Treatment Options in Knee Osteoarthritis

The Patient’s Perspective

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Background: The objectives of this study were to (1) examine patient treatment preferences for knee osteoarthritis, (2) determine the influence of specific medication characteristics on patients’ choices, and (3) examine whether patient preferences are consistent with current practice.

Methods: A total of 100 consecutive patients with symptomatic knee osteoarthritis completed an interactive computer questionnaire administered during a face-to-face interview. We measured the relative impact of specific medication characteristics (including administration, risks, benefits, and cost) on patients’ choice, and the percentage of patients preferring nonselective nonsteroidal antiinflammatory drugs (NSAIDs), cyclooxygenase-2 inhibitors, glucosamine and/or chondroitin sulfate, opioid derivatives, and capsaicin across varying risks, benefits, and costs.

Results: Of the characteristics studied, variation in the risk of common adverse effects and gastrointestinal ulcer had the greatest impact on patients’ choice. Assuming patients are responsible for the full cost of their medications, over 40% prefer capsaicin. Cyclooxygenase-2 inhibitors become patients’ preferred choice only if they are described as being 3 times as effective as capsaicin and are covered by insurance. Nonselective NSAIDs are among the least preferred options across all simulations.

Conclusions: When evaluating multiple alternatives, many older patients with knee osteoarthritis are willing to forgo treatment effectiveness for a lower risk of adverse effects. The patient treatment preferences derived in this study conflict with the current widespread use of nonselective NSAIDs in older patients with arthritis.

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Knee osteoarthritis (OA) is a leading cause of disability in the elderly. There is no cure for this disease, and treatment is aimed at improving quality of life by targeting symptoms and improving or maintaining function. Therapeutic options for knee OA include nonpharmacologic, pharmacologic, and surgical interventions. Nonpharmacologic measures such as weight loss, muscle-strengthening exercises, and joint protection techniques have no inherent risk and minimal costs, and are therefore advised for all patients. Joint replacement surgery is generally reserved for patients who are refractory to medical management.

Pharmacologic therapies, including acetaminophen, anti-inflammatory drugs, opioid derivatives, glucosamine and/or chondroitin sulfate, and capsaicin, all have modest efficacy in decreasing the pain associated with knee OA. Previous studies have found that patients with arthritis find traditional nonselective nonsteroidal anti-inflammatory drugs (NSAIDs) to be more effective than acetaminophen for the treatment of pain related to knee OA, and that physicians frequently choose nonselective NSAIDs as first-line therapy for patients with OA. However, to our knowledge, treatment preferences have not been assessed in patients who are fully informed of available treatment options. Explicit elicitation of patient preferences is of particular importance in the treatment of patients with knee OA, because pharmacologic options have relatively modest efficacy and differ significantly with respect to their risk of drug toxicity and cost. On a practical level, elicitation of preferences in this disease is feasible because decisions are rarely urgent.

Traditional methods of measuring patient preferences, such as the time tradeoff or standard gamble techniques, have been criticized as being too difficult to perform, especially in older patients, the demographic group most affected by OA. In contrast, conjoint analysis is an easy to use, reliable, and valid technique that has
been applied successfully by both researchers and managers to understand consumer preferences in diverse sociodemographic groups. This technique has been recently recognized as valuable means of assessing patient preferences for health care, and has been used to identify patient priorities in the doctor-patient relationship, as well as preferences for delivery of health care services and treatment alternatives.

When faced with multiple alternatives, people make decisions by making trade-offs between the specific features of competing products. Conjoint analysis derives preferences by examining these trade-offs through a series of rating and/or ranking exercises, and subsequently determines which combination of features would be most preferred by each respondent. Data derived from the conjoint task can be used to predict treatment preferences, weigh the amount of importance patients place on specific treatment characteristics, and estimate willingness to pay for more effective or less risky medications. Thus, unlike traditional methods of measuring preferences, conjoint analysis provides insight into the reasons underlying individual patient preferences.

There are several ways to collect data for conjoint analyses. Adaptive Conjoint Analysis (ACA) collects and analyzes preference data using an interactive computer program (Sawtooth Software; Sequim, Wash). ACA is unique in that it uses an individual respondent's answers to update and refine questions through a series of paired comparisons. The main advantage of ACA's interactive design is that it allows a large number of attributes to be evaluated without resulting in information overload or respondent fatigue.

The objectives of this study were to (1) examine older patients' treatment preferences for knee OA, (2) determine the influence of specific medication characteristics on patients' choices, and (3) examine whether patients' preferences are consistent with current practice.

**METHODS**

**PATIENTS**

Consecutive patients with radiographic knee OA, followed up in community rheumatology practices affiliated with a university hospital, were contacted by telephone approximately 1 week after having received a letter describing the study. Patients having pain in one or both knees on most days of the month, and not having rheumatoid arthritis, gout, pseudogout, or bilateral knee replacements, were asked to complete a questionnaire examining opinions about arthritis treatments. The study was approved by the Human Investigations Committee at our institution.

**DATA COLLECTION**

Demographic and clinical data were collected in face-to-face interviews. Patient characteristics were base on self-report and the Western Ontario and McMaster Universities OA Index (WOMAC). Preference data were collected using Adaptive Conjoint Analysis (ACA, version 4.0; Sawtooth Software) with respondents inputting their answers directly into a laptop computer.

**MEDICATION CHARACTERISTICS**

Medication characteristics were chosen to elicit preferences for agents commonly used when an inadequate response to acetaminophen is obtained: nonselective NSAIDs, cyclooxygenase-2 (COX-2) inhibitors, opioid analogics, glucosamine and/or chondroitin sulfate, and capsaicin. We did not assess preferences for acetaminophen, because many patients are already taking this medication when they present to a physician. We did not include intra-articular medications, because these agents are given on an intermittent basis.

We ascertained patient values (ie, utilities) for 7 medication characteristics including label, route of administration, time to benefit, response rate, common adverse effects, risk of ulcer, and monthly copayments. All characteristics were described using lay terminology adapted from patient information sheets published by the Arthritis Foundation. Each adverse effect was described in terms of severity and reversibility of symptoms, likelihood of occurrence, and sequelae. The face and content validity of the characteristic descriptions were assessed by rheumatologists, conjoint experts, and laypersons. The ranges of probabilities of benefits and adverse effects were based on randomized controlled data and long-term follow-up studies.

In view of the literature documenting significant variability in both patients' ability to interpret probabilities and preference for the presentation of probabilistic information, we used qualitative and quantitative frequency formats to describe the likelihood of adverse effects and illustrated probabilistic information using human figure charts. In addition, to improve understanding of the level of risk associated with rare events, we provided patients with familiar examples. For example: "A risk of a side effect happening in 1 person in 100 (one in a hundred) is the same as the risk of being audited by the Internal Revenue Service."

**ACA QUESTIONNAIRE**

Adaptive Conjoint Analysis assumes that each treatment option can be broken down into specific characteristics, and that each characteristic is defined by a number of levels. Levels refer to the range of plausible estimates for each characteristic. For example, the levels for the characteristic "risk of nausea" might be 0%, 10%, and 30%, depending on the specific medications being studied.

The second assumption is that respondents have unique values or utilities for each attribute level. In this context “utility” is a number that represents the value a respondent associates with a particular characteristic, with higher utilities indicating increased value. Differences in utilities allow the investigator to determine which features most strongly drive patients' treatment choices.

The final assumption is that utilities can be combined across attributes. For example, if the sum of a patient's utilities for the attributes of medication A is greater than the sum of utilities for the attributes of medication B, the patient should prefer medication A to B.

The adaptive conjoint task involved 3 groups of questions. First, patients ranked the estimates within each characteristic.

Second, respondents rated the importance of the difference between the best and worst estimates of each characteristic on a 4-point scale (1, not important at all; 2, somewhat important; 3, very important; 4, extremely important). For example: "If two medications were acceptable in all other ways, how important would this difference be?: Starts to work within 1 to 2 hours vs starts to work within 4 weeks. Attributes were presented in random order to eliminate any possible ordering effects.
Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SD</td>
<td>70 ± 7</td>
</tr>
<tr>
<td>Female, %</td>
<td>79</td>
</tr>
<tr>
<td>Duration of knee OA, mean ± SD, y</td>
<td>11 ± 9</td>
</tr>
<tr>
<td>White</td>
<td>92</td>
</tr>
<tr>
<td>College graduate</td>
<td>43</td>
</tr>
<tr>
<td>Employed</td>
<td>30</td>
</tr>
<tr>
<td>Annual income ≥$60 000</td>
<td>32</td>
</tr>
<tr>
<td>Prescription drug plan</td>
<td>88</td>
</tr>
<tr>
<td>Current health status fair or worse (vs good, very good, or excellent)</td>
<td>50</td>
</tr>
<tr>
<td>Previous ulcer or other stomach disease</td>
<td>22</td>
</tr>
<tr>
<td>Previously hospitalized for gastrointestinal bleeding</td>
<td>5</td>
</tr>
<tr>
<td>Dyspepsia from nonselective NSAID(s) use</td>
<td>34</td>
</tr>
<tr>
<td>Current or previous use of nonselective NSAID(s)</td>
<td>85</td>
</tr>
<tr>
<td>Current or previous use of COX-2 inhibitor(s)</td>
<td>76</td>
</tr>
<tr>
<td>Current or previous use of glucosamine and/or chondroitin sulfate</td>
<td>75</td>
</tr>
<tr>
<td>Current or previous use of opioid derivative(s)</td>
<td>30</td>
</tr>
<tr>
<td>Current or previous use of analgesic cream(s)</td>
<td>59</td>
</tr>
</tbody>
</table>

Abbreviations: COX, cyclooxygenase; NSAID, nonsteroidal anti-inflammatory drug; OA, osteoarthritis.

*Values are percentage of patients unless otherwise specified.

Third, to refine respondents' utilities, respondents evaluated a series of paired comparisons on scale of 1 to 9, where 1 indicates strongly prefer; 5, no preference; and 9, strongly prefer. For example: “Which would you prefer?”: $70 per month +75% of patients benefit or $10 per month +25% of patients benefit.

Adaptive Conjoint Analysis constructs pairs by examining all the possible ways the levels can be combined and then chooses pairs of options with similar utilities for which it expects respondents to be indifferent (based on previous responses). If one option is clearly superior to the other based on ACA’s initial estimate of utilities, no additional information is learned. Additional details regarding this methodology have been published previously.15,20-22

ANALYSES

Patient Characteristics

Patient characteristics were entered into SAS computer files (SAS Software, version 6.12; SAS Institute Inc, Cary, NC). Preference data derived from ACA (version 4.0) were imported into SAS and merged with the patient characteristics data set.

Patient Utilities

We first describe the mean ± SD utility for each characteristic. Initial utility estimates are derived from the set of questions evaluating the importance patients assigned to the difference between the best and worst levels of each characteristic. Estimates are subsequently updated based on respondents’ ratings of the paired comparison tasks. The least preferred level of each attribute is arbitrarily given a utility of zero, because conjoint analysis measures utilities on an interval scale. Details on how utilities are calculated by ACA have been published previously.26

We calculated the relative importance of the characteristics studied by dividing the range of utilities for each characteristic by the sum of ranges, and multiplying by 100. The relative importances reflect the extent to which the difference between the best and worst levels of each characteristic drives the decision to choose a particular product.

Choice Simulations

Choice simulations demonstrate the percentage of patients preferring specific treatment options defined by the researcher. We report treatment preferences for the “base-case” scenario (where levels were assigned to each option based on estimates from the literature) using the first-choice model, which assumes that the respondent chooses the product having the highest predicted utility. Although objective data comparing the efficacy of capsaicin with other medications are lacking, we described capsaicin as being less effective than the other 4 options based on feedback from clinicians. We subsequently performed simulations, analogous to sensitivity analyses, to examine how decreasing the risk of ulcer, improving the efficacy of anti-inflammatory agents compared with the remaining 3 options, and varying out-of-pocket costs influenced patients’ preferences. Associations between patient characteristics and treatment preferences were examined using χ² and t test statistics for categorical and continuous variables, respectively.

RESULTS

UTILITIES

One hundred older adults with symptomatic knee OA were interviewed (participation rate, 84%). Patient characteristics are described in Table 1. Patient values for the characteristics studied are presented in Table 2. The large standard deviations reflect substantial interpatient...
variability in the values that respondents placed on particular characteristics. Pertinent information is found in the relative differences between utilities.

### RELATIVE IMPORTANCES

The relative impact of the variation in each characteristic is presented in Table 3. The distribution of the relative importances suggests that the respondents considered multiple characteristics to arrive at their decision. Variation in risk of common adverse effects and gastrointestinal ulcer, however, had the greatest impact on choice, each accounting for approximately 19% of the total relative importance. This suggests that patients' treatment preferences are driven predominantly by a desire to avoid both common bothersome side effects as well as less frequent, but potentially more serious, drug-related toxic effects.

### TREATMENT PREFERENCES

Preferences assuming patients pay the full cost of their medications are presented in Table 4. Descriptions of the treatment options for the base-case scenario are described in Table 5. For the base-case scenario, which described capsaicin as being less effective than the other treatment options, capsaicin was the most popular choice with 44% of the respondents surveyed preferring this option. Relatively few patients preferred nonselective NSAIDs (2%) and COX-2 inhibitors (7%), assuming patients are responsible for the full cost of their medications.

Decreasing the risk of ulcers associated with nonselective NSAIDs and COX-2 inhibitors to 1% and 0.5%, respectively, increased the percentage of patients preferring nonselective NSAIDs from 2% to 9%, but had little influence on patients' preferences for the top 3 choices: capsaicin, glucosamine and/or chondroitin sulfate, and opioid derivatives. Forty-one percent of patients continued to choose capsaicin even when it is described as being 3 times less effective than anti-inflammatory drugs (ie, percentage of patients who improve on capsaicin is 25%, and on nonselective NSAIDs and COX-2 inhibitors is 75%).

Preferences assuming patients pay a monthly copayment for their medications are presented in Table 6. Cost significantly influenced patient treatment choices as seen in the change of the rank ordering of medications in Table 6. Assuming patients pay a fixed copayment for prescription medications and full cost for over-the-counter medications, 34% of patients preferred capsaicin while 23% preferred COX-2 inhibitors, and none chose traditional nonselective NSAIDs. As in Table 4, decreasing the risk of ulcer had little influence on treatment preferences. COX-2 inhibitors became more popular than capsaicin only when they are described as being 3 times more effective than the latter. Patients with prescription drug insurance never chose nonselective NSAIDs over the other treatment options included in this study.

### PATIENT CHARACTERISTICS AND TREATMENT PREFERENCES

We found no associations between demographic characteristics (age, annual income, and education level), clinical characteristics (previous adverse effects, knee pain, stiffness, or function as measured by the WOMAC scales), and treatment preference. However, patients rating their current health status as fair or worse were less likely to choose capsaicin compared with those who felt well or very well (26% vs 57%, P = .002) when capsaicin is described as being less effective than the other options. Health status was not related to preference for capsaicin when all options were described as being equally effective.

### COMMENT

In summary, we found that topical capsaicin appears to be the preferred treatment option for most older patients with knee OA, even when it is described as being much less effective than the other alternatives. Nonselective NSAIDs, the most widely prescribed medication for patients with arthritis, is the least preferred therapeutic option across almost all simulations. COX-2 inhibitors become the preferred choice only when they cost $10 per month (reflecting the typical copayment in an insured patient) and are described as being 3 times as effective as capsaicin.
The relative importance of the characteristics studied suggest that the risk of adverse effects had the strongest impact on patient decision making, which explains why patients with knee OA almost never preferred nonselective NSAIDs in this study. Preferences for capsaicin were unlikely due to a dislike for taking pills, since route of administration was one of the least influential medication characteristics. Despite the widespread use of complementary therapies among patients with arthritis, the label "natural supplement" also had little influence on treatment preferences when rated in comparison with other medication characteristics.

Patients with poorer self-reported health status were more willing to accept the risk of adverse effects for improved efficacy than those with better health status. However, patients reporting previous adverse effects related to nonselective NSAIDs were not more likely to prefer capsaicin. This finding is consistent with other studies showing that, contrary to intuition, patients who have had experience with side effects may be more willing to accept the risk of toxic effects compared with patients who have not experienced side effects. This may occur because patients' anticipated effects of adverse effects on quality of life are often worse than their actual effects.

Our findings contrast with those of Wolfe et al. and Pincus et al. who found that most respondents preferred nonselective NSAIDs over acetaminophen. The apparently conflicting results may be explained by differences in study design. Wolfe et al. asked patients to rate medications based on their previous experiences (which reflects patient satisfaction), and did not consider explicit trade-offs. In contrast, preferences in this study were predicted based on how individual patients value trade-offs between specific risks and benefits. We chose to omit the names of medications from the conjoint questionnaire to ensure that preferences were based on values for specific risks and benefits and not biased by recognition of specific brand names. Lastly, we did not assess preferences for acetaminophen, because in clinical practice many patients are already taking this medication when they present to their physician.

Numerous studies have demonstrated that ACA produces internally consistent responses, and that it is a reliable and valid method of measuring preferences.
Our results must be interpreted in view of the limitations of this study. First, we could not include all medication characteristics, since this would have overly complicated the questionnaire. However, inclusion of additional adverse effects (such as renal toxicity) would be expected to further widen the gap between patient preferences for safer, albeit less effective, treatment options and prescription drugs.

Second, the study was conducted in patients with prevalent disease currently taking medications, since recruiting treatment-naïve patients with new-onset disease would not have been feasible. Finally, despite recruiting patients from several community-based practices, our patient population was relatively homogeneous. Most patients were white, female, well educated, and had a prescription drug plan, thereby limiting the generalizability of the results. It is likely, for example, that out-of-pocket costs would have an even greater influence in patients with lower incomes.

We conclude that many older patients with knee OA might be willing to accept less effective treatments in exchange for a lower risk of adverse effects. The magnitude of the discrepancy between patient preferences in this study and the widespread use of nonselective NSAIDs raises important questions about how patient preferences are elicited and how treatment decisions for OA are made in clinical practice. Although not prescriptive, the results of this study underscore the importance of involving patients in treatment decisions for knee OA, where most treatment options are associated with relatively modest benefits, but differ significantly in both potential risks and out-of-pocket costs.

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REFERENCES


