**Development of a Pediatric Version of the Study Medication Withdrawal Questionnaire**

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**Introduction**

- Discontinuation of common medications used to treat attention-deficit/hyperactivity disorder (ADHD) may be associated with withdrawal symptoms.
- As withdrawal symptoms may negatively impact patients, it is important to develop a questionnaire to confirm the clinical efficacy of ADHD medications.

**The Study Medication Withdrawal Questionnaire (SMWQ) was developed for adults** for assessment of withdrawal symptoms in response to discontinuation of medication, but it has been suggested that different questions may be needed for pediatric use, as non-pediatric-specific adaptation exists.

**Objective**

- To develop a new pediatric questionnaire based on the SMWQ for assessment of withdrawal symptoms in children with ADHD

**Methods**

**Development of Initial Questionnaires**

- Literature searches were conducted for concepts related to medication withdrawal with ADHD, and results were validated using a 2-step process.
  1. Literature review to define concepts for the SMWQ and serve as a guideline for subsequent validation questions.
  2. Open-ended questions designed to understand participants’ experiences and expectations regarding medication withdrawal.

**Concepts for Mediation Withdrawal with ADHD**

- ADHD withdrawal symptoms may include, but not be limited to:
  - Emotional symptoms
    - Anhedonia
    - Sad mood
  - Sleep symptoms
    - Hypersomnia
  - Psychomotor symptoms
    - Hyperphagia
  - Cognitive symptoms
    - Difficulties concentrating
  - Irritability
  - Medication craving

**Questionnaire Finalization**

- The questionnaire was refined iteratively, and final version is a fit-for-purpose questionnaire with appropriate content validity designed to explore the understanding and answering of the word “craving.”

**Results**

**Table 1: Participant Demographics and Characteristics**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Parents of Children With ADHD</th>
<th>Children With ADHD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (range), years</td>
<td>47 (4-7)</td>
<td>12 (8-16)</td>
</tr>
<tr>
<td>ADHD subtype, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Predominantly inattentive</td>
<td>19</td>
<td>20</td>
</tr>
<tr>
<td>Predominantly hyperactive</td>
<td>19</td>
<td>10</td>
</tr>
<tr>
<td>Combined</td>
<td>19</td>
<td>10</td>
</tr>
<tr>
<td>Other</td>
<td>19</td>
<td>0</td>
</tr>
<tr>
<td>Gender identity, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>40</td>
<td>20</td>
</tr>
<tr>
<td>Female</td>
<td>7</td>
<td>11</td>
</tr>
<tr>
<td>Trans-male/nonbinary</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>ethnicity, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic/ non-Latino</td>
<td>19</td>
<td>11</td>
</tr>
<tr>
<td>Hispanic/Latino</td>
<td>31</td>
<td>10</td>
</tr>
<tr>
<td>Preferred to not answer</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>9</td>
<td>2</td>
</tr>
<tr>
<td>Black</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>Asian</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Current education level, n (%)</td>
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<td></td>
</tr>
<tr>
<td>Preschool</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Grade K-5</td>
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<td>11</td>
</tr>
<tr>
<td>Grades 6-9</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Grades 10-12</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Living situation, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Both parents</td>
<td>50</td>
<td>13</td>
</tr>
<tr>
<td>Both parents, 1 household</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>Both parents, 2 households</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Other family members</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**Figure 1: Overview of Study Methods**

- Literature review of the SMWQ
- Development of initial draft questionnaires based on concepts from literature review and the original SMWQ
- Open-ended interviews
- Data analysis and revision of questionnaires
- Cognitive debriefing interviews

**Concept Elicitation**

- Concepts elicited regarding holiday medication experiences included:
  - Felt more focused, feeling alert, on course, wanting to eat
  - Felt more energetic, positive, feeling excited (telling forgetful), feeling hyperactive (and related behavioral impacts), feeling overwhelmed, losing track of time, having a headache, feeling tired, and having a stomachache

**Response Options**

- “Have not felt that way” to “Tell that way all the time”

**Questionnaire Psychometrics**

- The SMWQ-PO and SMWQ-P have been operationalized in 2 ongoing phase 3 studies in pediatric ADHD
- Data from 233 participants on the SMWQ-PO in these ongoing clinical trials achieved an internal consistency of $\alpha = 0.76$, which was slightly below the target of $\alpha = 0.80$.
- Exploration of item-level reliability revealed that Item 1 (medication craving) was poorly related to other item (correct item total correlation $= 0.21$).
- Removing Item 1 resulted in an internal consistency of $\alpha = 0.79$ and good item-total standardized correlations.
- Confirmatory factor analysis was conducted to confirm the validity of using items 2 through 11 as a total score, which item 1 loaded separately.
- The model obtained strong fit (comparative fit index $= 0.95$; Tucker-Lewis index $= 0.93$; root mean square residual approximation $= 0.053$; standardized root mean square residual $= 0.047$).

**Discussion**

**Conclusions**

- The new SMWQ-PO and SMWQ-P are fit-for-purpose questionnaires with appropriate content validity designed to assess symptoms of withdrawal in pediatric ADHD.
- Based on the current results, the SMWQ-PO has a 2-items summary score (Item 2 and a mediation craving score (Item 1)). Additional analyses are planned to further validate this instrument.
- Evaluation of the psychometric properties of the SMWQ-PO is ongoing.

**References**


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**Limitations**

- The study is limited by a small sample size for each age group
- Participants were not in a withdrawal state during the interviews.
- Although drug holiday was used as a proxy for withdrawal, there may be concepts that were not elicited.
- Further research is necessary for psychometric validation and scoring development.

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- Andrew Palsgrove, Dorothee Oberdahn, Mark J. Atkinson, Jasen C. Cole, Mani Srisurapanont

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**Disclosures**

- Andrew Palsgrove, Dorothee Oberdahn, Mark J. Atkinson, and Caroline Ward are employees of Otsuka Pharmaceutical Development & Commercialization, Inc.
- Caroline Ward is a consultant for Otsuka.
- Andrew Palsgrove is an employee of Otsuka Pharmaceutical Development & Commercialization, Inc.
- Jaron C. Cole serves as a consultant for Otsuka.
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