Academic perspective on patient preference research

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Overview

To present the results of a survey of Prader-Willi Syndrome (PWS) caregivers that sought to:

1. Identifying caregiver priorities for outcomes
2. Quantifying caregiver preferences for treating PWS
3. Assessing the potential impact of hyperphagia on the quality of life of the PWS patients

We will also discuss:

4. What is a valid preference study?
5. What types of study do patients want?
Acknowledgement

• The project is support by International Consortium to Advance Clinical Trials for Prader-Willi Syndrome
• We would like to thank the members of our executive team, Sophie Tsai, Theresa V. Strong and Nathalie Kayadjanian.
• We are grateful for the guidance of the PWS Community Advisory Board
• Special thanks to the Prader-Willi Syndrome Association and Foundation for Prader-Willi Research for assisting with recruitment, and especially to Susan Hedstrom, Jessica Bohonowycz, and Lauren Roth
## Demographics (n=450)

<table>
<thead>
<tr>
<th>Category</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caregiver age (mean, range)</td>
<td>49.0 (20-83)</td>
</tr>
<tr>
<td>Parents</td>
<td>96%</td>
</tr>
<tr>
<td>Females</td>
<td>84%</td>
</tr>
<tr>
<td>Caucasian</td>
<td>87%</td>
</tr>
<tr>
<td>Familiar with FDA</td>
<td>46%</td>
</tr>
<tr>
<td>Annual household income &gt;$100,000</td>
<td>52%</td>
</tr>
<tr>
<td>Private insurance</td>
<td>68%</td>
</tr>
<tr>
<td>Patient age (mean, range)</td>
<td>15.9 (4-54)</td>
</tr>
<tr>
<td>Diagnosed via genetics (DNA/blood)</td>
<td>97%</td>
</tr>
<tr>
<td>Genetic subtype</td>
<td></td>
</tr>
<tr>
<td>Deletion</td>
<td>50%</td>
</tr>
<tr>
<td>UPD</td>
<td>37%</td>
</tr>
</tbody>
</table>
I. Caregiver treatment priorities
Potential treatment benefits

• The set of potential treatment benefits was identified from prior research and discussions with the PWS community advisory board.
  • Improves **intellectual** function
  • Decreases **gastrointestinal** problems
  • Improves **hyperphagia** symptoms
  • Decreases **overweight** problems
  • Decreases problems with **anxiety**
  • Decreases **temper outbursts**
  • Decreases **skin picking** problems
BWS example task

What do you think is **most important and least important** when choosing a treatment for your family member with PWS?

<table>
<thead>
<tr>
<th>Most Important</th>
<th>Benefits</th>
<th>Least Important</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Improves intellectual function</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Improves hyperphagia symptoms</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Decreases skin picking problems</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Decreases problems with anxiety</td>
<td></td>
</tr>
</tbody>
</table>
Best-worst scores

- Improves hyperphagia symptoms
- Decreases problems with anxiety
- Decreases temper outbursts
- Improves intellectual function
- Decreases overweight problems
- Decreases skin picking problems
- Decreases gastrointestinal problems
Benefit-risk assessment

• There is a paucity of available treatment options directly targeting hyperphagia
• The FDA weighs the benefit of a drug (effectiveness) against the risk of a drug (side effects) when making regulatory approval decisions.
• Discrete-choice experiment (DCE) is a stated-preference method used by the FDA to quantify patient benefit-risk preferences.
• Benefits were described as 5 and 10 point differences on the hyperphagia questionnaire for clinical trials (HQ-CT) scale
# DCE example task

<table>
<thead>
<tr>
<th></th>
<th>Drug A</th>
<th>Drug B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improvement in Hyperphagia</td>
<td>5-point improvement</td>
<td>10-point improvement</td>
</tr>
<tr>
<td>Improvement in obesity (weight loss)</td>
<td><img src="image" alt="5% weight loss" /></td>
<td><img src="image" alt="10% weight loss" /></td>
</tr>
<tr>
<td>Increased risk of skin rash</td>
<td><img src="image" alt="No additional risk" /></td>
<td><img src="image" alt="20% higher risk" /></td>
</tr>
<tr>
<td>Risk of liver damage</td>
<td><img src="image" alt="10 in 1000 risk" /></td>
<td><img src="image" alt="1 in 1000 risk" /></td>
</tr>
<tr>
<td>Which is the better drug?</td>
<td><img src="image" alt="☐" /></td>
<td><img src="image" alt="☐" /></td>
</tr>
</tbody>
</table>
Hyperphagia - acceptable tradeoffs

Maximal acceptable risk for 5-point improvement in hyperphagia

- Weight increase (%): 9.87
- Risk of skin rash (%): 11.44
- Risk of liver damage (1 in 1000): 6.23
III. Quality of Life
Impact of hyperphagia on QoL

• We sought to quantify the impact of treating hyperphagia (relative to treating obesity) on quality of life by estimating quality-adjusted life years (QALYS).
• Visual Analogue Scale (VAS) and Time-trade-off (TTO) were used to estimate QALYS.
• Caregivers were asked to evaluate three different health states for an individual (Alex) who was 18 years old:
  o PWS without treatment
  o PWS with no obesity
  o PWS with no obesity nor hyperphagia
On a scale of 0 to 100, 0 being the worst health that you can imagine, 100 is the best health you can imagine, how would you rate Alex’s current health?

65
TTO example task

Would it be better for Alex to:

Live in the current condition until age 38 (that is an additional 20 years)

OR

Live FEWER years but be completely healthy without excessive appetite for the rest of Alex’s life? Alex should give up _____ years (write the years) to live completely healthy for all of them.
QALY results (VAS)

- PWS untreated: 0.38
- PWS without obesity: 0.57
- PWS without obesity / hyperphagia: 0.69

P < 0.001
QALY results (TTO)

- PWS untreated: 0.76
- PWS without obesity: 0.83
- PWS without obesity / hyperphagia: 0.9

P<0.001
IV. What is a valid preference study?
Acknowledgements

• This project is funded by the Patient-Centered Outcomes Research Institute Methods Program Award (ME-1303-5946) and by the Johns Hopkins Center of Excellence in Regulatory Science and Innovation and the Food and Drug Administration (U01FD004977).

• I would like to thank all study coinvestigators, including: Albert Wu, Daniel Longo, Lee Bone, Karen Bandeen-Roche, Jodi Segal, Tanjala Purnell, Ellen Janssen, Allison Oakes, Mo Zhou

• I am grateful for the guidance of the Diabetes Action Board (DAB) and Johns Hopkins Community Research Advisory Committee (C-RAC).
Dot voting process

Identify

• In small groups:
  • Discuss important characteristics of preference studies
  • Create a list of the five most important characteristics
  • Present list to large group

Desirable

• Individually:
  • Take 12 red dots
  • Consider all study characteristics identified by all groups
  • Allocate dots to the most desirable study characteristics

Actionable

• Individually:
  • Take 12 green dots
  • Consider all study characteristics identified by all groups
  • Allocate dots to the most actionable study characteristics
Desirable and Actionable

![Bar chart showing dot voting scores for various criteria: Respondents understanding, Stakeholder relevance, Appropriate research question, External validity, Diverse samples, Transparency of methods, Internal validity, Patient/Population centered. The x-axis represents the criteria, and the y-axis represents the dot voting score. The bars are color-coded with blue for desirable and red for actionable.](image-url)
Desirable and actionable combined

[Bar chart showing dot voting scores for various factors: Respondents understanding, Appropriate research question, Diverse samples, Transparency of methods, Stakeholder centeredness, Stakeholder relevance, Internal validity, External validity]

Dot voting score

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V. What types of study do patients want?
## Sample DCE task

A local hospital is conducting a study to learn about the preferences of patients. Choose the study that you think is better.

<table>
<thead>
<tr>
<th>Attributes</th>
<th>Study A</th>
<th>Study B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Validity</td>
<td>High Validity (★★★★☆)</td>
<td>Low Validity (★★☆☆☆)</td>
</tr>
<tr>
<td>Relevance</td>
<td>Low Relevance (★★☆☆☆)</td>
<td>High Relevance (★★★★☆)</td>
</tr>
<tr>
<td>Bias</td>
<td>Medium Bias (★★★★☆)</td>
<td>Medium Bias (★★★★☆)</td>
</tr>
<tr>
<td>Burden</td>
<td>Low Burden (★★★★☆)</td>
<td>High Burden (★★☆☆☆)</td>
</tr>
<tr>
<td>Time</td>
<td>45 minutes</td>
<td>30 minutes</td>
</tr>
<tr>
<td>Payment</td>
<td>$50</td>
<td>$25</td>
</tr>
<tr>
<td>What study do you think is better?</td>
<td>□</td>
<td>□</td>
</tr>
</tbody>
</table>
Latent class results

- Increase in validity (1 step)
- Increase in relevance (1 step)
- Decrease in bias (1 step)
- Decrease in burden (1 step)
- Decrease in time (15 minutes)
- Increase in payment ($25)

Preference estimate

Class1 - convenience focused (24%)
Class2 - quality focused (76%)
DCE completion time, Latent Class

Mean class 1 = 6.7 min
Mean class 2 = 9.0 min
P = <0.001
Motivating factors, Latent Class

Considered the motivations in their choices:

- Completion rate
- Decision making
- Respondent burden
- Research results*
- Patient benefit
- Society’s wellbeing*
- Scientific publication
- Community centered

Class1 - convenience focused (24%)
Class2 - quality focused (76%)
*significant at 0.01 level
DCE evaluation, Latent Class

Class 1 - convenience focused (24%)  
Class 2 - quality focused (76%)  

* significant at 0.01 level
Protecting Health, Saving Lives—
*Millions at a Time*