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## ARTICLE

# Patient preferences for the pharmacological treatment of osteoarthritis using adaptive choice-based conjoint (ACBC) analysis: A pilot study

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### Abstract

**Background:** Patient preferences for pharmaceutical treatment of osteoarthritis have been investigated using Conjoint Analysis. Studies have identified the importance of side effects in determining preferences, but noted that methodological limitations precluded further investigation of additional attributes such as hepatic and renal toxicity.

**Objective:** Following on from a feasibility study of adaptive choice-based conjoint (ACBC) analysis, the aim of this study was to evaluate 8 medication attributes for the pharmaceutical treatment of osteoarthritis (OA).

**Setting and Participants:** Eleven participants were recruited from members of a Research Users' Group (RUG) who had been diagnosed with osteoarthritis. RUG members individually complete the ACBC task.

**Main outcome measures:** The relative importance of each attribute and the utilities (part-worth) of each level of each attribute were estimated using ACBC built-in Hierarchical Bayes (HB).

**Results:** The combined relative importance of the 4 risk side-effect attributes when selecting osteoarthritis medication (kidney and liver side effects, heart attack and stroke side effects, stomach side effects and addiction) was 66% while the effectiveness attribute accounted for 8% of the relative importance of the medication decision.

**Conclusions:** In this study, the gap between relative importance of 4 side-effect attributes and expected benefit was 66% vs 8%. These preliminary findings indicate that OA patients are most concerned with the avoidance of adverse events and that there is a threshold above which expected benefit has little impact on patients' medication preferences. The study highlights methodological features of ACBC that may be useful more generally in health services research, but the results must be interpreted in conjunction with the study limitations.

### Keywords

Adaptive choice-based conjoint analysis, osteoarthritis, patient preferences, person-centered healthcare, pharmaceutical treatment

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## Introduction

Medication preference may be influenced by a wide range of factors including the efficacy in reducing serious outcomes of disease and, especially for a non-fatal but long-term symptomatic disease such as osteoarthritis (OA), in dealing with important but less serious symptoms such as pain or stiffness in the joints [1]. Such clinical benefits may be judged alongside practical characteristics of different medications, such as dosage, frequency and the nature of delivery of the medication [2,3]. Against the benefits of treatment and the practical features of the medication will also be weighed the potential side effects of taking the medication. This will be so particularly when the condition itself (OA) is in its effects (pain and

restricted activity) troublesome rather than serious in the sense of life-threatening.

OA medications are associated with several side effects such as gastric ulcer, hepatic and renal toxicity and cardiovascular side effects. The prevalence of these side effects varies between medications. For example, although, gastrointestinal side effects of NSAIDs are well documented as common side effects, others such as cardiovascular and hepatic side effects are less common. Heart failure occurs in approximately 1 per 100 patients using NSAIDs [4] and hepatotoxicity occurs in 1.7 per 100,000 individuals using NSAIDs [5]. The annual incidence of NSAID-related clinical upper gastrointestinal events is estimated to be between 2.5% to 4.5%, with the annual incidence of serious complications (severe

bleeding, perforation and obstruction) about 1% to 1.5% [6].

The degree of joint aches, the degree of physical mobility and the risk of experiencing serious side effects from OA treatment are important attributes in influencing OA treatment preferences [7]. Of particular concern are serious side effects, even when these are associated with a low prevalence rate [7]. In a study by Fraenkel and colleagues [1] examining 7 attributes in relation to the pharmaceutical treatment of knee OA, the relative importance of each attribute was expressed in percentage terms. Their results suggested that avoidance of side effects, especially those with more serious drug-related toxicity, is central to patients' treatment preferences even if this involves foregoing treatment. The method used by Fraenkel and colleagues [1] was adaptive conjoint analysis (ACA). ACA involves participants' rating their preference between 2 sets of attribute configurations [8]. Compared to paper-based rating methods that used pre-determined choice comparison sets, ACA choice sets adapt at each stage based on the individual's ratings at earlier stages of the process. Fraenkel and colleagues [9] indicated that the range of side effects that they were able to study was limited, because the inclusion of more attributes would have created an overly complicated ACA task. They hypothesized that the inclusion of additional adverse effects (such as renal toxicity) would lead to greater avoidance of drugs with side effects and that therefore patients would choose other treatment options such as exercise.

Another approach that has been used to investigate patient preferences for attributes associated with the efficacy and side effects for treatment in OA is choice-based conjoint (CBC) analysis [10]. Choice-based methods have become more popular than rating-based methods as a way of eliciting patient preferences [8]. The main characteristic distinguishing CBC from ACA is that instead of rating or ranking individual attributes, respondents are shown sets of treatment attributes and asked to indicate which set they would prefer [10]. CBC has been recently used to investigate patient preferences for potential disease-modifying drugs for osteoarthritis (DMOADs) [11]. This study involved 4 attributes, each with 3 levels; (1) route of administration, (2) expected benefit, (3) risk of drug toxicity and (4) cost [11]. In this study potential benefit was the most influential factor (39.4% of the relative importance followed by risk of side effects (26.9%), cost (24.9%) and route of administration (8.8%)).

As part of the preparation for the current study, the feasibility of adaptive choice-based conjoint (ACBC) analysis was evaluated [12]. ACBC contains elements of ACA and CBC. ACBC features adaptation of scenarios based on a respondent's earlier choices (from ACA) and the use of choice rather than ranking of scenarios (from CBC). The feasibility study reported on the steps taken to develop an ACBC task that enabled participants to evaluate a wide range of medication attributes for the treatment of OA. The results showed that older patients (who predominate among patients with OA), even without computer experience or computer literacy, can use a computer-based adaptive choice-based questionnaire to

produce quantitative estimates of the relative importance of the different attributes preferences. Detailed analyses of 3 individuals' medical priorities using this method are reported elsewhere [13].

The aim of the present study was to evaluate the use of ACBC in eliciting treatment preferences by determining the relative importance of 8 attributes in selecting pharmaceutical treatment of OA. While the present study reports on a small group of participants and is not claimed to be representative of OA patients in general, the intention is to evaluate the use of ACBC with a larger range of side effect attributes than previous studies.

## Methods

### Participants

Participants were drawn from members of a Research Users' Group (RUG) who had been diagnosed with OA and had reported one or more of hip, knee, hand and foot joint pain in the past 12 months. Eleven RUG members were recruited. Participants were OA patients age 50 or above. Having established the feasibility and practicality of the methods, we proceed to conduct a pilot study to investigate the relative importance and utilities of the attributes, while acknowledging that the sample would be too small to extrapolate these to all patients with OA.

### Ethical statement

All participants in this project were members of the extended Patient and Public Involvement (PPI) group of the Arthritis Research UK Primary Care Centre at Keele University, England, UK. These members had signed an agreement which permits the Centre to use their expertise in the development of research. This project was approved by the PPI team of the Arthritis Research UK Primary Care Centre at Keele University and complied with Keele University guidelines for the storage of sensitive and confidential data on laptops.

### Data collection and analysis

The data were collected from the 11 participants in the computer laboratory at the Arthritis Research UK Primary Care Centre at Keele University over 2 days in 2012. A Hierarchical Bayes (HB) model was used to estimate: (a) the relative importance of each attribute and (b) utilities of each level of each attribute.

### Relative importance of each attribute

The relative importance of all attributes adds up to 100%. A higher relative importance represents a greater impact of the attribute concerned on patients' preferences. Relative importance is ratio-scaled and relative, such that an attribute with relative importance of 20% is twice as important as an attribute with relative importance of 10% within [14].

Utilities (part-worth) of each level of each attribute

The order of the levels in each attribute is reported using utilities. Utilities are interval data and scaled within each attribute. The utilities of levels in each attribute are scaled to sum to "0". The utility for each level is a number that represents the weight that respondents place on that particular level in context with other levels within the same attribute. The level with the highest utility is the most favourable. Utilities are estimated through the maximum likelihood of each level [14].

## Results

### Participants' characteristics

There were 11 participants (4 male and 7 female) with OA in the hips, knees, shoulders, hands, ankles and/or spine. All participants were over 50 years of age. The modal age category was 60-69 years (see Table 1 for frequency of age groups). The majority of patients (72.8%) had suffered with OA for over 5 years. All participants reported that joint pain affected their normal life and 81.8% reported that effect to be moderate to extreme.

Table 1 Participant characteristics

Participants characteristics	Percentage
<b>Age groups</b>	
50-59	9.1
60-69	63.6
Over 69	27.3
<b>Years with osteoarthritis</b>	
1-2 years	9.1
3-4 years	18.2
More than 5 years	72.8

The participants reported using paracetamol (81.8%), NSAIDs and COX-2 inhibitors (81.8%), opioids (63.6%) and glucosamine (63.6%) for the management of OA. None of the participants reported previous or current use of capsaicin.

### The relative importance of attributes

Table 2 shows the relative importance of each attribute, representing the impact of that particular attribute on patients' preferences. The most important attribute was "risk of kidney and liver side effects", which accounted for 22.2% of the relative importance. The second most important attribute was "risk of heart attacks and strokes" with 17.4%. The least important attributes were "expected benefit" (7.5%) and "way of taking the medication" (6.9%).

Table 2 Relative importance scores of the eight medication attributes for the eleven participants [Mean  $\pm$  standard deviation (SD); mean scores sum to 100.]

Attribute (wording from the current study)	Relative importance scores for the medication attributes (with standard deviation)
Stomach side effects	16.5 $\pm$ 5.3
Risk of kidney and liver side effects	22.2 $\pm$ 5.8
Risk of heart attacks and strokes	17.4 $\pm$ 3.6
Risk of addiction	9.6 $\pm$ 8.7
How much you would expect to benefit	7.5 $\pm$ 4.8
Way of taking medication	6.9 $\pm$ 6.7
Availability	12.7 $\pm$ 3.7
Frequency	7.3 $\pm$ 4.8
Total	100

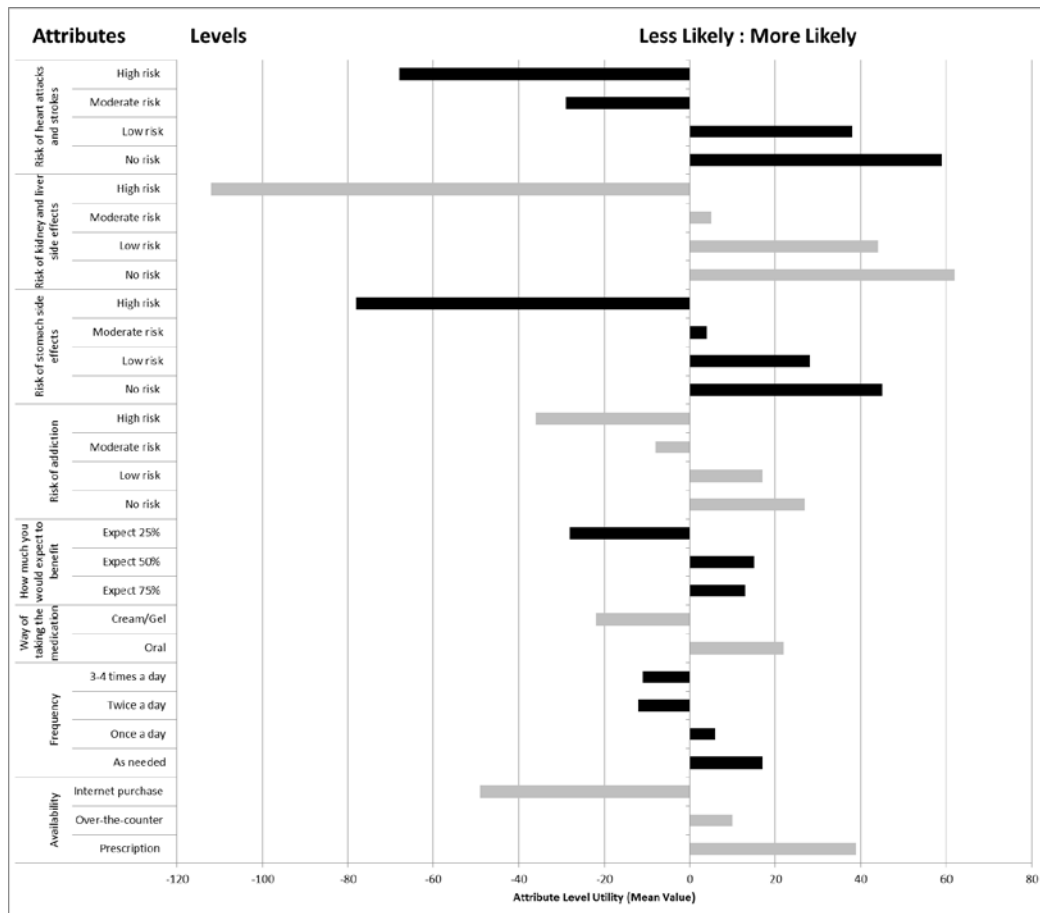
### Utilities of levels of attributes

Figure 1 shows the mean utility for each level. These results suggest that the preferred levels for each attribute are a prescription drug, taken orally when needed, with 50% benefit expected and no risk of addiction, stomach ulcer, kidney or liver impairment or heart attacks and strokes. Participants were avoiding medications that are to be taken frequently (2 or more times a day) and favouring those in the form of cream/gel rather than taken orally. Furthermore, participants were avoiding medications that are purchased *via* the internet.

## Discussion

This study collected data from 11 patients with established painful OA, all with experience of using medication for the condition. The study examined their medication preferences by using an ACBC task involving 28 levels of 8 medication attributes. The aim of the present study was to evaluate the use of ACBC in eliciting treatment preferences by determining the relative importance of 8 attributes in selecting pharmaceutical treatments for OA. As the present study had a small sample size, the generalisability of the results is therefore limited. Given this caveat, the results generally support the suggestion by Fraenkel *et.al.* [1-3] that the inclusion of more serious side effect attributes would elicit a preference for safer treatment options such as exercise. In the current study the effectiveness attribute accounted for only 8% of the relative importance of the medication decision compared to

Figure 1 Group utilities for all levels, showing propensity to select medication with indicated attribute/level



15% in an earlier study [9]. There was little difference in the utility value for medication effectiveness (expect 50% or 75% benefit), although the values at these levels were higher than those at the lowest level (expect 25% benefit). This finding indicates that there is a threshold above which expected benefit has little impact on patients' medication preferences.

The relative importance of these attributes should be interpreted in relation to all attributes included in the conjoint task. To further evaluate this issue, it would be necessary to conduct an ACBC study in which different attributes (i.e., with different combinations of benefit and risk should be administered to the same sample). Hauber and colleagues [15] used a form of choice-based conjoint (CBC) analysis to study patients' willingness to risk adverse events for improved function and pain control in OA. Their study involved 6 attributes of which 2 related to adverse events. They reported that patients tended to attach greater importance to eliminating the risks of adverse events than to reducing pain. Thus, the importance of side effects is also confirmed in a study where fewer attributes related to adverse events.

This study was preceded by a detailed feasibility study to identify attributes and levels that may influence patients' preferences regarding pharmaceutical treatment of

osteoarthritis [12,13]. Eight attributes and 28 levels were identified and considered to potentially influence patients' preferences regarding pharmaceutical treatment of OA. Taken together with the feasibility study, the current findings indicate that ACBC is a potentially valid method of evaluating patients' preferences for pharmaceutical treatment of OA. It remains to be seen whether more attributes can be studied and whether this will alter the basic finding that avoidance of side effects is the major determinant of patients' preferences regarding pharmaceutical treatment of osteoarthritis.

## Conclusion

This study is the first conjoint analysis study to have included 8 attributes related to patients' preferences for pharmaceutical treatment of OA and in addition including liver, kidney, gastric, heart attacks, strokes and addiction side effects. This study addresses the issues raised by Fraenkel and colleagues [9] regarding the need for conjoint techniques that could include attributes on hepatic and renal toxicity. The study extends our understanding of factors influencing patients' preferences for

pharmaceutical treatment of OA and highlights methodological features of ACBC that maybe be useful in health services research.

## Acknowledgements and Conflicts of Interest

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