

Patients' Stated Health Outcome Preferences for Confounded Patient-Reported Outcome Domains for Osteoarthritis

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BACKGROUND

- Patient-reported outcome (PRO) instruments yield scores for outcomes that cannot be measured clinically
- Scores from PRO instruments assume that domains and scales are separable and additive
- PRO scores may not indicate patients' perceptions of the relative importance of therapeutic endpoints
- Discrete-choice experiments can elicit patients' preferences over PRO domains and scales to quantify the relative importance to patients of therapeutic benefits and risks

HYPOTHESIS

- Patient preferences in the United Kingdom (UK) for osteoarthritis (OA) outcomes are separable and additive in PRO domains

METHODS

Survey Instrument

- Web-enabled survey instrument
- Discrete-choice experiment (choice-format conjoint survey method)
 - Elicits patient tradeoffs among alternatives with varying levels of different endpoints
 - Repeated choices over treatment profiles with varying severity of outcomes provide reliable information for quantifying preferences¹⁻⁴
- Patients evaluated 10 pairs of hypothetical OA treatments
 - Treatments defined using 7 endpoints (Table 1)
 - 4 benefit endpoints derived from Western Ontario and McMaster Universities Arthritis Index (WOMAC) PRO instrument (visual analog scales)
 - 3 adverse-event endpoints
 - Patients chose the option they preferred if these were the only medications available to them (Figure 1)
- Experimental design
 - Combinations of endpoint levels in each medication profile were determined using an experimental design with known statistical properties⁵⁻⁷
 - Reduces the number of paired comparisons to the smallest number necessary for efficient estimation of preference weights

Subjects

- Inclusion criteria
 - Age 45 years or older
 - Resident of the UK
 - Self-reported diagnosis of OA
- Recruitment
 - Harris Interactive UK Consumer Panel
 - All patients provided online informed consent

Table 1. Outcomes and Risks in the Survey Instrument

Outcome or Risk	Label	Levels
Pain while moving around 1 hour after taking the medicine	Ambulatory pain	None (0 mm) Mild (25 mm) Moderate (50 mm) Severe (75 mm)
Pain while sitting, lying down, or sleeping 1 hour after taking the medicine	Resting pain	None (0 mm) Mild (25 mm) Moderate (50 mm) Severe (75 mm)
Stiffness 1 hour after taking the medicine	Stiffness	None (0 mm) Mild (25 mm) Moderate (50 mm) Severe (75 mm)
Difficulty doing daily activities 1 hour after taking the medicine	Difficulty doing daily activities	None (0 mm) Mild (25 mm) Moderate (50 mm) Severe (75 mm)
Chance of a bleeding ulcer requiring an operation within the next year because of the medicine	Ulcer risk	None 10 out of 1,000 (1.0%) 50 out of 1,000 (5.0%) 100 out of 1,000 (10.0%)
Additional chance of a heart attack within the next 5 years because of the medicine	Heart attack risk*	No chance 5 out of 1,000 (0.5%) 15 out of 1,000 (1.5%) 30 out of 1,000 (3.0%)
Additional chance of a stroke within the next 5 years because of the medicine	Stroke risk*	No chance 5 out of 1,000 (0.5%) 15 out of 1,000 (1.5%) 30 out of 1,000 (3.0%)

mm = millimeters

* Half of the questions in the survey elicited preferences for treatment-related heart-attack risk and half elicited preferences for stroke risk

Figure 1. Example Choice Question

Medicine Features	Medicine A	Medicine B
Pain while moving around 1 hour after taking the medicine	None	None
Pain while sitting, lying down, or sleeping 1 hour after taking the medicine	Mild	Mild
Stiffness 1 hour after taking the medicine	Mild	Mild
Difficulty doing your daily activities 1 hour after taking the medicine	Mild	Mild
Chance of a bleeding ulcer requiring an operation within the next year because of the medicine	10 people out of 1,000 (1.0%)	50 people out of 1,000 (5.0%)
Additional chance of a stroke within the next 5 years because of the medicine	30 additional people out of 1,000 (3.0%) will have a stroke	15 additional people out of 1,000 (1.5%) will have a stroke
Which medicine would you choose if these were the only medicines available?	Medicine A	Medicine B

Analysis

- Estimated relative preference weights using random-parameters (mixed) logit⁸
- Estimated two specifications for relative preference weights:
 - A categorical main-effects model that does not control for clinical correlation of endpoints
 - A model that controls for clinical correlation of ambulatory pain and difficulty doing daily activities

RESULTS

Sample

- Data collected from 294 subjects (Table 2)
- Five subjects had no variation in their responses and were omitted from subsequent modeling

Table 2. Demographic Characteristics (N = 294)

Category	%
Gender	
Male	35%
Female	65%
Age, mean (standard deviation), years	59 (8.3)
45-65	77%
Older than 65	23%
Marital status	
Married	62%
Widowed	7%
Divorced or separated	21%
Single	8%
Other	2%
Race/ethnicity	
White	99%
Other	1%
Highest education	
Less than secondary school education	2%
Some secondary school education	12%
Secondary school qualification (e.g., O levels, CSEs, GCSEs)	33%
Vocational qualification gained in further education (e.g., BTEC National, ONC, OND)	15%
Further education qualification (e.g., A-levels, Scottish Highers or equivalent)	11%
Vocational qualification from higher education (e.g., HND, HNC)	11%
University first degree (e.g., BA, BSc)	8%
Some postgraduate education but no higher degree obtained	1%
Postgraduate or professional qualification (e.g., MBA, MSc, PhD)	7%

Hypothesis Test

- Log-odds parameter estimates are preference weights indicating the relative strength of preference for each endpoint level
- Larger parameter estimates represent more preferred outcomes
- Main-effects categorical model that did not account for clinical correlation (Figure 2):
 - Preference weights correctly indicate that lower side-effect risks are preferred to higher risks
 - 3 of the 4 benefit endpoints are incorrectly ordered (e.g., 50 mm ambulatory pain is preferred to 25 mm ambulatory pain)
 - The perceived benefit of reducing pain from 75 mm to 0 mm is **less than** the perceived risk of increasing risk of either heart attack or stroke from 0% to 1.5%
- Categorical model that accounts for perceived correlation in PRO domains (Figure 3):
 - Difficulty doing daily activities is confounded with the level of ambulatory pain. Patients perceive outcomes that combine daily-activity restrictions and little ambulatory pain implausible, including:
 - 50 mm or 75 mm difficulty doing daily activities with 0 mm ambulatory pain
 - 75 mm difficulty doing daily activities with 25 mm ambulatory pain
 - **REJECT HYPOTHESIS** that patient preferences for OA outcomes in the UK are separable and additive in PRO domains

Benefit-Risk Analysis

- Main-effects model: The perceived importance of reducing pain from 75 mm to 0 mm is less than the perceived importance of increasing risk of heart attack from 0% to 1.5% (Figure 2)
- Correlation-corrected model: The perceived importance of reducing pain from 75 mm to 0 mm is more than the perceived importance of increasing risk of heart attack from 0% to 1.5% (Figure 3)

Figure 2. Categorical Main-Effects Model (Log-Odds)

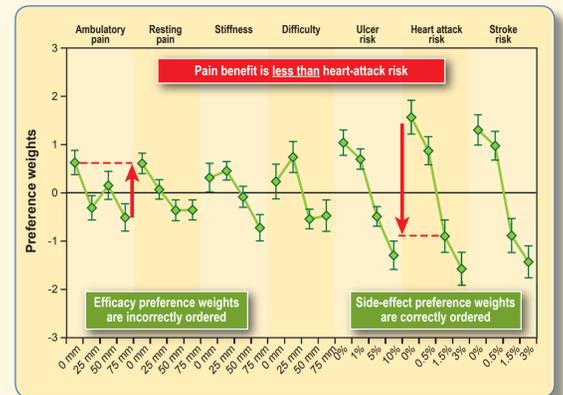
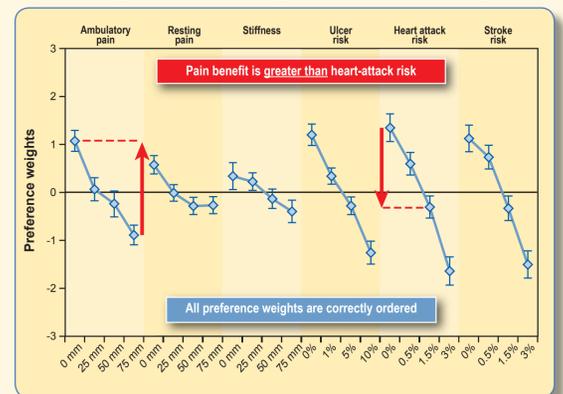


Figure 3. Categorical Model Controlling for Confounded Domains (Log-Odds)



CONCLUSIONS

- PRO domains for OA are not separable and additive and thus complicate estimating valid preference weights
- Patients may reject certain domain combinations as implausible
- Effect of implausible combinations of endpoint levels may be controlled to obtain valid preference weights
- In this case, controlling for confounding in PRO domains reversed the benefit-risk implications of the analysis

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