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Exploring Heterogeneity in Preferences for Attributes of Pharmaceutical Treatments for Osteoarthritis and Chronic Low Back Pain in the United States: A Latent Class Approach

BREAKOUT SESSION 2
PATIENT PREFERENCE STUDIES
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Presented by Marco Boeri

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DISCLOSURE

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DISCLAIMER

The views and opinions expressed in this presentation are those of the presenting author and do not necessarily represent those of other authors or of the institutions of affiliation.

NC = North Carolina; UK = United Kingdom; USA = United States of America.

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Background

- Patient preferences for pharmacologic treatments for chronic OA pain and CLBP have been previously and formally measured. However, none of the previous studies:
  - Elicited preferences for long-acting, nonopioid, injectable alternatives for the treatment of chronic pain, including features of opioids and NSAIDs
  - Elicited preferences for chronic pain treatments from patients with moderate-to-severe pain related to OA, CLBP, and comorbid OA/CLBP, comparing preferences across groups
- The study objective was:
  - To quantify patients' preferences for attributes of treatments for chronic moderate-to-severe musculoskeletal pain associated with OA and CLBP that both differentiate NGF inhibitors, NSAIDs, and opioids and that are relevant to patients, Exploring preference heterogeneity.

CLBP = chronic lower back pain; NGF = Nerve Growth Factor; NSAIDs = Non-steroidal anti-inflammatory drugs; OA = osteoarthritis;

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Inclusion and Exclusion Criteria

- Inclusion criteria
  - Aged 18 years or older, residents of the US, and provided informed consent
  - Had a self-reported physician diagnosis of hip or knee OA only, CLBP only, or comorbid OA and CLBP received at least 3 months ago
  - Had self-reported moderate-to-severe pain in the hip, knee, and/or lower back, defined as a self-assessed rating of 5 or greater on average in the past week on an 11-point numeric pain scale ranging from 0 (no pain) to 10 (worst possible pain)
  - Have taken or tried 3 or more classes of pain treatment in the past 2 years or have taken or tried 2 prior classes of pain treatment and for whom NSAIDs are contraindicated or were unwilling to take opioids
- Exclusion criteria
  - Had Alzheimer's disease, axial spondyloarthritis, fibromyalgia, major depressive disorder, migraine headaches, myopathy, neuropathic pain, psoriatic arthritis, radiculopathy or sciatica, rheumatoid arthritis, spinal stenosis, or spondyloarthropathy, or had pain as a result of having had surgery in the past 3 months

NSAIDs = nonsteroidal anti-inflammatory drugs; US = United States.

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Discrete-Choice Experiment Attribute Identification

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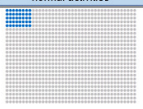
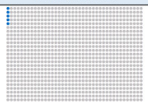
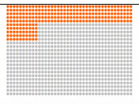
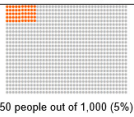
Attributes Important to Patients *(from focus groups)*	Attributes That Differentiate NSAIDs, Opioids, and NGF Inhibitors	Attributes Included in the DCE
Efficacy	Efficacy	Symptom control (patient global assessment)
Side effects	NGF inhibitor risks and side effects	Incremental treatment-related risk of severe rapidly progressive joint problems requiring total joint replacement
Risk of addiction/dependence	NSAID risks and side effects	Incremental treatment-related risk of heart attack
Mode of administration	Opioid risks and side effects	Treatment-related risk of physical dependency
Frequency of administration	Risk of addiction/dependence	Mode and frequency of administration
Out-of-pocket cost	Mode of administration	
	Frequency of administration	
	Out-of-pocket cost	Personal (out-of-pocket) monthly cost

DCE = discrete-choice experiment; NGF = Nerve growth factor.

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DCE Questions

- Experimental design generated in SAS
  - 48 choice questions were split into 6 blocks of 8 hypothetical choice questions
  - Each respondent randomly assigned to 1 block of questions
  - Questions were randomly ordered to avoid ordering effects and were not repeated across blocks
- The chosen alternative yields higher utility than the alternative that was not chosen
  - The utility of each alternative in a choice question is a function of the attribute levels defining that alternative

Medicine Feature	Medicine A	Medicine B
Symptom control: Symptom control while you are taking the medicine	GOOD mild symptoms; no limitations on normal activities	VERY GOOD no symptoms; no limitations on normal activities
Additional risk of severe joint problems: Additional risk each year of having joint problems that are severe enough that you would need a total joint replacement while you are taking the medicine or within 6 months of stopping the medicine	 40 people out of 1,000 (4%)	 5 people out of 1,000 (0.5%)
Additional risk of heart attack: Additional risk each year of having a heart attack while you are taking the medicine	 5 people out of 1,000 (0.5%)	 No additional risk (0%)
Risk of physical dependence: Risk each year of becoming physically dependent on the medicine	 250 out of 1,000 people (25%)	 50 people out of 1,000 (5%)
How you take the medicine	 Oral pills once a day	 Injection every 8 weeks (about every 2 months)
Cost: Personal cost of the medicine to you every month	$30 every month	$55 every month
Which medicine would you choose if these were the only 2 medicines available?	☐	☐

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Discrete-Choice Experiment Data Modeling

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- Random-parameters logit (RPL) model
  - Controls for preference heterogeneity by also estimating a continuous (e.g., normal) distribution across the sample for each preference weight
  - Subgroup analysis was also executed using an interacted RPL model
- Latent class (LC) model
  - Controls for preference heterogeneity by assuming discrete distribution of preferences
    - Assumes that there is heterogeneity between classes (or segments) but not within each class
  - Data reveal the number of latent segments (i.e., preference classes)
  - Each preference weight is the mean preference weight for the class (or segment)
  - Same subgroups explored in the RPL were explored in the class membership probability function of the LC model

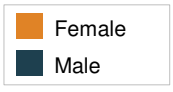
LC = latent class; RPL = random-parameters logit.

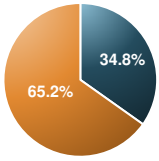
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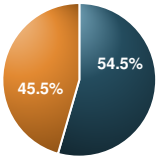
The Sample: Demographic Characteristics

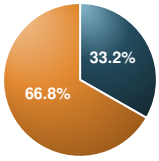
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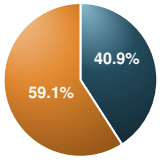
Gender











	OA Only (n = 201)	CLBP Only (n = 202)	OA and CLBP (n = 199)	Full Sample (n = 602)
Age (in years)				
Mean (SD)	**65.7** (8.7)	**60.1** (12.8)	**65.2** (9.5)	**63.7** (10.8)
Median	**66**	**63**	**66**	**66**
Min, max	**21, 87**	**21, 83**	**25, 90**	**21, 90**

Max = maximum; min = minimum; SD = standard deviation.

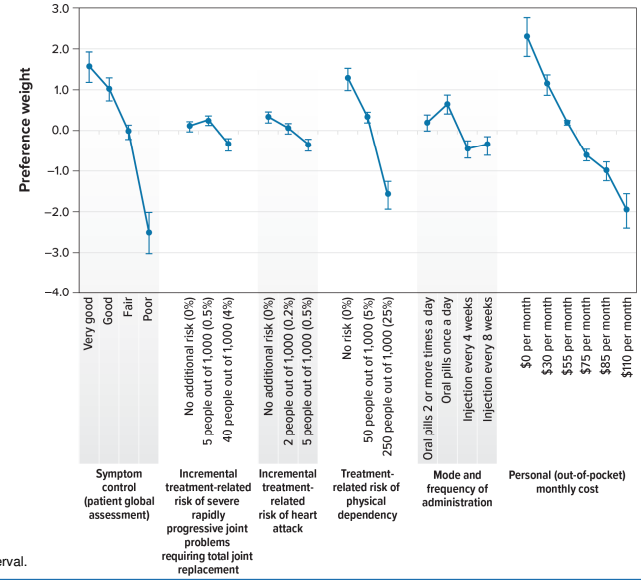
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Preference Analysis

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Preference Weights From Random-Parameters Logit Model (N = 602)



CI = confidence interval.

The results indicate that respondents prefer no symptoms ("Very good" symptom control as defined in the patient global assessment), lower adverse event risks, and lower monthly out-of-pocket costs

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Exploring Preference Heterogeneity

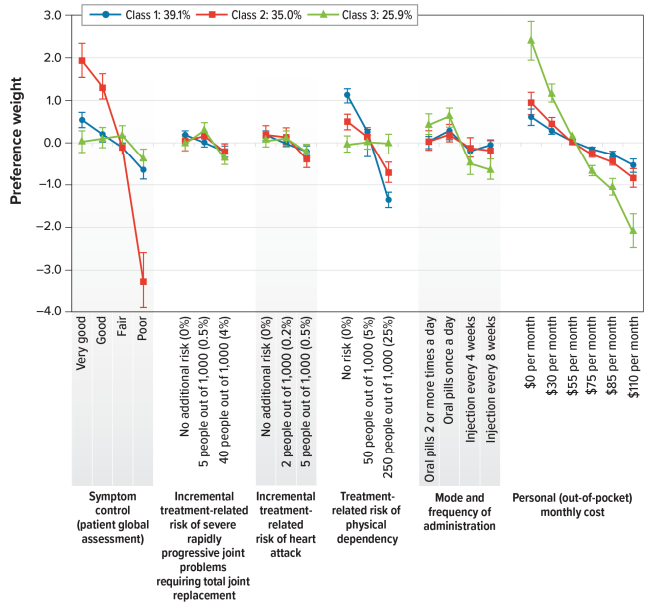
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- 10 subgroups explored using the random-parameters logit model
  - Only the subgroup pair based on incorrect answers to the comprehension questions presented systematic differences in preferences
    - The preference weights and conditional relative importance estimates for the 2 subgroups in this pair were similar and resulted in very similar WTP and MAR
- Latent class analysis
  - ➢ Based on the BIC and AIC criteria, a 3 classes model was considered optimal
    - 4 classes was another candidate; it was excluded because of other considerations on the classes and probability and the amount of information added by the additional class
  - ➢ The LC model and the RPL subgroup analysis uncovered different patterns of preference heterogeneity

AIC = Akaike information criteria; BIC = Bayesian information criteria; LC = latent class; MAR = Maximum acceptable risk; RPL = random-parameters logit; WTP = Willingness to pay.

Latent Class Analysis (N = 585)[a]

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- **Class 1 (blue, 39.1%); cautious of physical dependency:** strongly preferred low risk of physical dependence
- **Class 2 (red, 35.0%); efficacy focused:** strongly preferred better symptom control
- **Class 3 (green, 25.9%); avoid injection, averse to cost:** strongly averse to paying a personal (out-of-pocket) cost and strongly preferred oral pills (best if one, once a day) to injections

Note: the vertical bars surrounding each mean preference weight denote the 95% confidence interval (computed by the delta method).
[a] Seventeen respondents did not answer the questions used to model the membership probability function and were excluded from this latent class analysis.

Latent Class Analysis: Membership Probability Model (N = 585)[a]

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Covariate	Class 1 (Averse to dependency)		Class 2 (Focused on efficacy)	
	γ estimate	*P* value	γ estimate	*P* value
Constant	0.623	0.231	0.518	0.304
Respondents with concurrent OA and CLBP	**Reference**			
Respondents with OA only	0.452	0.174	–0.264	0.408
Respondents with CLBP only	0.123	0.704	–0.616	0.055
Respondents without opioid experience	**Reference**			
Respondents with opioid experience	–0.578	0.029	0.014	0.959
Age: younger than median age	**Reference**			
Age: median age or older	0.066	0.801	0.407	0.114
Respondents living with chronic pain for less than 5 years	**Reference**			
Respondents living with chronic pain for 5 years or more	–0.387	0.203	0.282	0.401
Respondents with moderate baseline pain (ranked 5-6)	**Reference**			
Respondents with severe baseline pain (ranked 7-10)	0.135	0.610	–0.036	0.893
Respondents who provided incorrect responses to fewer than three comprehension questions	**Reference**			
Respondents who provided incorrect responses to three or more comprehension questions	–0.210	0.422	–1.070	<0.001

Modeling class membership (γ) showed that respondents with ***opioid experience*** were *less likely to be in class 1 than in class 3 (avoid injection, averse to cost), and* respondents who **incorrectly answered 3 or more *comprehension questions*** were *less likely to be in class 2 than in class 3.*

Note: The membership probability model also included the 3 dimensions of the locus of control.
[a] Seventeen respondents did not answer the questions used to model the membership probability function and were excluded from this latent class analysis.

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Summary of Key Results

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- On average, the 2 most important clinical attributes over the full sample were improvements in symptom control and treatment-related risk of physical dependence
- Improving symptom control from poor to very good was approximately
  - 1.4 times as important as avoiding the risk of physical dependence
  - 6.1 times more important than avoiding the risk of heart attack
  - 9.1 times more important than avoiding the risk of rapidly progressive severe joint problems
- Preference heterogeneity was found to be important in the sample
  - 3 distinct segments of patients were identified in the LC Analysis
    - 1 class is focused on avoiding risk of physical dependency (39.1%)
    - 1 class is focused on symptoms control (35.0%)
    - 1 class is focused on cost and strongly prefers an oral pill once a day compared with injections (25.9%)

LC = latent class.

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Conclusions

- It is important to recognize that not everyone has the same preferences, and analysis should explore preference heterogeneity
- The preference heterogeneity found in these data suggests that not all patients will agree on treatment options for chronic pain
- The LC analysis indicated that there are 3 distinct preference segments in the sample
- The LC analysis results highlighted 2 patient characteristics explaining preference heterogeneity (opioid experience – not identified by the RPL subgroup analysis – and incorrect answers to comprehension questions)
- It is important for physicians to discuss options with patients and to try to find the treatment plan that is most consistent with the patient's preferences

LC = latent class.

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Thank You
Questions?



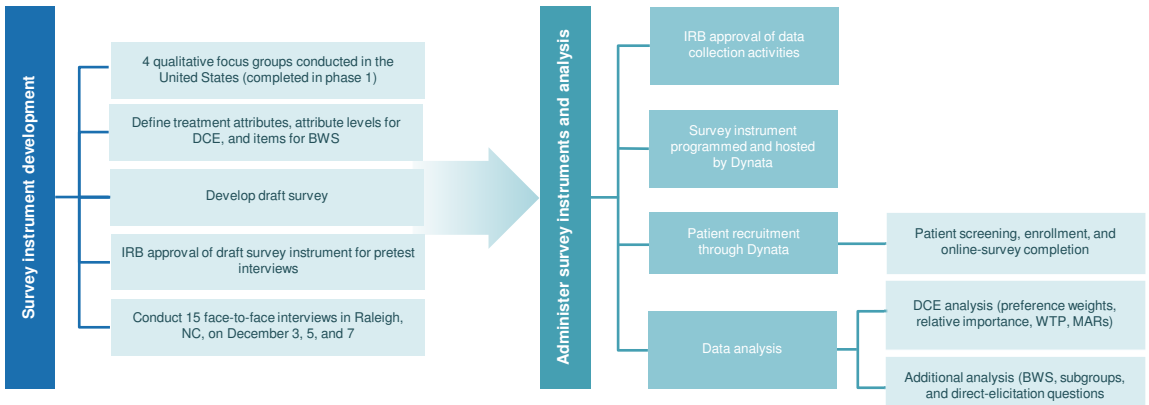
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Additional Slides: Study Plan and Survey Development

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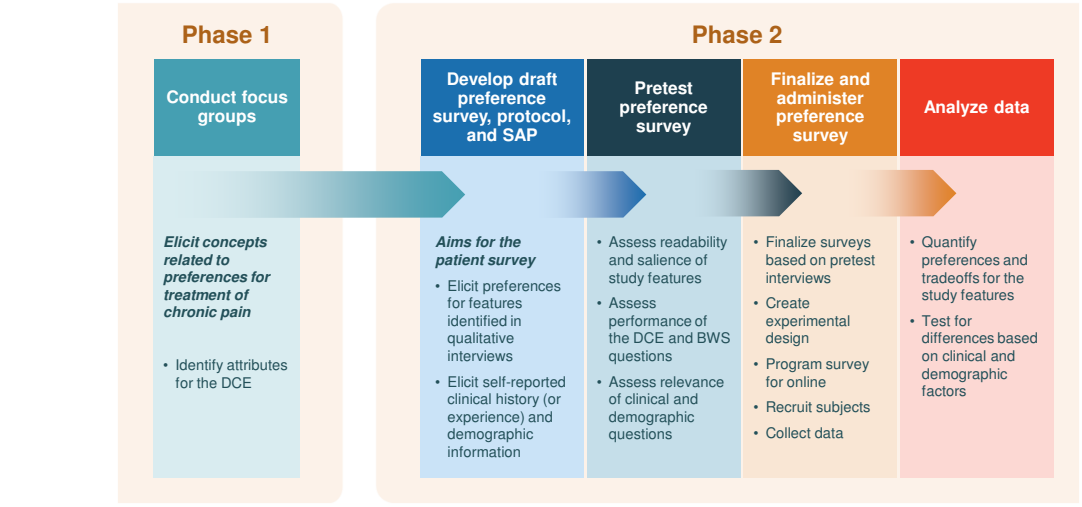
Study Plan



BWS = best-worst scaling; IRB = institutional review board; MAR = maximum acceptable risk; WTP = willingness to pay.

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Study Design



SAP = statistical analysis plan.
Note: Approval from the IRB was obtained for the study, including the recruitment material, the interview guide used in phase 1, the draft survey instrument used in pretest interviews, and the final survey instrument administered online.

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Focus Groups and Survey Instrument Development

Phase 1: qualitative interviews

- 4 focus groups, with a total of 30 US patients, were conducted with the following objectives
  - To identify the attributes of treatments for moderate-to-severe OA pain and CLBP that are important to patients
  - To gain insight into the extent to which different medication attributes may affect continuation on medication
  - To assess whether the drivers of medication satisfaction differ between patients with OA and those with CLBP
- 6 categories of treatment attributes were identified as being particularly important to patients
  - Efficacy, side effects (both narcotic and nonnarcotic), out-of-pocket cost or insurance coverage of the medication, risk of addiction/dependence, frequency of administration, and mode of administration

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Survey Instrument Pretesting

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- The survey instrument was first developed in the United States and pretested during 15 in-person interviews in Raleigh, NC
- Objectives of the pretest
  - Confirmed that the attributes included in the survey were of concern to respondents and that no important attributes were omitted
  - Assessed survey length, respondents' comprehension, and respondents' willingness to trade off among treatment attributes
  - Resulted in minor survey revisions to improve comprehension and readability