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If You Want Patients with Knee Osteoarthritis (OA) to Exercise: Tell them about NSAIDS

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Abstract

Purpose—Exercise is an important adjunctive treatment for knee OA; however it is underutilized, in part because of the known difficulties related to initiating and adhering to exercise programs. Although there are ample data documenting the latter, patient preferences for exercise in comparison to other options have not been examined.

Methods—Participants were recruited as part of an intervention trial to improve decision-making in knee OA. Patients with knee pain on most days of the preceding month completed an Adaptive Conjoint Analysis interactive computer survey designed to elicit patient preferences for a cream (capsaicin), oral medications, [acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs)], intra-articular (IA) injections (up to four times per year) and exercise (low impact aerobic exercise and/or strength training three times per week). Preferences were determined based on individual respondent's trade-offs between: route of administration, probability of having less pain, probability of improved strength and endurance, risk of dyspepsia, and risk of ulcer. Preferences were calculated as "shares" which sum to 100.

Results—90 subjects completed the computer tool; mean age $\pm$ SD = 68 $\pm$ 9 (range = 53–87). Patients preferred exercise over other treatment options whether IA injections and NSAIDs were described as being 20% or 50% more effective at decreasing symptoms compared to other options. The relative importance assigned to treatment benefits and risks were 29% and 41% respectively. Patient demographic characteristics were not related to preferences; however, patients with more self reported knee pain were less likely to prefer exercise compared to their counterparts ($r = -0.3$, $p=0.004$).

Conclusions—In this study, patients preferred exercise over pharmacologic options for treatment of knee OA. Preferences were driven by patients' unwillingness to accept the risk of adverse effects. Our findings also suggest that subjects with greater knee pain may be more reluctant to exercise compared to their counterparts. Presentation of exercise in the context of other available therapies might increase patient willingness to try exercising by making the trade-offs between exercise and medications more apparent.

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. Currently available drug therapies for knee OA generally offer only modest benefit and many are associated with significant toxicity. Joint replacement surgery is generally reserved for patients who are refractory to medical management.

Nonpharmacologic measures such as weight loss, exercise, and joint protection techniques have also been advocated for knee OA. Of these measures, exercise is the best studied. In a recent review, Roddy et al (1) found pooled effect sizes of 0.52 for aerobic exercise and 0.39 for quadriceps strengthening on knee pain. Exercise has also been shown to improve function (2), decrease the risk of disability (3), and it may decrease the risk of disease progression (4). These studies indicate that exercise is an important adjunctive treatment for knee OA.

Despite its benefits, exercise is underutilized in older adults in part because of the known difficulties related to initiating and adhering to exercise programs. Although there are ample data documenting the latter (5–7), patient preferences for exercise in comparison to other options have not been examined. The objective of the study was to gain insight into patients' preferences for exercise in the context of other available treatment options (excluding surgery).

Methods

The study took place in the VA Connecticut Healthcare System primary care outpatient clinics. A research assistant recruited participants by approaching patients waiting in the primary care waiting room area. She described the study, determined eligibility among those interested in participating, and obtained written consent.

Eligibility criteria included: at least 60 years old, self-report of pain involving one or both knees on most days of the month, the ability to read and understand English, and the ability to perform a choice task. This task asked the participant to examine three hypothetical treatment options and to choose the one they would prefer (Figure 1). The options were described such that one was objectively preferable because it maximized benefit while minimizing risk. Use of a choice task was chosen to identify patients who do not have the cognitive skills required to perform an Adaptive Conjoint Analysis (ACA) task without the risk of upsetting patients with formal mental status questionnaires.

Patients were excluded if they were judged to be too ill to participate as determined by the medical staff, were scheduled for an urgent visit, had a disease other than OA which causes knee pain (inflammatory arthritis, Paget's disease, cancer, hyperparathyroidism), or had relative or absolute contraindications to one or more of the proposed treatment options (i.e. on warfarin or heparin, renal disease, heart or other disease requiring limitation of physical activity).

Independent variables were collected in face-to-face interviews and included sociodemographic characteristics (age, ethnicity, maximum level of education attained, and marital status) and clinical factors (level of knee pain with walking (8), global health status (9), and history of peptic ulcer disease. All characteristics were ascertained by self-report.

Preferences were elicited using ACA (Web System Version 3.5, Sawtooth Software Inc., Seattle, WA). ACA is an interactive computer survey that enables patients to construct their treatment preferences by asking them to make tradeoffs between competing treatment characteristics in a series of rating tasks. Preferences are predicted based on tradeoffs between specific treatment characteristics and not the treatments themselves. Therefore, bias due to product recognition, brand preferences, or previous experience with any particular treatment is minimized.

For this study, the ACA task was designed to assess patients' preferences for the treatment characteristics corresponding to four treatment options: a cream (capsaicin), oral medications, [acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs)], intra-articular (IA) injections (up to four times per year) and exercise (low impact aerobic exercise and/or strength training three times per week). Preferences were determined based on individual respondent's

trade-offs between: route of administration (pills, cream, injection, exercise), likelihood of expected benefit (decrease in pain and improvement in strength and endurance), and risk of adverse effects (dyspepsia and ulcer) (Table 1). All characteristics and possible sequelae of the adverse effects were described using lay terminology. Risk information was obtained from randomized controlled trials (10) and presented using natural frequencies and pictographs to facilitate communication of probabilistic data (11,12).

The ACA task included 16 questions. The first question asked participants to rate the routes of administration on a seven point scale ranging from “Not Desirable At All” to “Extremely Desirable”. The next five questions asked respondents to rate the importance of the difference between the best and worst alternative for each treatment characteristic. Lastly, participants completed 10 paired comparison tasks. Two attributes were presented in the first five paired comparison tasks and three were included in the last five. An example is provided in Figure 2. Further details regarding the use of this procedure in eliciting patient preferences have been previously published (13).

Analyses

We used ACA’s randomized first choice model to calculate patients’ preferences for capsaicin, acetaminophen, anti-inflammatory drugs, intra-articular injections, and exercise. ACA predicts preferences based on the utilities derived from the conjoint questionnaire using least squares regression analysis. Preferences are calculated by first summing the utilities of the levels corresponding to each option. The utilities are then exponentiated and rescaled so that they sum to 100. For this study preferences were predicted using the randomized first choice model. Details on how ACA calculates utilities and predicts treatment preferences using this model are available at <http://www.sawtoothsoftware.com/download/techpap/acatech.pdf> and <http://www.sawtoothsoftware.com/download/techpap/asmtech.pdf> respectively.

Utilizing the part-worths generated from the ACA tasks, preferences were calculated for two scenarios. In the base case scenario capsaicin, acetaminophen, and exercise were modeled as relieving pain in 3 out of 10 people and NSAIDs as relieving pain in 5 out of 10 people. We used the same part worths to examine preferences when effectiveness of decreasing pain attributed to NSAIDs and injections was increased to 8 out of 10 people (Benefits Maximized). Only exercise was assumed to increase strength and endurance. The relative importance of risk and benefits were calculated by dividing the range of each characteristic (difference between levels) by the sum of ranges of all characteristics, and multiplying it by 100. These values sum to 100, and reflect the extent to which the difference between the levels of each characteristic impacts subjects’ choices. We subsequently used multivariable linear regression to ascertain associations between respondent characteristics and treatment predicted preference.

Results

Of 114 patients approached for participation, 90 completed the computer tool (16 patients refused to participate and eight failed the screening choice task); mean age $\pm$ SD = 68 ± 9 (range = 53–87); 73% Caucasian; 17% college graduates; 43% married; 53% retired; mean $\pm$ SD level knee pain (WOMAC pain scale) = 9.5 ± 3.7 ; and 36% reported having excellent or very good health status.

Across scenarios patients consistently preferred exercise over other treatment options (Table 2). NSAIDs were the least preferred option. This was true whether the more effective therapies (intra-articular injections and NSAIDs) were described as being 20% (Base Case) or 50% more effective (Benefits Maximized) at decreasing symptoms compared to the other options.

Patients' preferences for exercise were explained by the relative impact of each treatment characteristics on patients' choice. (Table 3) Patients' preferences were more strongly influenced by the risk of side effects compared to the chance of benefit. Patient demographic characteristics (age, ethnicity, employment status, education) were not related to preferences (Table 4); however, patients with greater WOMAC knee pain scores were less likely to prefer exercise compared to their counterparts ($r = -0.3$, $p=0.004$).

Discussion

Despite the benefits of exercise for arthritis as well as many other treatment conditions, this modality is exceptionally underutilized, presumably because of patient unwillingness to initiate or adhere to exercise programs. To the best of our knowledge this is the first study to examine preferences for exercise in the context of other possible treatment options. We found that when patients are asked to construct preferences based on the trade-offs related to the specific risks and benefits for treatment options for OA, patients preferred exercise over pharmacologic options for treatment of knee OA.

Although, patients valued the potential benefits associated with therapy, preferences were driven primarily by patients' unwillingness to accept the risk of adverse effects. The risk aversion demonstrated in this study is consistent with other studies of older adults' treatment preferences for chronic pain (14–16) and suggests that when informed of the risks associated with commonly prescribed medications for arthritis, many older patients would opt to choose safer treatment options, even when they are less effective and less convenient.

Preference for exercise was however inversely associated with level of knee pain, suggesting that patients with greater levels of pain may have reservations about their ability to perform exercise, the safety of exercise, or the effectiveness of exercise in patients with painful knee arthritis. This finding is supported by a recent qualitative study describing beliefs about exercise in patients with knee OA (17) and suggests an opportunity for physicians to educate their patients about the safety and benefits of exercise in knee OA.

Numerous studies have demonstrated that ACA produces internally consistent responses, and that it is a reliable and valid method of measuring preferences (18–21). Other strengths of this technique are the minimization of interviewer bias, the elimination of brand name or product recognition bias, and the ability to ensure that respondents evaluate all characteristics under consideration. In addition, ACA allows a large number of characteristics to be evaluated without resulting in information overload or respondent fatigue.

In view of the known difficulties associated with communicating probabilistic information, we tried to maximize understanding of risk magnitude using several strategies. We provided both numerical estimates (natural frequencies) as well as pictographs. In addition, all characteristics were described using a standardized script written in lay terminology.

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 associated with NSAIDs) would be expected to further widen the gap between patient preferences for exercise and prescription drugs. In addition, our patient population was relatively homogenous thereby limiting the generalizability of the results. Finally, 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. However, ascertainment of preferences in patients with established disease is an appropriate task for patients with chronic disease in whom preferences should be ascertained over time as they

would be expected to vary with response to therapy, the development of adverse events, and fluctuations in disease activity.

The results of this study suggest that presentation of exercise in the context of other pharmacologic treatment options for knee OA may highlight the potential benefits of this treatment modality. Our findings add to the literature emphasizing the importance of ensuring that patients understand the safety of exercise. Further research is needed to determine whether elicitation of preferences using approaches in which patients are enabled to make trade-offs between all available treatment options increases willingness to engage and adhere to exercise programs.

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If these were the only options to treat your knee pain, which would you choose?

	<u>Number of times a day</u> you take this pill	<u>How many people</u> get <u>good pain relief</u> taking this pill	<u>How many people</u> get <u>stomach upset</u> taking this pill
Pill #1	4 times a day	3 out of 10	2 out of 10
Pill #2	2 times a day	8 out of 10	1 out of 10
Pill #3	3 times a day	6 out of 10	4 out of 10

Figure 1.
Screening Choice Task

Figure 2.
Example of an ACA Paired-Comparison Question.

Table 1

Characteristics Included in the ACA Questionnaire

Attribute	Level
Route of administration	Cream applied up knee Pills Injections into the knee (up to four times per year) Exercise (low impact aerobic/strength training for minimum of 30 minutes 3 times per week)
Decrease in pain	8 out of 10 people have less pain 5 out of 10 people have less pain 3 out of 10 people have less pain
Improved strength	Improves strength and endurance Does not improve strength and endurance
Risk of dyspepsia	Causes stomach upset or heartburn in 3 out of 10 people Does not cause stomach upset or heartburn
Risk of bleeding ulcer	Causes a bleeding ulcer in 1 in 100 people Does not cause bleeding ulcers

Table 2

Patient Treatment Preferences

Option	Base Case	Benefits Maximized
Capsaicin	13	10
Acetaminophen	13	10
NSAIDs	4	5
IA Injections	24	35
Exercise	40	42

Table 3

Relative Importances

Attribute	Median Relative Importances (Interquartile Range)
Route of administration	24.0 (18.3–32.1)
Decrease in pain	14.7 (11.1–23.0)
Improved strength	14.2 (9.4–21.5)
Risk of dyspepsia	22.2 (16.2–26.7)
Risk of bleeding ulcer	19.1 (13.3–26.3)

Table 4

Association of Patient Characteristics and Preference for Exercise

Characteristics	Standardized Estimate	P value
Age	0.17	0.19
Race	−0.09	0.39
Education	0.11	0.29
Employment status	−0.16	0.22
Knee pain	−0.31	0.008