pay (WTP) for these attributes was estimated. Findings from ODGs and DCE were compared to understand WTP and preference heterogeneity.

Key findings

Men mostly valued medicine that reduced urgency and night time frequencies of urination, but avoided sexual side effects. We find heterogeneity in the effect of sexual side effects on men's preferences. The ODGs suggest this is, because several men may be sexually inactive due to their age, being widowed or having comorbidities. The ODGs also raised concern about men's awareness of LUTS.

Conclusion

We argue that the insights gained into men's preferences for treatment and how LUTS affects men's QoL, could not have been obtained by either the qualitative research or the DCE alone.

Key Points for Decision Makers

- Guidelines recommend that DCEs should be informed by qualitative evidence. We go beyond these guidelines in a mixed methods approach (MMA) that treats qualitative findings and DCE results as being equally important.
- In our study about men's treatment preferences for lower urinary tract symptoms (LUTS), we find treatment should relieve urgency and night-time symptoms while limiting sexual side effects.
- The MMA has provided a richer understanding of treatment preferences than the DCE or qualitative research could have provided alone. Our qualitative data was collected in online discussion groups, which may offer a practical alternative to face-to-face interviews, especially for target populations with limited mobility or sensitive research topics.

1 Introduction

Discrete choice experiments (DCEs) are widely used to elicit patient and population preferences for healthcare [1]. DCE surveys ask respondents to choose repeatedly between mutually exclusive hypothetical healthcare options characterised by a set of common attributes that take different levels [2]. Researchers select these attributes using literature reviews, pre-defined outcome measures, underlying behavioural hypotheses or qualitative research [3]. Attribute selection is fundamental to DCEs and previous research finds that the number and type of attributes may affect the study outcome [4, 5]. While too many attributes may overburden respondents [6, 7], too few attributes might induce omitted variable bias [8, 9]. Guidelines therefore recommend to use qualitative research to identify and describe DCE attributes [3, 10]. This has improved the reporting of qualitative approaches in the DCE literature over the last years, and is increasingly considered as an important quality aspect of DCE studies [11]. Systematic literature reviews of health DCEs find that qualitative research has informed attribute selection in 54% of studies, level selection in 35% of studies and is used to test the quality of questionnaires [1, 12, 13]. However, few studies use qualitative research after the attribute selection and survey pre-testing phases of a DCE. For example, Vass et al. [11] find that only 4% of all health DCEs use qualitative research to collect additional evidence about individuals' preferences or attitudes. There are two potential explanations for this: First, journals have tight word limits and second, guidelines only focus on the role of qualitative research for DCE design.

In this paper we argue, that limiting the use of qualitative research to attribute selection does not uncover its full potential. Qualitative research is an established method in public health and other disciplines to gain insights into individuals' health care preferences, quality of life and care context [14-18]. Qualitative research largely focusses on uncovering heterogeneity in views, contexts and opinions. Hence, qualitative research has a potential to provide detailed insights into causes and types of preference heterogeneity that is often only accounted for in DCE analysis by allowing preferences to be randomly distributed in the population [19]. We aim to demonstrate how qualitative and quantitative methods can be analysed and reported in parallel using an example study about patients'

preferences for medical treatment of lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia (BPH). Our mixed method approach (MMA) recognises that qualitative and quantitative methods are complementary and together create a detailed understanding of individuals' preferences for healthcare. We are also the first to explore the use of online discussion groups (ODGs) as an alternative to traditional face-to-face focus groups to collect qualitative data alongside a DCE. ODGs can make qualitative research alongside a primarily quantitative study more practical than face-to-face alternatives. They may also be useful to collect data from a population with limited mobility. In case of online DCEs, ODGs can also be used to ensure that all study participants are sampled from the same population.

2 Background of the case study

BPH is a chronic, progressive urologic condition that affects aging men and is often associated with LUTS [20, 21]. LUTS comprise storage symptoms (day-time urinary frequency, night-time urinary frequency, urgency), voiding symptoms (e.g. slow stream, splitting or spraying, hesitancy, terminal dribble) or post-micturition symptoms (e.g. sensation of incomplete emptying). These symptoms reduce men's quality of life (QoL) and the health status of their partners [23-25].

Several medical treatments are available for LUTS [21, 25]. These medicines have different profiles with regards to efficacy (e.g. reduced urge or frequency of voiding, or reduced prostate size) and side effects (e.g. reduced sexual functionality, and multiple non-sexual side effects). Previous studies have shown that men prefer medicine that maintains sexual activity in addition to relief of short-term and long-term symptoms [26, 27]. Preferences were also found to vary between men [27]. We suggest that qualitative research can help to better understand why men have different preferences for medical treatment of LUTS.

3 Mixed methods

3.1 Study overview

Our MMA was the first study that combined qualitative data from ODGs with quantitative online DCEs. The collected data was used in three ways (Figure 1): First, qualitative analysis of the online discussion groups explored how LUTS affects men's life and men's attitudes towards medical treatment. Second, the ODGs were used to identify the DCE attributes, to frame the choice tasks and to define the 'no treatment' baseline. Third, the ODG results motivated the DCE analysis, informed the interpretation of the estimated trade-offs and provided insights into the overall validity of the quantitative findings.

[FIGURE 1]

While literature reviews, validated outcome measures, theoretical arguments and interviews have been used to inform the design of DCEs, face-to-face discussion groups have become increasingly popular for the identification of attributes and levels [1, 3, 11]. These discussion groups are usually recorded, transcribed verbatim and systematically analysed. In contrast, ODGs do not take place in real time, instead participants access a purpose build website at any time during a pre-arranged period [28]. On this website, ODG participants can read comments of other participants or comment themselves.

ODGs are increasingly used in qualitative healthcare research [29-31]. Data quality from ODGs are found to be comparable to face-to-face discussion groups, but researchers can reach a broader population with ODGs [32, 33]. The dedicated website is accessible from home at a time that is suitable for participants, which facilitates the inclusion of people who are housebound, have reduced mobility, or have busy schedules. ODGs can also be anonymous, which may facilitate the discussion of sensitive topics such as incontinence due to LUTS or sexual side effects of medicine [34, 35].

3.2 Data collection

3.2.1 Online discussion groups

Five moderated ODGs were conducted over two weeks to understand how LUTS affects men's QoL; to understand men's experience of, and attitudes towards treatment of LUTS; to develop DCE attributes and levels; and to help inform subsequent DCE analysis.

Each ODG was 'live' for one week, started on Monday morning and was moderated by three researchers (SH, DI, VW) identified by their names. At least one moderator was present daily between 8am and 10pm. A new question was posted every weekday (Table 1). Participants could respond to these questions and other participants' comments. Moderators prompted for information and encouraged discussions. The final question was posted on Friday and the website remained open until Monday morning.

[TABLE 1]

All posted comments were downloaded and analysed independently by the moderators using an inductive thematic approach [36, 37]. Each researcher assigned codes that described topics, concerns, or emotions in each post on the website. The codes were used to identify overarching themes. The three moderators discussed coding strategies and emerging themes in a two-day workshop with the objectives: First, to gain insights into the effect of LUTS on men's QoL as well as attitudes towards medical treatment. Second, to identify themes or sub-themes from the qualitative analysis that could be included as treatment attributes in the DCE. These themes or sub-themes had to be actionable, plausible in the context of treatment choice and tradeable [2]. This means that complex themes may require to be broken down into sub-themes (e.g. into different classes of side effects). Other themes may not be suitable at all for the inclusion as an attribute in the DCE (e.g. if it is unaffected by treatment choice). Third, qualitative insights guided the statistical analysis plan and should inform the interpretation of the DCE results at a later stage. For the purpose of the workshop it was agreed in advance that disagreements were to be resolved through discussion and if this did not result in agreement, by majority vote. No voting was required in this study. As part of the workshop, a conceptual map was developed that linked themes and codes to explore interdependencies, by comparing which themes were discussed jointly in the ODGs. The purpose of the conceptual map was to graphically represent the wider context of the identified themes as well as how the different aspects that were raised in the ODGs relate to each other. The conceptual map therefore illustrates the

complexity of the disease and treatment context, whereas the DCE reduces this complexity to the key attributes.

3.2.2 Discrete choice experiment

The DCE quantified the trade-offs that men make when choosing between LUTS treatments in terms of their willingness to pay (WTP) for each attribute and explored preference heterogeneity among men. Seven attributes were used to describe medical treatments of LUTS (Table 2). Three attributes (day-time and night-time frequency of urination and day-time urgency) represented symptoms that men experience and that medication can potentially improve. Two attributes describe the side effects of medications. A cost attribute allowed the estimation of WTP for changes in each attribute and was described as *'all the costs involved in obtaining a prescription and having it dispensed including the travel costs such as bus fares, petrol costs, car parking charges, time off work, and any prescription fee'*. The cost attribute levels were based on previous studies [26, 27].

[TABLE 2]

A D-efficient design with flat priors combined the attributes and levels into 30 choice sets, which were split into three blocks of equal size [38]. Each choice set included two hypothetical LUTS treatments and an opt-out option. The opt-out was described as a no-treatment option with a day-time frequency of 14 times, a night time frequency of 4 times, urge incontinence and no side effects. These relatively severe levels were chosen to allow for sufficient variation in symptoms improvement by medicine [42]. Figure 2 presents an example choice set.

[FIGURE 2]

Attribute levels of the treatment alternatives and the opt-out were chosen such that treatment could not worsen LUTS. The opt-out levels were introduced by asking men to imagine that they urinated 14 times during the day, woke up 4 times to urinate during the night and experienced urge incontinence (Figure 2). A link to a description of this baseline scenario was placed above each choice set.

The data analysis was based on random utility theory [39] and assumed that utility u_{jnt} that respondent n derived from alternative j in choice t can be split into a deterministic part v_{jnt} and a random part ε_{jnt} , such that

$$u_{jnt} = v_{jnt} + \varepsilon_{jnt} \quad (1)$$

The deterministic part of equation (1) was specified as a linear function of the attributes:

$$v_{jnt} = \beta'_n x_{jnt} \quad (2)$$

with β_n being an individual specific vector of marginal utilities and x_{jnt} denoting the vector of attributes. The ODGs suggested that preferences varied between men and marginal utilities were therefore assumed to be distributed with a probability distribution $f(\beta_{kn} | \bar{\beta}_k, \sigma_k)$, where $\bar{\beta}_k$ denotes the mean and σ_k the standard deviation (SD). The resulting mixed logit was estimated with 3,000 Halton draws from $f(\beta_{kn} | \bar{\beta}_k, \sigma_k)$ [40]. Day-time and night-time frequency were assumed to be log-normal distributed to avoid that an implausibly large share of respondents preferred a higher frequency of urination. The cost attribute was fixed to ensure that probability distributions of parameter ratios have existing moments and the number of tablets was fixed, because no specification resulted in either a significant mean or a significant standard deviation. The remaining attributes were normal distributed. Mean WTP estimates were obtained as the ratio between the estimated coefficient for an attribute and the negative cost coefficient; 95% confidence intervals for WTP estimates were calculated using the delta method [41]. All categorical attributes were dummy coded. More details about the model is provided in a separate publication [42].

3.2.3 Recruitment

Men residing in the UK, who were registered with a commercially managed online access panel were invited to participate in the study, if they were of ≥ 45 years and had a self-reported International Prostate Symptom Score (IPSS) of ≥ 8 . These criteria are associated with increased prevalence of storage symptoms [21].

Forty-eight eligible men were invited to participate in an ODG and received detailed information. Informed consent was obtained and men were asked to provide dates on which they would be available. Men registered with a username and password to the website and were identified in the ODG only by their username. Users registered to the website were split into groups of 7–10 men with similar distributions of age and IPSS. Participants received £30 for contributing at least three comments.

5,212 men who did not participate in the ODGs were invited to the DCE. Men received information about the medical background, the survey structure and completion time. Respondents received £1.50 for a completed questionnaire. The sampling was paused for one week after 63 respondents had completed the questionnaire and this data was used as pilot and has resulted in a minor adjustment of the cost attribute based on an unexpected opt-out rate of 33%. Further details on the pilot are presented in a separate publication [42].

4 Results

4.1 Online discussion groups

22 men actively participated in the ODGs. Men had a mean age of 59.82 years and mean IPSS of 16.41. 223 comments were made across all ODGs (3–22 posts per active participant).

Seven themes were identified: 1) men's symptom *awareness*; 2) experience of *day-time frequency* and urgency; 3) experience of *night-time frequency* and urgency; 4) determinants and experiences of consulting a *doctor*; 5) attitudes to *side effects*; 6) *psychological well-being*; and 7) determinants of *self-care*. Figure 3 presents the conceptual map of these themes.

[FIGURE 3]

1) Awareness

All men found their LUTS bothersome, but not all men associated their symptoms to a medical condition and some men were unaware that their symptoms were more severe than what is 'normal' for men their age. For example, Participant 1 in group 5 wrote:

“It is [...] accepted that as a man when you grow older you are likely to want to use the toilet a lot more and is sometimes treated as a bit of a joke, which probably contributes to men not paying too much attention to it.”

Some men had spoken with their general practitioner (GP) and were told that their symptoms were age related. Participant 3 in group 4 wrote:

“I have been to see a doctor [...] when I was having to go to the toilet 2 or 3 times [at night]. She said it was of no concern and that it is normal for a man my age.”

2) Day-time symptoms

Men often discussed the impact of day-time frequency and urgency on their life. Frequently needing to urinate was annoying, disruptive, embarrassing and confining to men. For example, Participant 10 in group 1, wrote:

“I would normally only go to places where I know where the toilet is. If it’s a new place I have to make sure I go before leaving the house. This can take a while so going anywhere always takes longer than it would for others.”

If men’s careful plans were disrupted, by delays or traffic congestion this was stressful. Participant 9 from group 2 wrote:

“Until recently, I had a 3.5 hour drive most Monday mornings and the same on Thursday nights. I would anticipate wanting to stop around 1.5 to 2 hours out and judge which service station to stop at. Occasionally I misjudge it, or get stuck in traffic, and then it becomes uncomfortable. This tends to results in a lot of swearing at other road users or traffic lights, if I’m [...] getting near my limit.”

Working men were concerned about how urination frequency affected their work. For example, Participant 3 in group 4 wrote:

“Recently, it has started to affect my work and I have to go at least four times during the shift.”

Urinary urgency restricts men’s lives and decreases their self-confidence. Several men seldom leave home and restrict their social life, because they are afraid of not reaching the toilet on time. For example, Participant 8 in group 3 wrote:

“To minimize accidents I use incontinence pads, which although are a nuisance they help me feel more confident if I am going out. This condition wears me down and makes me feel like a lesser man.”

3) Night-time symptoms

The most frequent response to how LUTS affected men’s life was related to night-time urination frequency. Night-time urgency was also mentioned and linked to wetting the bed. For example, Participant 6 in group 5 wrote:

“I am still getting up during the night, it is such a horrible thing. You are fast sleep one moment and the next you are awake and trying to get to the toilet as quick as possible.”

Some men reported that their disturbed sleep meant that they were tired during the day. Participant 2 in group 2 wrote:

“I often feel tired and sleepy in the afternoons and frequently fall asleep on the sofa in the evenings. This means I get very little leisure time as when I finally sit down and read a book or watch TV I am too tired and will fall asleep.”

Men who experienced urgency symptoms at night had experienced incontinence or were worried about it. This reduced their confidence, enjoyment of trips away from home and caused worry about the effect on their partner whose sleep was disturbed, too. For example, Participant 6 in group 5 said:

"[...] I have been as many as four times during the night. [...] it is putting a strain on my relationship with my wife. [...] She is such a light sleeper that I wake her up when I am getting in and out of bed. [...] We now have separate beds, and also sometimes I have been in such a deep sleep that I have accidents during the night, and then my wife has to change the bed in the middle of the night. [...] My wife never says anything she just does it as if it is a part of normal life, but I can tell after 40 years of being together she does find it all stressful."

4) Doctor

Not all men had consulted their general practitioner (GP). Men gave three main reasons for not consulting a GP. First, their symptoms were perceived as not "too bad". Second, they believed doctors could not do anything. Third, they didn't want to take medication. A minority of men were also scared of their symptoms being associated with prostate cancer. In general, LUTS getting "too bad" was not an absolute concept, but related to a deterioration in symptoms that substantially decreased QoL. For example, Participant 9 in group 2 wrote:

"I put up with the situation for quite a while and just thought 'well that's just the way I am'. Also inherited a fear of doctors (they find nasty stuff and maybe I'd rather not know). What finally forced the issue was when I started getting urine infections and the pain and frequency of needing to go to the toilet and loss of control..."

5) Side effects

Sexual side effects were perceived as more important than non-sexual side effects for most men. For example, Participant 16 in group 2 wrote:

“Headaches, dizziness, a dry mouth are not too bad, but I am having enough issues with no fluid during ejaculation, inability to get or maintain an erection, decreased sexual desire as it is ...”

The importance of sexual side effects to a man depended on his circumstances. Some men were already experiencing sexual symptoms. Men who were living alone and were no longer sexually active stated that the sexual side effects were irrelevant to them. For example, Participant 5 in group 3 wrote:

“I am totally impotent, prior to this my GP wanted to prescribe Viagra. As a widower of advanced years (72) the impotence does not bother me, so the sexual side of my life is one less problem to worry about [...].”

6) Psychological well-being

LUTS affects men’s psychological well-being. Many worried about going to the toilet when being out, about having an accident and about staying overnight away from home. Men felt guilty about how their symptoms affected their family or felt trapped at home, because they were afraid of not finding a toilet. For example, Participant 6 in group 5 who experienced severe storage symptoms wrote:

“I am unable to just nip into town as the only public toilet that was there has been closed. [...] This is a terrible strain on my relationship with my wife, although she fully understands and is very comforting to me when I get upset, because I feel like a prisoner in my own home at times, because of this problem.”

7) Self-care

Men had different strategies to self-care or manage their LUTS. They were conscious of, and sometimes limited, their fluid intake. Not all men believed that this worked. Other men wrote about trying to hold on and not to “give in” to the urge to urinate. For example, Participant 1 in group 5 wrote:

"[I am] [g]enerally more conscious about how much I drink during the day, mainly tea, especially with regard to what I will do in the following hours, e.g., long drive. Usually do not drink anything after about 6pm or I will almost certainly have to get up in the night."

The ODGs showed that LUTS reduce men's QoL and that men organise their day to manage the symptoms. Many men were not aware that LUTS is treatable by medicine and many had not contacted their GP. This supports our use of online recruitment from the general population using symptom score as an inclusion criteria. In doing so we have included a wider group of men that would have been reached by patient groups.

The ODG informed our attributes. We include day-time and night time frequency of urination and urgency as attributes, because these were symptoms most frequently discussed and those that potentially can be improved with treatment. The attribute and levels echo the ways in which men discussed frequency and urgency in the ODGs. We expected men to value reduced day-time urination frequency, because they can take part in more daily activities, and to value reduced night-time frequency, because they would have better sleep quality. We included a broad range of side effects. In the ODGs, men's circumstances affected their willingness to take medication with side effects. Men who were sexually inactive were less concerned about sexual side effects of treatment, therefore we expected to find significant preference heterogeneity for side effects in the DCE results. The range of experiences and symptoms reported in ODG meant that we chose to define a baseline situation in the DCE to ensure that the DCE made sense to all respondents.

4.2 Discrete choice experiment

1,097 men opened the online survey, of which 450 were screened out. 136 men met the eligibility criteria, but were over the sampling quota of 310 respondents. 201 men dropped out before completing all the questions and 63 were used as pilot study. The final survey was completed by 247 men, resulting in 7,410 observations for the DCE analysis. Men had a mean age of 62.32 years and a

mean IPSS of 15.69. In the sample, 112 men had discussed LUTS with their GP, and 65 (58.04%) of these men had received medical treatment.

Figure 4 presents the mean WTP estimates based on the mixed logit model results. A full set of estimates is reported by Mankowski et al. [42]. WTP estimates show how much men are willing to pay per month for marginal change in each of the significant attributes (p -value < 0.05). The DCE showed that men value medicine, especially if it reduces urinary urgency. However, men's valuation is reduced by side effects, especially sexual side effects. Three coefficients were insignificant (estimate, p -value): the reduction in urgency from incontinence to severe urgency, the side effect of dry mouth, and number of tablets per day. While it is surprising that a change from urge incontinence to severe urgency is not significantly valued by men, one explanation may be that even under severe urgency, men are still afraid of wetting themselves while rushing to the toilet. It may be this fear together with the requirement of rushing to toilets that prevents the change in urgency to be valued by men. Men may also be affected by past experience of incontinence. For example, participant 231 in ODG 1 stated:

“Several years ago I did wet the bed and this sometimes makes me a little apprehensive when we are away.”

Men were willing to pay more to improve urination urgency than to reduce urination frequency. Reducing urgency from incontinence to mild urgency was valued at £25.33 per month, and from incontinence to moderate urgency was valued at £23.93 per month. Men were willing to pay more for a one-time reduction in night-time frequency than day-time frequency of urination (£6.65 per month and £1.39 per month, respectively).

[FIGURE 4]

Erectile dysfunction was the worst side effect and reduced the value of medication by £30.07 per month. The remaining sexual side effects (no fluid during ejaculation and decreased sexual desire) and non-sexual side effects (headache and dizziness) reduced the value of medication by similar values (between £16.26 and £19.66 per month).

Preferences were found to be heterogeneously distributed in the population for both frequency attributes, all levels of the urgency attribute except for an improvement to mild urgency, all levels of the sexual side effects attribute except no fluid during ejaculation and all levels of the non-sexual side effect attribute except dry mouth. In line with our expectations, we find significant preference heterogeneity for the 'decreased sexual desire' and 'impotence levels' of the sexual side effects attribute (Figure 5). More details on estimated SDs are provided in [42].

[FIGURE 5]

5 Discussion

This paper has presented one of the first MMAs in the health literature that combines a DCE with qualitative research [11]. Previous studies have mostly published qualitative findings and DCE results separately [44-47] or conducted an MMA using non-economic quantitative techniques, such as rating or ranking [50]. Current DCE guidelines recommend the use of qualitative research at the study design stage. Our findings suggest that qualitative research can complement DCEs at the analysis and interpretation stage as well. Qualitative research can provide insights into patients' preferences and attitudes that cannot be obtained by a DCE. For example, the inclusion of random parameters in our statistical analysis of the DCE data allowed us to control for preference uncertainty [19], but it did not explain these idiosyncratic differences between respondents in terms of differences in personal circumstances, tastes and expectations. Qualitative research can also provide insights into causes of relative attribute importance. In our DCE, we found that reducing night time frequency was more important than day-time frequency. The ODGs suggested that this is because night-time frequency disturbs patients' sleep as well as the sleep of their partners. Therefore, WTP for improving night-time frequency in the DCE includes the value of improved sleep for men and their family. Other aspects of patients' treatment choice may simply not be picked up by a DCE. For example, a key finding of our qualitative analysis was that men were often unaware of LUTS being treatable and therefore had not talked about their symptoms with their doctor or family.

While our findings suggest that a MMA would enhance most, if not all DCEs, some issues remain to be resolved. Reporting guidelines for DCEs and qualitative research have become complex and require the provision of several method-specific study details [51-53]. Fulfilling all of these recommendations may not be possible in one journal publication. The high interdependency between qualitative research and DCEs also results in an unclear and potentially unnatural presentation ordering. While the DCE attributes are results of the qualitative research, they are not the only qualitative research output. This may suggest that all qualitative research should be presented before the DCE is discussed. However, such a reporting structure would reduce researchers' ability to discuss and compare qualitative evidence together as a common picture that emerges from studying treatment preferences in an MMA. We therefore advocate a more interwoven reporting approach. To make such an approach more practical and transparent, future discussions about reporting standards of MMAs are needed.

Our study was also the first to combine an online DCE with ODGs. ODGs may offer a practical and less costly alternative to face to face interviews or focus groups. When ODG are undertaken alongside online quantitative surveys then ODGs allow researchers to sample all study participants from the same population. ODG also enable people with limited mobility to participate in the study. Furthermore, we found that using an anonymous username as an identifier helped in the discussion of sensitive topics. One participant in discussion group 3 for example stated:

"As you are only a username and not a physical being it is easier to express your feelings as you are not watched and are unaccountable. It gives you more freedom and lifts the 'taboo' barrier."

There are some disadvantages of ODGs over face to face discussion groups. The asynchronous nature of ODGs reduces the amount of interaction between participants and moderators are less likely to be able to engage all participants in discussions. However, these issues may be reduced by providing a participation based incentive (e.g. a minimum number of postings). Furthermore, little is known about how the anonymity affects the validity of participants' responses. Future studies should therefore build on this study by exploring the ODGs in a different health context by comparing ODGs with face to face qualitative methods.

Our study contributes to a broad range of different literatures. First, the DCE adds to the limited evidence of patients' preferences for medical treatment of LUTS associated with BPH. Previous studies have mainly focussed on men's preferences for treating BPH (e.g. by decreasing the size of the prostate) [26,27]. In contrast, our study focusses on how men experience LUTS and how this experience changes due to medical treatment. Second, our qualitative research extends the findings from other studies that show LUTS can have a severe effect on the QOL of men and their partners [22-24]. Third, our discussion of combining and reporting DCEs together with qualitative research in a MMA builds on and extends previous work that explores how qualitative research can inform the design of DCEs [3,10,11,54-63].

Our analysis is subject to some limitations: 1) The ODGs suggested that some of the preference heterogeneity around the sexual side-effects attribute is caused by the degree to which men are sexually active. We did not collect such data in the DCE questionnaire and could therefore not account for sexual activity in our analysis. However, sexual activity is only one of several reasons for preference heterogeneity in the valuation of the sexual side effects attribute. This is why we assumed parameters to be randomly distributed in the population. 2) As noted by Mankowski et al. [42], our results may not be representative for all patients suffering from LUTS due to BPH. Using the online access panel, we achieved an estimated recruitment rate of 14.58%, but have no information about how responders differed from non-responders or UK population that is not signed up to the panel. 3) Our DCE assumes that taking no medicine results in a fixed set of symptoms and does not allow for any changes in LUTS due to progression of BPH. We have chosen to fix the opt-out alternative to a defined scenario to make choices comparable and to avoid instances in which taking medicine resulted in worse scenarios than taking no medicine. 4) Our sampling criteria relies on self-reported IPSS, which is not equivalent to a clear medical diagnosis and as a result, men may be suffering from other diseases such as urinary tract infections or prostatic cancer. Using self-reports also allowed us to explore men's disease awareness in the ODGs, which is in line with studies that find low consultation rates for men suffering from LUTS [43]. 5) the DCE only considered storage symptoms of LUTS, because these symptoms were found to

be the most bothersome to men in the ODGs. However, this is in line with findings from other studies in the literature [64, 65].

6 Conclusion

This paper went beyond the recommendations of DCE guidelines by showing how qualitative methods can complement a DCE. Our MMA informed the DCE attributes and levels, provided behavioural insights on its own and informed the interpretation of DCE parameter estimates. As a result, the MMA provided more detailed insights into patients' preferences than qualitative or quantitative research could have provided alone.

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Figure 1 Flow chart of the mixed method study

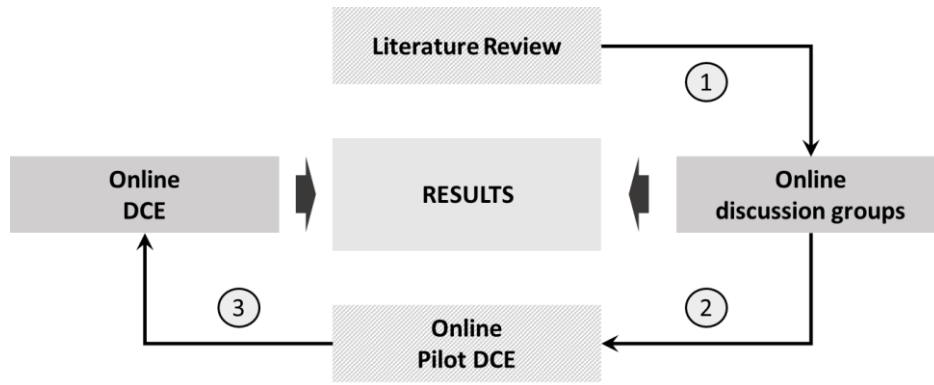
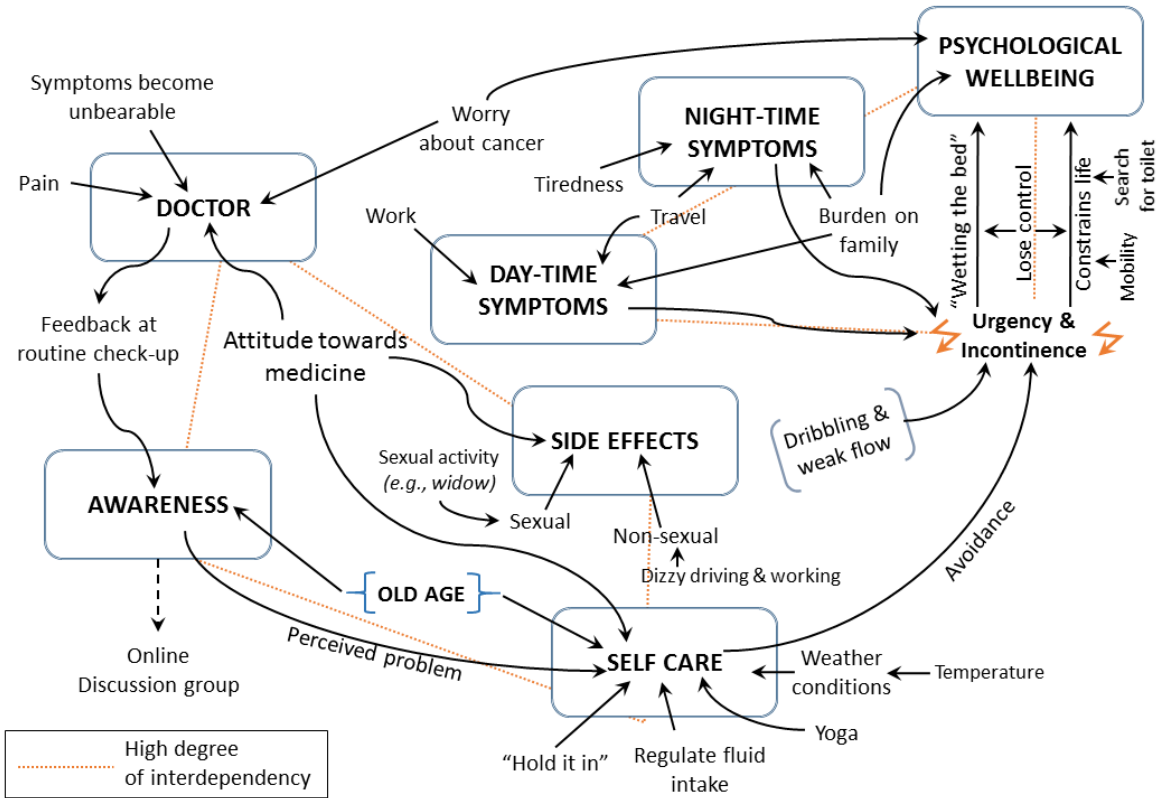


Figure 2 Example choice set

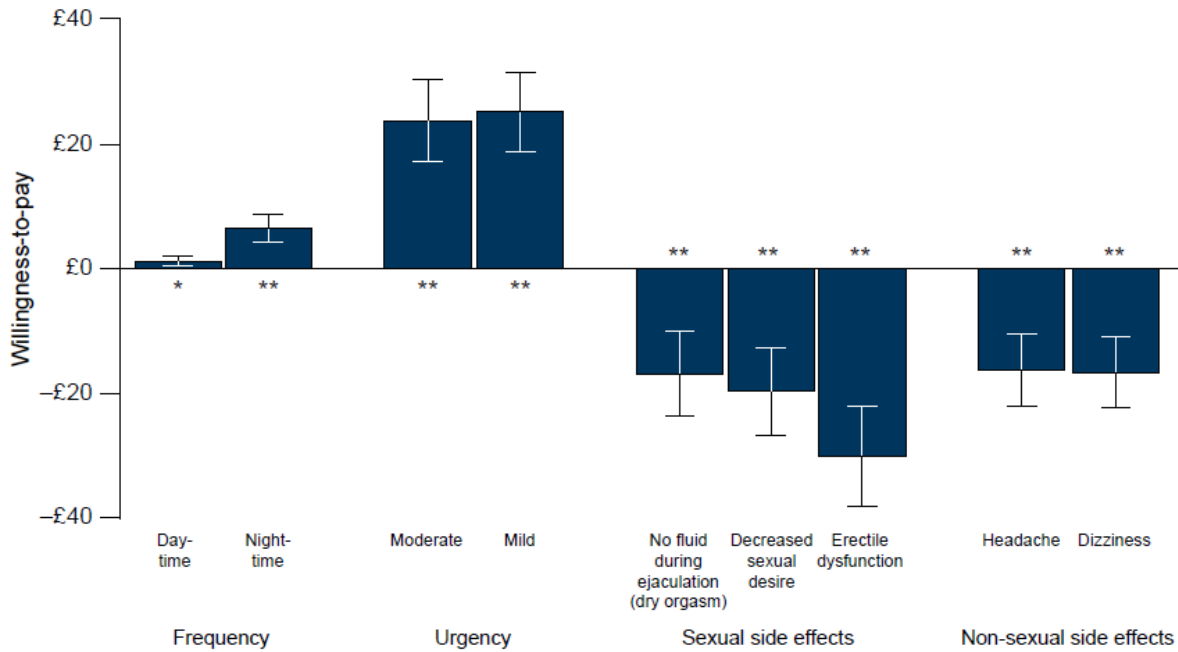
| Please compare the medicine and select which, if any, you would take. | | | |
|---|--|--|--|
| Description | Medicine A | Medicine B | No medicine |
| Day-time frequency of urination | 12 times | 14 times | 14 times |
| Nigh-time frequency of urination | 4 times | 2 times | 4 times |
| Urgency - when you need to urinate you usually | Have to rush to the toilet and leak before you get there | Can postpone as long as necessary, without fear of wetting yourself. | Have to rush to the toilet and leak before you get there |
| Sexual side effects of medicine | Decreased sexual desire | No sexual side effects | You do not have any side effects |
| Non-sexual side effects of medicine | Dry mouth | Headaches | You do not have any side effects |
| No. of tablets per day | One tablet | Two tablets | You do not take any medicine |
| Cost per month | £10 | £20 | £0 |
| Please select your answer here: | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

Figure 3 Conceptual map illustrating interdependencies between themes, codes and topics ^a



^a Themes are represented by boxes, arrows connect sub-themes to themes and indicate relationships between themes, and orange dotted lines represent complex relationships between sets of themes.

Figure 4 Men's mean willingness to pay for each attribute ^{a,b,c,d}



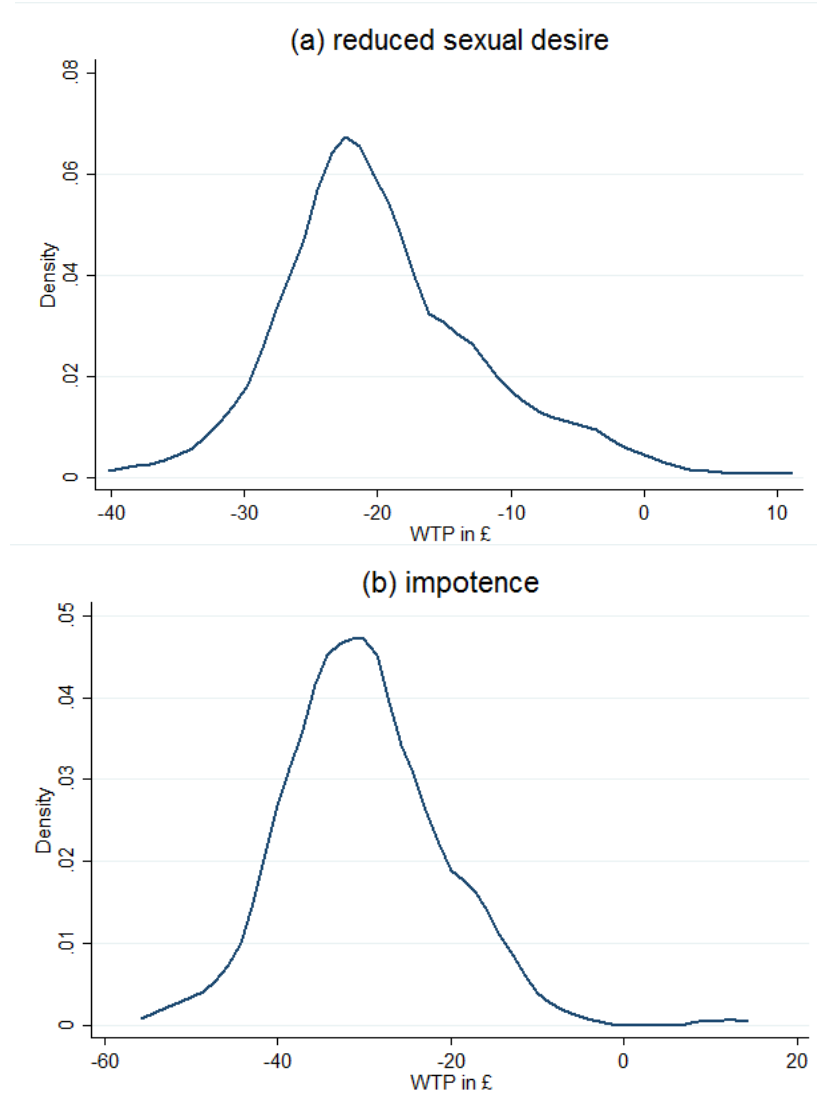
*, p<0.005; **, p<0.001

^a WTP estimates show the value that men put on each attribute (and level) of medication. For urinary frequency, the estimates are for a reduction in frequency of 1 time. For urinary urgency, the estimates are for a change from urge incontinence to the specified level of urgency. For side effects, the estimates are for the occurrence of the stated side effect versus no side effect. Bars above the horizontal axis denote attributes that have a positive effect on utility and men are willing to pay for that attribute. Bars below the horizontal axis denote attributes that have a negative effect on utility and men are willing to pay to avoid that attribute.

^b Error bars denote 95% confidence intervals.³

^c insignificant WTP estimates are excluded from the graph: Constant = -£6.53 [-£16.73; £3.68], Severe urgency = -£1.93, Dry mouth = -£2.85 [-£9.14;£3.44], Number of tablets = £1.43 [-£2.10; £4.96]

Figure 5 The distribution of WTP for sexual side-effects in the DCE sample ^{a,b}



^a Distributions are based on the conditional parameter distribution of the sample [5,19]

^b The negative WTP means that men's valuation decreases if a medicine has side effects

Table 1 Online discussion groups: questions posed by moderators

Welcome (Day 1)

Welcome to this online bulletin board about the treatment of urinary symptoms. Your answers to the short questionnaire last week indicate that you experience symptoms such as:

- A frequent need to go to the toilet, day or night
- The feeling of delay or hesitation when you start to urinate
- The feeling that you cannot empty your bladder completely
- The feeling that you must urinate right away

We would like to understand:

- How these symptoms affect your day-to-day life
- If you receive treatment
- What men like you think about different aspects of the available treatments for these symptoms.

To help us understand, each day we will ask you a question. We are interested in your answers to these questions and the answers of the group. You might find other people's answers interesting and/or different from your own. Throughout there are no right or wrong answers, we are interested in your opinion. Thank you very much for agreeing to take part and sharing your opinion with us.

Urinary symptoms and your day-to-day life (Day 1)

In the short questionnaire last week, you indicated that you experience symptoms such as:

- A frequent need to go to the toilet, day or night
- The feeling of delay or hesitation when you start to urinate
- The feeling that you cannot empty your bladder completely
- The feeling that you must urinate right away

Can you tell us how these symptoms affect your day-to-day life?

Managing your symptoms (Day 2)

Thank you for all your comments on Monday. They were really useful to help us understand how your symptoms affect your life. Today, we would like to understand how you manage your symptoms. Do you take any medicine to help manage your symptoms? If you take medicine, are you satisfied with the effect this has on your symptoms? If you don't take medicine, could you tell us why? (There are no right or wrong answers, we are interested in your opinion). Thanks again for all your help.

Medicine side effects (Day 3)

Yesterday we were discussing medicines. Some people take medication and they said it can help with their symptoms. Other people don't take medication for several reasons. Today we would like to discuss the different side effects that medicines might have. Different medicines have different side effects. But the most frequently reported side effects of medicine to treat urinary symptoms are:

- Headaches
- Dizziness
- A dry mouth
- No fluid during ejaculation (dry orgasm)
- Inability to get or maintain an erection
- Decreased sexual desire

Would/have these side effects put you off taking medicine? How do you weigh up the possible benefits of treatment against the possible side effects? Thanks for all your comments so far they are really helpful. Best wishes.

Consulting a doctor (Day 4)

From your answers, we understand there is mix of people on the bulletin board. Some of you are taking medication and others are not. Those of you not taking medication have told us that you might consider taking medication if your symptoms got worse. Today, we would like to understand what would make you visit the doctor and discuss medication in the future? If you are taking medication – what made you visit the doctor to discuss your symptoms? Thank you for all your help. Best wishes.

Final comments (Day 5)

Today is the last day on which we will post a new topic to the bulletin board. The bulletin board will close on Monday morning. We have found all of your thoughtful responses and comments very helpful, and we would like to thank you very much for taking the time to contribute. Today we would like to ask you questions about the bulletin boards this week: Have you been surprised by the topics that we have discussed? Did we miss something that you expected to come up? Overall, how have you found the experience of taking part in the bulletin board this week? Many thanks and best wishes.

Table 2 Attributes of the discrete choice experiment

| Attributes | Levels |
|-----------------------------|---|
| Day-time frequency | 8, 10, 12, 14 times |
| Night-time frequency | 1, 2, 3, 4, times |
| Day-time urgency | <i>Mild</i> can postpone as long as necessary, without fear of wetting yourself <i>Moderate</i> can postpone temporarily, without fear of wetting yourself <i>Severe</i> cannot postpone and have to rush to the toilet in order not to wet yourself <i>Urge incontinence</i> have to rush to the toilet and leak before you get there |
| Sexual side effects | No fluid during ejaculation Decreased sexual desire Impotence |
| Non-sexual side effects | Dry mouth Headache Dizziness |
| Number of tablets per day | 1, 2 |
| Cost of treatment (monthly) | £5, £10, £20 and £40 |