How generalizable are estimates in preference studies? A weight and test approach

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Patient-Centered Outcomes at Open Health

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Outline

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Project background and objectives

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Project Background

Background

- The growing demand for quantitative patient preference information (PPI) from regulators and health technology assessment bodies underscores the critical need for accurate and generalizable results.
- Challenges in achieving representativeness and generalizability in PPI samples are well known
- Traditional approaches often rely on oversampling specific subsamples (underserved populations) or setting specific target sample sizes to explore preference heterogeneity
- However, PPI samples frequently exhibit skewness towards specific patient demographics, such as white, women or more highly educated individuals.

Objectives of study

- To use data from an existing PPI study to explore techniques to enhance generalizability
- To set a path forward in transferability of preference estimates, marginal tradeoffs, and preference shares across target populations or countries

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Data

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Case study

- Data from a preference study on
  - Osteoarthritis (OA)
  - Chronic low back pain (CLBP)
- Data collected in
  - the United States (US)
  - the United Kingdom
- 6 attributes
  - Symptom control
  - Risks of 3 AEs
  - Mode and frequency of administration
  - Out-of-pocket Cost
- Experimental design:
  - 48 sets of two treatments split into 6 blocks of 8 choice questions each

Attribute	Respondent-facing attribute levels	
Symptom control (patient global assessment)	Very good (no symptoms; no limitations on normal activities)	
	Good (mild symptoms; no limitations on normal activities)	
	Fair (moderate symptoms; limitations on some normal activities)	
	Poor (severe symptoms; unable to carry out most normal activities)	
Incremental treatment-related risk of severe, rapidly progressive joint problems requiring total joint replacement	No additional risk (0%)	
	5 people out of 1,000 (0.5%)	
	40 people out of 1,000 (4%)	
Incremental treatment-related risk of heart attack	No additional risk (0%)	
	2 people out of 1,000 (0.2%)	
	5 people out of 1,000 (0.5%)	
Incremental treatment-related risk of physical dependence	No risk (0%)	
	50 people out of 1,000 (5%)	
	250 people out of 1,000 (25%)	
Mode and frequency of administration	Oral pills 2 or more times a day	
	Oral pills once a day	
	Injection every 4 weeks (about once a month)	
	Injection every 8 weeks (about once every 2 months)	
Personal (out-of-pocket) cost per month	Narrow range	Wide range
	$0 every month	$0 every month
	$30 every month	$30 every month
	$55 every month	$75 every month
	$85 every month	$110 every month

Walsh, Boeri, et al., 2022; Eur J Pain. 2022 Mar;26(3):648-67. doi: 10.1002/ejp.1892
Turk, Boeri et al., 2020; Osteoarthritis Cartilage. 2020 Sep 1;28(9):1202-13. doi: 10.1016/j.joca.2020.06.006.

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Fielding

- N = 602 US residents
  - OA (n = 201)
  - CLBP (n = 202)
  - both OA and CLBP (n = 199)

- N = 437 UK residents
  - OA (n = 171)
  - CLBP (n = 188)
  - both OA and CLBP (n = 78)

Walsh, Boeri, et al., 2022; Eur J Pain. 2022 Mar;26(3):648-67. doi: 10.1002/ejp.1892
Turk, Boeri et al., 2020; Osteoarthritis Cartilage. 2020 Sep 1;28(9):1202-13. doi: 10.1016/j.joca.2020.06.006.

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Methods

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Two Approaches to applying weights

Study sample and target sample were based on a set of observed or known participant/patient characteristics

Study Sample (fixed)
- Characteristic 1 (X_1) %
- Characteristic 2 (X_2) %
- Characteristic 3 (X_3) %
- …

Target Population
- Characteristic 1 (Y_1) %
- Characteristic 2 (Y_2) %
- Characteristic 3 (Y_3) %
- …

Use sample weighting (Y/X) to yield results that are generalizable to the target population

Approach 1 (based on literature):

Reweight the study sample so that sample used in analysis reflects the target population and generate preference result estimates (eg, MAR) for Target population (Vass et al. 2022).

Approach 2 (exploratory):

Estimate the preference model on the study sample, retrieve individual conditional posterior parameters (Bayesian) and use the output to reflect the target population (re-weighting individual characteristics).

Vass CM, Payne K, Feng Y, et al. Med Decis Making. 2022 Apr;42(3):291-306. doi: 10.0161/j.jocm.2022.100367

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Estimation of weights 1: Post-Stratification

- **Steps:**
  1. **Definition of Population Margins**:
     - Percentage of the population in each subgroup were identified (e.g., age-gender-location combinations) from external data.
  2. **Creation of Stratified Groups**:
     - Trial sample was divided into subgroups based on combinations of age, gender, and location (e.g., young males in urban areas).
  3. **Calculation of Weights**:
     - For each subgroup, weights were computed so that their sample representation aligned with the target population margins:

$$Weight = \frac{Population\ Proportion}{Sample\ Proportion}$$

  4. **Application of Weights**:
     - Weights were applied in the estimation of MNL and RPL models

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Estimation of weights 2: Iterative Proportional Fitting

- **Steps:**
  1. **Definition of Population Margins**:
     - Target population distributions (margins) were obtained for **age**, **gender**, and **duration of disease and race**.
  2. **Assignment of Initial Weights**:
     - Equal weights for all sample participants was assumed to start.
  3. **Adjustment of Weights Iteratively**:
     - **Iteration 1**: Weights were adjusted so the sample matched the target population distribution for **gender**.
     - **Iteration 2:** Weights were adjusted so the sample matched the target population distribution for **race**.
     - **Iteration 3**: Weights were adjusted so the sample matched the target population distribution for **duration of osteoarthritis**.
     - **Iteration 4**: Weights were adjusted so the sample matched the target population distribution for **duration of age**.
  4. **Application of Weights**:
     - Weights were applied in the estimation of RPL models

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Modelling Approach: Random Parameter Logit (RPL) Model

- A Mixed MNL model accommodates for taste heterogeneity by allowing the estimated coefficients to follow a mixing distribution. The RPL model uses continuous distributions

- The choice probability is obtained by integrating the product of Logit probabilities over the distribution of:

$$\Pr(i_{nt}) = \int \prod_{t=1}^{T_n} \frac{\exp(\beta' x_{nit})}{\sum_{j=1}^{J} \exp(\beta' x_{nj})} (\beta) d(\beta).$$

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Conditional Individual Post-Estimations

- After estimating the RPL model, individual-specific parameter estimates (posterior means) can be computed using Bayes' Rule, conditioning on the choices made by each individual.
- This is a well-established (Huber and Train, 2001; von Haefen, 2003; Scarpa and Thiene, 2005; Greene et al., 2005; Train, 2009).

$$\hat{\beta}_n = \frac{\frac{1}{R}\sum_{r=1}^{R} \widehat{\beta_{x,n}^r}\, L(\widehat{\beta_{x,n}^r}|y_n, \pi_n)}{\frac{1}{R}\sum_{r=1}^{R} L(\widehat{\beta_{x,n}^r}|y_n, \pi_n)},$$

Huber J, Train K. Mark Lett. 2001;12(3):259–69. doi: 10.1023/a:1011120928698.von Haefen RH. J Environ Econ Manage. 2003 Mar;45(2):145–65. doi: 10.1016/s0095-0696(02)00047-5.Scarpa R, Thiene M. Land Econ. 2005 Aug;81(3):426–44. doi: 10.2307/4129695.Scarpa R, Alberini A. Appl Simul Methods Environ Resour Econ. Springer; 2006.Train K. Discrete Choice Methods with Simulation. Cambridge University Press; 2009. https://eml.berkeley.edu/books/choice2.html

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Estimation of Marginal Rates of Substitution

- The utility function can be described as:

$$U_{in} = g(\alpha, Risk_i) + h(\beta, X_i) + \varepsilon_{in}$$

Marginal effect of Risk (or others)

Marginal effect of other attributes

- The MAR (which is a Marginal Rate of Substitution), can be expressed as the change in Risk (DRisk) that decreases the respondents' utility by the same amount a given improvement (DX*) increases it. Therefore:

$$h(\beta, \Delta X^*) = -g(\alpha, \Delta Risk)$$

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Approach (Comparing RPL mean vs. HB – individual post-estimations)

- Estimate multinomial logit on original sample and weighted sample (benchmark)
- Estimate RPL

  original sample → Individual β → average with weights

- Estimate weighted

  (larger confidence intervals)

- Compare results

- Three samples considered:
  - US sample → Trial population (Schnitzer et al., 2021)
  - UK sample → Trial population (Schnitzer et al., 2021)]
  - US sample weights → UK sample population

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Results

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MAR results – Trial weights applied to US sample

Maximum acceptable risk (MAR) for risk of heart attack

Attribute	From level	To level	Mean estimate (RPL)	Mean estimate (w-RPL)	Mean estimate (w-postRPL)
Symptom control (patient global assessment)	Poor	Very Good	2.507 [1.287 ; 3.727]	1.962 [1.026 ; 2.898]	2.423
	Poor	Good	2.191 [1.142 ; 3.239]	1.767 [0.952 ; 2.581]	2.115
	Poor	Fair	1.510 [0.837 ; 2.184]	1.145 [0.653 ; 1.637]	1.436
Incremental treatment-related risk of severe rapidly progressive joint problems requiring total joint replacement	40 people out of 1,000 (4%)	No additional risk (0%)	0.321 [0.114 ; 0.529]	0.234 [-0.041 ; 0.509]	0.325
	40 people out of 1,000 (4%)	5 people out of 1,000 (0.5%)	0.416 [0.228 ; 0.605]	0.386 [0.175 ; 0.596]	0.424
Treatment-related risk of physical dependence	250 people out of 1,000 (25%)	No risk (0%)	1.741 [0.938 ; 2.545]	1.456 [0.752 ; 2.161]	1.791
	250 people out of 1,000 (25%)	50 people out of 1,000 (5%)	1.201 [0.668 ; 1.734]	0.990 [0.556 ; 1.424]	1.239
Mode and frequency of administration	Oral pills 2 or more times a day	Oral pills once a day	0.232 [0.003 ; 0.46]	0.274 [0.054 ; 0.495]	0.244
	Oral pills 2 or more times a day	Injection every 4 weeks	0.290 [0.033 ; 0.547]	0.038 [-0.338 ; 0.414]	0.279
	Oral pills 2 or more times a day	Injection every 8 weeks	0.270 [-0.013 ; 0.554]	0.092 [-0.222 ; 0.406]	0.256
	Oral pills once a day	Injection every 4 weeks	0.483 [0.224 ; 0.742]	0.327 [0.018 ; 0.635]	0.499
	Oral pills once a day	Injection every 8 weeks	0.464 [0.179 ; 0.749]	0.381 [0.121 ; 0.642]	0.477
	Injection every 4 weeks	Injection every 8 weeks	0.024 [-0.237 ; 0.284]	-0.051 [-0.262 ; 0.16]	0.026
LL			-1490.03	-1669.05	-1490.03

RPL = unweighted RPL model; w-RPL = RPL model with iterative proportional fitting weights applied pre-estimation; w-postRPL = Individual conditional parameters from the unweighted RPL weighted with iterative proportional fitting.
Note: weights were based on gender, race, age and time since diagnosis

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MAR results – UK sample weights applied to US sample

Maximum acceptable risk (MAR) for risk of heart attack

Attribute	From level	To level	Mean estimate (RPL)	Mean estimate (w-RPL)	Mean estimate (w-postRPL)
Symptom control (patient global assessment)	Poor	Very Good	2.367 [0.491 ; 4.243]	1.3 [0.622 ; 1.977]	1.661
	Poor	Good	1.885 [0.42 ; 3.35]	1.149 [0.592 ; 1.706]	1.378
	Poor	Fair	1.458 [0.397 ; 2.519]	0.95 [0.516 ; 1.383]	1.055
Incremental treatment-related risk of severe rapidly progressive joint problems requiring total joint replacement	40 people out of 1,000 (4%)	No additional risk (0%)	0.228 [-0.107 ; 0.563]	0.168 [-0.191 ; 0.528]	0.315
	40 people out of 1,000 (4%)	5 people out of 1,000 (0.5%)	0.07 [-0.145 ; 0.284]	0.055 [-0.196 ; 0.306]	0.420
Treatment-related risk of physical dependence	250 people out of 1,000 (25%)	No risk (0%)	1.547 [0.392 ; 2.701]	1.091 [0.559 ; 1.624]	1.860
	250 people out of 1,000 (25%)	50 people out of 1,000 (5%)	0.885 [0.249 ; 1.521]	0.877 [-0.439 ; 2.194]	1.263
Mode and frequency of administration	Oral pills 2 or more times a day	Oral pills once a day	-0.02 [-0.254 ; 0.213]	-0.126 [-0.469 ; 0.216]	0.215
	Oral pills 2 or more times a day	Injection every 4 weeks	0.466 [-0.152 ; 1.085]	0.409 [0.13 ; 0.688]	0.310
	Oral pills 2 or more times a day	Injection every 8 weeks	0.117 [-0.199 ; 0.432]	0.158 [-0.218 ; 0.534]	0.316
	Oral pills once a day	Injection every 4 weeks	0.483 [0.07 ; 0.896]	0.333 [0.023 ; 0.642]	0.499
	Oral pills once a day	Injection every 8 weeks	0.096 [-0.2 ; 0.392]	0.032 [-0.267 ; 0.33]	0.505
	Injection every 4 weeks	Injection every 8 weeks	0.372 [-0.013 ; 0.757]	0.314 [0.03 ; 0.597]	-0.006
LL			-976.17	-1174.40	-976.17

RPL = unweighted RPL model; w-RPL = RPL model with iterative proportional fitting weights applied pre-estimation; w-postRPL = Individual conditional parameters from the unweighted RPL weighted with iterative proportional fitting.
Note: weights were based on gender, race, age and time since diagnosis

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MAR results – Trial weights applied to UK sample

Maximum acceptable risk (MAR) for risk of heart attack

Attribute	From level	To level	Mean estimate (UK RPL)	Mean estimate (UK w-RPL)	Mean estimate (UK w-postRPL)
Symptom control (patient global assessment)	Poor	Very Good	2.367 [0.491 ; 4.243]	2.47 [0.971 ; 3.969]	2.653
	Poor	Good	1.885 [0.42 ; 3.35]	2.085 [0.895 ; 3.276]	2.305
	Poor	Fair	1.458 [0.397 ; 2.519]	1.487 [0.686 ; 2.287]	1.565
Incremental treatment-related risk of severe rapidly progressive joint problems requiring total joint replacement	40 people out of 1,000 (4%)	No additional risk (0%)	0.228 [-0.107 ; 0.563]	0.315 [0.07 ; 0.56]	0.310
	40 people out of 1,000 (4%)	5 people out of 1,000 (0.5%)	0.07 [-0.145 ; 0.284]	0.467 [0.246 ; 0.688]	0.423
Treatment-related risk of physical dependence	250 people out of 1,000 (25%)	No risk (0%)	1.547 [0.392 ; 2.701]	1.642 [0.722 ; 2.562]	1.906
	250 people out of 1,000 (25%)	50 people out of 1,000 (5%)	0.885 [0.249 ; 1.521]	1.133 [0.546 ; 1.719]	1.307
Mode and frequency of administration	Oral pills 2 or more times a day	Oral pills once a day	-0.02 [-0.254 ; 0.213]	0.295 [0.043 ; 0.547]	0.224
	Oral pills 2 or more times a day	Injection every 4 weeks	0.466 [-0.152 ; 1.085]	0.307 [-0.043 ; 0.657]	0.285
	Oral pills 2 or more times a day	Injection every 8 weeks	0.117 [-0.199 ; 0.432]	0.427 [0.064 ; 0.79]	0.275
	Oral pills once a day	Injection every 4 weeks	0.483 [0.07 ; 0.896]	0.547 [0.186 ; 0.907]	0.512
	Oral pills once a day	Injection every 8 weeks	0.096 [-0.2 ; 0.392]	0.667 [0.253 ; 1.081]	0.502
	Injection every 4 weeks	Injection every 8 weeks	0.372 [-0.013 ; 0.757]	-0.167 [-0.542 ; 0.209]	0.010
LL			-976.17	-1372.17	-976.17

RPL = unweighted RPL model; w-RPL = RPL model with iterative proportional fitting weights applied pre-estimation; w-postRPL = Individual conditional parameters from the unweighted RPL weighted with iterative proportional fitting.
Note: weights were based on gender, race, age and time since diagnosis

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Discussion

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Discussion

- In this case study, the application of weighting pre or post estimation had no statistically significant effect on results, suggesting that it did not influence the overall findings.
- This lack of impact from weighting implies that the results would not affect policy conclusions or recommendations and can potentially be generalized to the broader public without concern for model-specific adjustments.
- We recommend adopting a similar approach across studies to ensure consistency in analysis and findings.
- The decision to generalize results (for example, through benefit transfer or other methods) should be made on a case-by-case basis, depending on the specifics of each study and context.
- Future studies should assess whether further efforts to generalize results are necessary or if the current findings are already applicable to broader populations.

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Thank you

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