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ORIGINAL RESEARCH

Adult Patient Preferences for Long-Acting ADHD Treatments: A Discrete Choice Experiment

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M Janelle Cambron-Mellott[1]
Jaromir Mikl[2]
Joana E Matos[1]
Jennifer G Erensen[2]
Kathleen Beusterien[1]
Marc J Cataldo[2]
Bernadette Hallissey[1]
Gregory W Mattingly[3–5]

[1]Kantar Health, New York, NY, USA; [2]Purdue Pharma L.P./Adlon Therapeutics, L.P., Stamford, CT, USA; [3]Department of Psychiatry, Washington University School of Medicine, St. Louis, MO, USA; [4]Midwest Research Group, St. Charles, MO, USA; [5]St. Charles Psychiatric Associates, St. Charles, MO, USA

Background and Objective: Treatment for attention deficit hyperactivity disorder (ADHD) requires a multifaceted approach including psychosocial interventions and pharmacological treatment. This study evaluates preferences for specific attributes associated with different long-acting stimulant treatment among US adults with ADHD.

Methods: Patients completed an online, cross-sectional survey, incorporating a discrete choice experiment to assess preferences for attributes.

Results: Analyses included 200 adults with ADHD (mean age 33.0 years; 60% self-reporting moderate severity); the mean (SD) Adult ADHD Self-Report Scale-v1.1 score was 45.9 (12.4). Overall, patients valued speed of onset most and risk of rebound least. Three population groups with distinct preferences were identified: side effect-driven (n=69, 35%), quick onset-driven (n=47, 24%) and quick onset and long duration-driven (n=84, 42%).

Conclusion: This study shows differences in how adults with ADHD value and assess benefit-risk trade-offs when considering the desired attributes of stimulant treatments, highlighting the importance of patient-physician shared decision-making to optimize the desired benefits of individualized treatment.

Keywords: attention deficit hyperactivity disorder, choice behavior, CNS stimulants, discrete choice experiment, patient preference

Introduction

Attention deficit hyperactivity disorder (ADHD) is a common neurodevelopmental disorder characterized by symptoms of inattention and/or hyperactivity/impulsivity such as an inability to focus, forgetfulness, and excessive fidgeting or restlessness.[1] Fifty-seven percent of children with ADHD continue to meet full diagnostic criteria for ADHD as an adult according to the World Health Organization's World Mental Health report and the prevalence of ADHD is estimated to be 5.2% among adults in the United States (US).[2]

Clinical presentation of ADHD often changes through adolescence into adulthood. Hyperactivity may be expressed as extreme restlessness, inability to relax or wearing others out with their activity. Other symptoms such as inattention may manifest as disorganization, procrastination, boredom and sensitivity to stress.[3] Untreated adult ADHD is associated with various clinical and sociological outcomes such as impaired quality of life, elevated morbidity and mortality, impaired relationships, reduced employment, vulnerability to depression and anxiety, and/or suicide.[4]

Stimulant medication, including methylphenidate hydrochloride, dextroamphetamine, lisdexamfetamine, and mixed amphetamine salts (dextro- and levoamphetamine), are recommended as first-line medication treatment for adults with

Correspondence: M Janelle Cambron-Mellott
Kantar Health, 3 World Trade Center, 175 Greenwich Street, 35th Floor, New York, NY, 10007, USA
Tel +1 212 706 3961
Email janelle.cambron-mellott@kantar.com

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ADHD.[5–7] Longer-acting stimulants are recommended by most consensus guidelines for adults with ADHD.[8,9] Research suggests that patients who use longer-acting stimulants tend to be more compliant, miss fewer doses, and are adherent to their medication longer than those using short-acting stimulants.[10,11]

Shared decision-making and partnership between physicians and patients is recommended to individualize both psychological and pharmacological ADHD treatment. This is particularly critical given the plethora of stimulant products available for ADHD treatment in the US. While both methylphenidate and amphetamine-based products are highly effective in improving ADHD symptoms, individual formulations differ in their onset and duration of action.[10–13] Selection of treatment is often based on preferences of patients, who must weigh the desired benefits and risks of each medication option with their health-care provider.[14] Therefore, it is critical to understand patients' preferences for ADHD treatment, identifying the features that may be of most value to patients and the tradeoffs they are willing to make among the attributes. For example, whether patients are willing to accept an increased risk of a bothersome side effect in exchange for an improvement in efficacy (eg, speed of onset).

The majority of prior patient preference research has focused on the preferences of parents of children with ADHD. Most studies only examined a single attribute versus multiple aspects related to various stimulant preparations, and they often lacked rigorous methods for assessing preference.[15–25] Largely missing from these studies is the voice of the adult patient with ADHD[17] The primary aim of this study was to evaluate preferences for specific features associated with long-acting stimulant treatment among adult patients with ADHD in the US.

Methods

This was a multi-phase study, conducted in consistency with the recommendations of the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Good Research Practices for Conjoint Analysis Task Force,[26,27] and involved three phases: 1) Literature review and qualitative research to identify key attributes of stimulant treatment that are important to adult patients and physicians for incorporation into the preference survey; 2) cognitive interviews among adults with ADHD to confirm comprehension of the final survey content; and 3) fielding of the resulting online, cross-sectional, quantitative survey, which incorporated a discrete choice experiment (DCE) to elicit the preferences of adults with ADHD for features (attributes) of long-acting ADHD treatments.[28] A DCE enables assessment of benefit-risk trade-offs that respondents are willing to make among treatment attributes.

Participants were recruited in the US via a patient panel maintained by Kantar Profiles or through panel partners who are fellow members of the Trust Alliance. To qualify, patients had to be at least 18 years old and self-report a physician's diagnosis of ADHD. As this study was designed to evaluate preferences for long-acting stimulant treatment, only patients who need control of symptoms throughout the day were eligible to participate. This criterion was determined by respondents' current medication; patients were required to be currently treated with ≥1 dose of a long-acting or ≥2 doses of a short-acting ADHD stimulant medication, or a combination of both a long-acting and a short-acting ADHD stimulant medication, for one month or longer. The survey was available for completion from June 14 to July 9, 2019. All patients provided their informed consent electronically. This study received exemption from ethics review by Pearl IRB (Indianapolis, IN; IRB Study Number: 19-KANT-183), as the data from the interview and survey procedures were not linked with personally identifying information, and this study was conducted in accordance with the Declaration of Helsinki.

Literature Review and Qualitative Research

This process involved an initial review of the literature, which included review of product labels/full prescribing information, grey literature search and peer-reviewed publications, followed by a qualitative research phase comprised of interviews with 10 patients and 3 physicians (2 psychiatrists and 1 primary care physician). The literature review and interviews helped identify the attributes and levels included in the DCE exercise. Specifically, the attributes were developed to meet the following criteria: 1) reflect attributes that are influential in treatment decision-making, 2) capture the full range of attribute performance (maximum and minimum levels) across competitive treatments, 3) be consistent with literature and medical guideline specifications, and 4) be objective and measurable, so that it is clear to the respondents what trade-offs they are being asked to consider. The interviews began with open-ended questions to capture patient experience with ADHD, reasons for treatments used, important aspects of treatment from the perspective of each stakeholder, followed by more targeted

probing to explore specific treatment attributes and levels. Finally, cognitive interviews were conducted with 8 patients to obtain feedback on the draft survey and ensure it was clear and interpreted as expected.

Survey Content

The survey incorporated a DCE exercise during which they were asked to evaluate a series of 10 choice tasks, each comparing two hypothetical ADHD treatments, and indicate which they would prefer. These hypothetical treatment profiles consisted of combinations of attributes, each at a particular intensity or severity (called "levels"). Six attributes were included: speed of onset, duration of effect, risk of insomnia/sleep disturbance, risk of headache, risk of nervousness/anxiety/irritability, risk of rebound effect. The attributes had three to four levels (eg, risk level, etc.) each. Figure 1 shows an example DCE choice task. By asking patients to choose between different combinations of attributes and levels, the benefit-risk trade-off can be evaluated. All respondents answered a different set of choice tasks. The combinations of levels shown across treatment profiles in the DCE were based on a balanced design with minimal overlap.[27]

Attribute levels were derived from data extracted from the stimulant medications indicated for the treatment of adult ADHD in the US.[29–57]

The survey also collected sociodemographic data, including information on occupation, work burden, general health information, and clinical and ADHD treatment history data. The Adult Self-Report Scale (ASRS-v1.1) was incorporated to assess the severity of patients' ADHD.[58,59] Each of the 18 items is rated on a scale of 0 (never) to 4 (very often) and then summed to compute ADHD symptom severity [range: 0 to 72]. Occupation was identified by having patients who indicated they were employed (full-time, part-time, or self-employed) select the option that best described their primary occupation from a list of the 32 major groups of the 2018 Standard Occupational Classification System.[60] Work burden was computed by summing the number of work stressors selected from a list of potential work stressors for each respondent; severity of work burden was based on approximate tertiles of this sum of work stressors.

To help familiarize respondents to the attributes and levels used in the DCE, they first rated each attribute level on a 5-point scale where 1 = "Very Bad" and 5 = "Very Good". These questions were also used to identify those who may have been inattentive in their responses to increase the validity of the results.[61] This was done by flagging respondents with two or more "illogical" responses (ie, rating a more favorable attribute level lower than a less

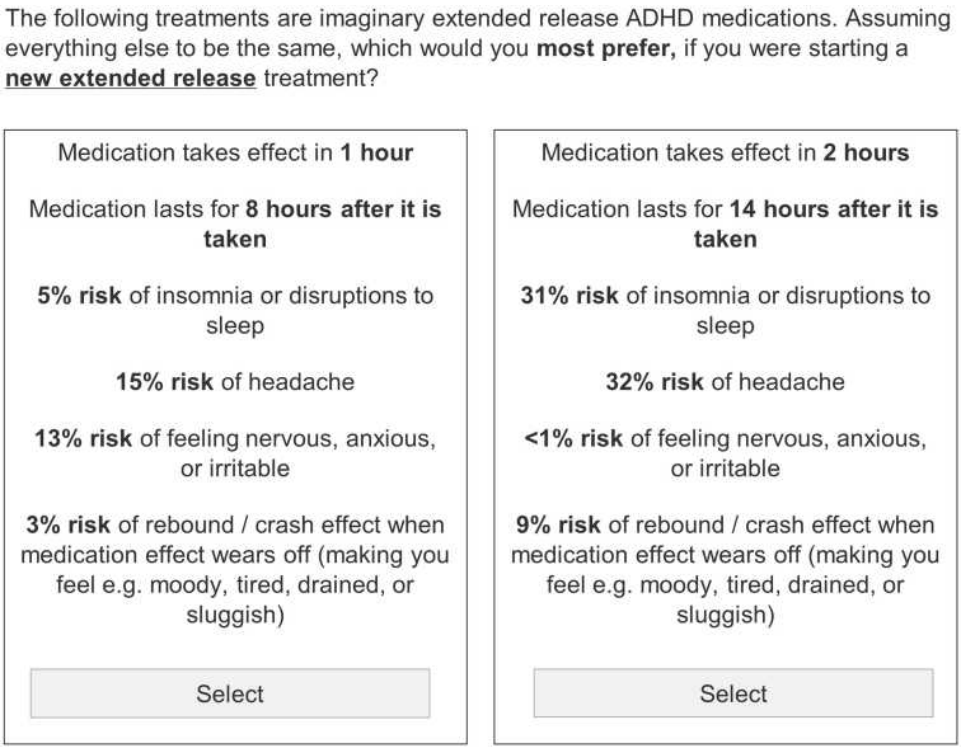

Figure 1 Example of a DCE choice task seen by respondents.

favorable attribute level of the same attribute; the duration of effect attribute was excluded from this evaluation).

Statistical Analysis

Descriptive statistics were calculated for all study measures, including means, standard deviations, quartiles, and minimums and maximums for continuous and count variables, and frequency and percentage for categorical variables. Analyses were conducted per the ISPOR Good Research Practices for Conjoint Analysis Task Force recommendations;[62] Specifically, a hierarchical Bayesian model (HB) was fitted to the choice data from the DCE to estimate preference weights for each attribute and attribute level. Mean preference weights were calculated as point estimates of the HB model coefficients, as well as standard errors and 95% confidence intervals. The magnitude of change between levels of one attribute was compared to the magnitude of change between levels of a different attribute. The conditional relative importance of each attribute was calculated at the respondent level by dividing the range of each attribute (utility of most favorable level minus utility of least favorable level) by the sum of the ranges of all attributes and multiplying by 100.

A latent class analysis of the HB preference weights for the DCE data was performed to identify potential groups of people that differed in their distributions of preferences using multinomial logistic regression. Identification of the optimal latent class solution was based on Bayesian Information Criteria[63] and evaluation of the group preferences. Each group identified in the latent class analysis was further characterized by demographic, clinical, and treatment characteristics to examine potential signals between the groups. One-way analysis of variance was utilized to examine whether attribute-level preference weights and relative importance estimates differed by latent class group.

Data were analyzed using SPSS Version 23 for descriptive statistics and Sawtooth Software Lighthouse Studio 2018 Version 6.9.1 for the DCE analyses.

Results

A total of 214 adults with ADHD completed the survey. The preference weights were examined with and without 14 respondents who were flagged for quality control issues (n=2 had ≥2 illogical responses to the rating items, n=12 completed the DCE portion of the survey in less than 70 seconds). Given the findings, 14 respondents were removed from further analysis, resulting in a final sample size of 200. The mean (*SD*) age of respondents was 33.0 (9.4), and the mean (*SD*) length since diagnosis was 12.0 years (9.1). The majority were female (78.5%), more than half were Caucasian (57.5%), and 43.5% were in a committed relationship or married. In addition, nearly half had at least a college degree or higher (48.5%). Comorbidities with ADHD were high, with 78.5% of patients reporting having been diagnosed with an anxiety or mood disorder. Major depressive disorder diagnosis and insomnia or other sleep disturbance diagnoses were reported at 34.5% and 31.0%, respectively (Table 1).

The proportion of patients taking one dose a day of an extended-release (ER) oral medication (38.5%) was similar to the proportion of those taking ≥2 doses a day of an immediate-release (IR) oral medication (39.5%). Amphetamine use was most common both among the patients using an ER medication (84.3%) and among those using an IR medication (81.9%). The majority of patients (76.0%) reported they took their medication daily (Table 1). More than half (58.0%) of patients had been on their current treatment for more than 4 years, indicating stability of treatment plans among these patients. Patients perceived the effect of their ER medication to last a mean (SD) of 9.1 hours (3.1) and the effect of their IR medication to last a mean (SD) of 5.5 hours (2.6). Patients reported needing the effects of their medication to last a mean (SD) of 11.9 hours (3.6).

Almost all patients (92.5%) self-reported their ADHD as moderate or severe in severity; the mean (*SD*) ASRS-v1.1 symptom severity score across all patients was 45.9 (12.4; range: 7–72) (Table 1). Patients who described their ADHD as "mild" had a mean (*SD*) ASRS-v1.1 score of 38.7 (12.6), while patients who described their ADHD as "moderate" or "severe" had mean (*SD*) ASRS-v1.1 scores of 43.7 (11.9) and 51.5 (11.2), respectively.

On average, employed patients with ADHD (n=150) reported experiencing 3.1 (*SD* = 2.1) different types of work stressors, with "high stress" being the most common and reported by 59.3% of respondents, followed by "little time for meals" (44.0%) and "very long work hours" (41.3%). Severity of work burden was reported as high (≥4 stressors) by 36.0%, moderate (2–3 stressors) by 39.3% and low (0–1 stressors) by 24.7% of the employed respondents (Table 2). Descriptive statistics for employment status and occupation are shown in Supplemental Table 1.

Table 1 Patient Characteristics: Total and by Latent Class Group

Characteristic	Total (n=200)	Side Effects (n=69)	Quick Onset (n=47)	Quick Onset and Long Duration (n=84)
Age (years), mean (SD)	33.0 (9.4)	33.2 (11.1)	33.8 (9.0)	32.4 (8.1)
Gender, female, n (%)	157 (78.5)	53 (76.8)	36 (76.6)	68 (81.0)
Marital status, n (%)				
Single/separated/divorced/widowed	113 (56.5)	47 (68.1)	21 (44.7)	45 (53.6)
Committed relationship/married	87 (43.5)	22 (31.9)	26 (55.3)	39 (46.4)
Education, n (%)				
No college degree	103 (51.5)	40 (58.0)	22 (46.8)	41 (48.8)
College degree or higher	97 (48.5)	29 (42.0)	25 (53.2)	43 (51.2)
Race/ethnicity, n (%)				
Hispanic/Latino/a	70 (35.0)	19 (27.5)	13 (27.7)	38 (45.2)
Caucasian/White	115 (57.5)	43 (62.3)	31 (66.0)	41 (48.8)
African-American/Black	11 (5.5)	6 (8.7)	2 (4.3)	3 (3.6)
Other	13 (6.5)	3 (4.3)	3 (6.4)	7 (8.3)
Employed, yes, n (%)	150 (75.0)	46 (66.7)	37 (78.7)	67 (79.8)
Has children in household, yes, n (%)	100 (50.0)	29 (42.0)	26 (55.3)	45 (53.6)
Diagnosed comorbidities ≥ 10%, n (%)				
Anxiety/mood disorder	157 (78.5)	51 (73.9)	42 (89.4)	64 (76.2)
Major depressive disorder	69 (34.5)	22 (31.9)	15 (31.9)	32 (38.1)
Insomnia/sleep difficulty	62 (31.0)	20 (29.0)	12 (25.5)	30 (35.7)
Bipolar disorder	47 (23.5)	17 (24.6)	13 (27.7)	17 (20.2)
Obsessive compulsive disorder	32 (16.0)	12 (17.4)	10 (21.3)	10 (11.9)
Substance abuse disorder	25 (12.5)	6 (8.7)	10 (21.3)	9 (10.7)
Restless legs syndrome	23 (11.5)	7 (10.1)	5 (10.6)	11 (13.1)
Time since diagnosis (years), mean (SD)	12.0 (9.1)	11.1 (8.0)	13.8 (8.8)	11.8 (10.0)
ASRS-v1.1 symptom severity, mean (SD)	45.9 (12.4)	44.5 (10.6)	44.8 (12.6)	47.6 (13.5)
Severity of ADHD – self reported, n (%)				
Mild	15 (7.5)	7 (10.1)	5 (10.6)	3 (3.6)
Moderate	120 (60.0)	42 (60.9)	26 (55.3)	52 (61.9)
Severe	65 (32.5)	20 (29.0)	16 (34.0)	29 (34.5)
Current medication type, n (%)				
≥2 IR doses	79 (39.5)	29 (42.0)	22 (46.8)	28 (33.3)
1 ER dose	77 (38.5)	23 (33.3)	16 (34.0)	38 (45.2)
1 ER dose and ≥1 IR oral dose	26 (13.0)	11 (15.9)	5 (10.6)	10 (11.9)
≥2 ER oral doses	17 (8.5)	6 (8.7)	4 (8.5)	7 (8.3)
ER patch	1 (0.5)	0 (0.0)	0 (0.0)	1 (1.2)
Current ER prescription medication[a], n (%)				
Amphetamines	102 (84.3)	32 (80.0)	20 (80.0)	50 (89.3)
Methylphenidate	20 (16.5)	9 (22.5)	5 (20.0)	6 (10.7)
Non-stimulants	3 (2.5)	1 (2.5)	0 (0.0)	2 (3.6)
Current IR prescription medication[b], n (%)				
Amphetamines	86 (81.9)	31 (77.5)	25 (92.6)	30 (78.9)
Methylphenidate	21 (20.0)	10 (25.0)	4 (14.8)	7 (18.4)
Other IR	1 (1.0)	0 (0.0)	0 (0.0)	1 (2.6)

(*Continued*)

Table 1 (Continued).

Characteristic	Total (n=200)	Side Effects (n=69)	Quick Onset (n=47)	Quick Onset and Long Duration (n=84)
Perceived duration of effect (hours), mean (SD)				
Current ER medication[a]	9.1 (3.1)	9.3 (3.2)	8.5 (2.8)	9.3 (3.1)
Current IR medication[b]	5.5 (2.6)	5.5 (2.4)	6.5 (3.3)	4.7 (1.9)
Medication taken daily, yes, n (%)	152 (76.0)	46 (66.7)	42 (89.4)	64 (76.2)
Number of ER medications tried, mean (SD)	1.6 (1.1)	1.4 (1.0)	2.0 (1.3)	1.5 (1.0)

Notes: [a]Among patients on ER medication, N=121. [b]Among patients on IR medication, N=105.
Abbreviations: ASRS, Adult ADHD Self-Report Scale; ER, extended release; IR, immediate release; SD, standard deviation.

Table 2 Work Stressors and Work Burden Among Employed Patients (n=150): Total and by Latent Class Group

Characteristic	Total (n=150)	Side Effects (n=46)	Quick Onset (n=37)	Quick Onset and Long Duration (n=67)
Work stressors, n (%)				
High stress	89 (59.3)	29 (63.0)	18 (48.6)	42 (62.7)
Little time for meals	66 (44.0)	20 (43.5)	14 (37.8)	32 (47.8)
Very long work hours	62 (41.3)	17 (37.0)	15 (40.5)	30 (44.8)
Little rest during shifts	56 (37.3)	20 (43.5)	8 (21.6)	28 (41.8)
Work schedule is irregular/unpredictable	41 (27.3)	14 (30.4)	7 (18.9)	20 (29.9)
Many work days in a row without days off	38 (25.3)	14 (30.4)	8 (21.6)	16 (23.9)
Night work	34 (22.7)	6 (13.0)	7 (18.9)	21 (31.3)
Little time off between shifts	22 (14.7)	6 (13.0)	5 (13.5)	11 (16.4)
Frequent driving	21 (14.0)	5 (10.9)	7 (18.9)	9 (13.4)
Operate machinery	12 (8.0)	4 (8.7)	4 (10.8)	4 (6.0)
Frequent travel	10 (6.7)	3 (6.5)	3 (8.1)	4 (6.0)
Frequent business dinners or entertaining clients	6 (4.0)	2 (4.3)	2 (5.4)	2 (3.0)
Restrictions against taking certain prescription medications	3 (2.0)	2 (4.3)	0 (0.0)	1 (1.5)
Work burden, count (number of stressors), mean (SD)	3.1 (2.1)	3.1 (2.0)	2.6 (1.9)	3.3 (2.3)
Severity of work burden, n (%)				
Low (0–1 stressors)	37 (24.7)	9 (19.6)	12 (32.4)	16 (23.9)
Moderate (2–3 stressors)	59 (39.3)	23 (50.0)	15 (40.5)	21 (31.3)
High (≥4 stressors)	54 (36.0)	14 (30.4)	10 (27.0)	30 (44.8)

Notes: The work burden variable was computed by summing each work stressor a respondent selected. Severity of work burden was based on approximate tertiles.
Abbreviation: SD, standard deviation.

DCE Results

The magnitude of the differences in preference weights within attribute levels indicates that patients are willing to make trade-offs between speed of onset, duration, and risk of side effects. Larger changes in preference weights across attribute levels indicate more importance to the patient, and smaller changes indicate that such changes are not as important to the patient (the absolute value of the differences is what is relevant). For example, patients are willing to accept an increase in the risk of insomnia from 18% to 31% (respective change in preference weight: |-0.07-[−1.27]|=1.19) in exchange for reducing speed of onset from 4 to 2 hours, where the change in preference weights is larger (|-3.32-[0.17]|=3.49). In another example, patients would be willing to accept an increased risk of headache from <1% to 15% (|1.57–0.32|=1.25) in

Table 3 Attribute-Level Preference Weights: Total and by Latent Class Group

		Total (n=200)	Side Effects (n=69)	Quick Onset (n=47)	Quick Onset and Long Duration (n=84)
Attribute	**Level**	**M (95% CI)**	**M (95% CI)**	**M (95% CI)**	**M (95% CI)**
Speed of onset - "Medication takes effect in __"	4 hours	−3.32 (−3.55–3.09)	−1.86 (−2.11–1.60)	−4.65 (−5.05–4.26)	−3.78 (−4.04–3.52)
	2 hours	0.17 (0.10–0.23)	−0.03 (−0.13–0.06)	0.16 (−0.01–0.33)	0.34 (0.25–0.43)
	1.5 hours	1.25 (1.18–1.32)	0.91 (0.80–1.02)	1.51 (1.37–1.64)	1.38 (1.29–1.47)
	1 hour	1.90 (1.73–2.08)	0.98 (0.75–1.21)	2.99 (2.65–3.32)	2.06 (1.85–2.26)
Duration of effect - "Medication lasts for __ after it is taken"	8 hours	−1.28 (−1.48–1.07)	−0.62 (−0.88–0.35)	−0.15 (−0.52–0.22)	−2.45 (−2.66–2.24)
	12 hours	0.21 (0.15–0.27)	0.34 (0.24–0.45)	0.04 (−0.09–0.17)	0.20 (0.11–0.28)
	14 hours	0.64 (0.56–0.72)	0.33 (0.21–0.44)	0.50 (0.33–0.66)	0.98 (0.88–1.08)
	16 hours	0.42 (0.27–0.58)	−0.05 (−0.26–0.16)	−0.39 (−0.68–0.10)	1.27 (1.10–1.44)
Insomnia/sleep disturbance - "__ risk of insomnia or disruptions to sleep"	31%	−1.27 (−1.37–1.16)	−1.64 (−1.80–1.47)	−0.54 (−0.70–0.38)	−1.37 (−1.52–1.23)
	18%	−0.07 (−0.13–0.02)	−0.16 (−0.27–0.06)	0.06 (−0.07–0.18)	−0.07 (−0.15–0.00)
	5%	1.34 (1.23–1.46)	1.80 (1.63–1.97)	0.48 (0.31–0.66)	1.45 (1.30–1.60)
Headache - "__ risk of headache"	32%	−1.89 (−2.02–1.75)	−2.66 (−2.86–2.46)	−1.01 (−1.20–0.83)	−1.74 (−1.90–1.58)
	15%	0.32 (0.26–0.38)	0.29 (0.19–0.38)	0.16 (0.04–0.27)	0.44 (0.35–0.52)
	<1%	1.57 (1.42–1.71)	2.37 (2.17–2.57)	0.86 (0.66–1.06)	1.30 (1.12–1.48)
Nervousness/anxiety/irritability - "__ risk of feeling nervous, anxious, or irritable"	13%	−0.91 (−1.01–0.80)	−1.24 (−1.39–1.09)	−0.37 (−0.60–0.14)	−0.93 (−1.07–0.79)
	7%	0.14 (0.09–0.20)	0.21 (0.10–0.32)	0.15 (0.03–0.27)	0.08 (0.01–0.16)
	<1%	0.77 (0.66–0.87)	1.04 (0.86–1.21)	0.22 (0.01–0.43)	0.85 (0.71–0.99)
Rebound - "__ risk of rebound/crash effect when medication effect wears off (making you feel eg, moody, tired, drained, or sluggish)"	9%	−0.62 (−0.74–0.50)	−0.50 (−0.69–0.30)	0.01 (−0.20–0.22)	−1.08 (−1.23–0.93)
	3%	−0.04 (−0.12–0.05)	−0.46 (−0.56–0.35)	0.05 (−0.13–0.24)	0.26 (0.14–0.38)
	<1%	0.66 (0.56–0.76)	0.96 (0.79–1.12)	−0.06 (−0.24–0.12)	0.82 (0.70–0.94)

Note: Text appearing in quotations shows the text seen by respondents for each attribute.
Abbreviations: CI, confidence interval; M, mean.

exchange for increasing the duration of effect from 8 to 14 hours (|-1.28–0.64|=1.92) (Table 3).

Preference weights increased as attribute levels improved (eg, as speed of onset or risk of side effects decreased), with the exception of duration of effect, where 14 hours was most preferred followed by 16 hours. Reducing the speed of onset from 4 hours to 1 hour was most important to patients, as it showed the highest change in preference weight (preference weight increase=5.23); reducing the risk of rebound from 9% to <1% was least important as it showed the smallest change in preference weight (preference weight increase=1.28) (Table 3).

Latent Class Analysis

The latent class analysis performed for the DCE data identified three population groups that differed in their overall preferences and were mostly driven by the following attributes: (a) Side effects (n=69, 34.5%), (b) Quick onset (n=47, 23.5%) and (c) Quick onset and long duration (n=84, 42.0%). The relative importance of improving each attribute differed significantly across the three groups (*p*s<0.01; Figure 2). All attribute-level preference weights differed significantly among the three groups with the exception of a 7% risk of feeling nervous, anxious, or irritable (Table 3).

The "Side effects" group most valued the reduction in risk of side effects in their decision-making. The most important attribute change for this group was decreasing the risk of headache from 32% to <1%, followed by decreasing the risk of insomnia/sleep disturbances from 31% to 5%. The duration of medication effect was not a major concern for this group (Figure 2) with most patients in this category preferring a 12- or 14-hour duration (Table 3).

The "Quick onset" group valued reducing the speed of onset from 4 hours to 1 hour more than any other attribute change. Increasing the duration of effect and decreasing the risk of headache from 32% to 1% were the second and third most important attributes (Figure 2). The most

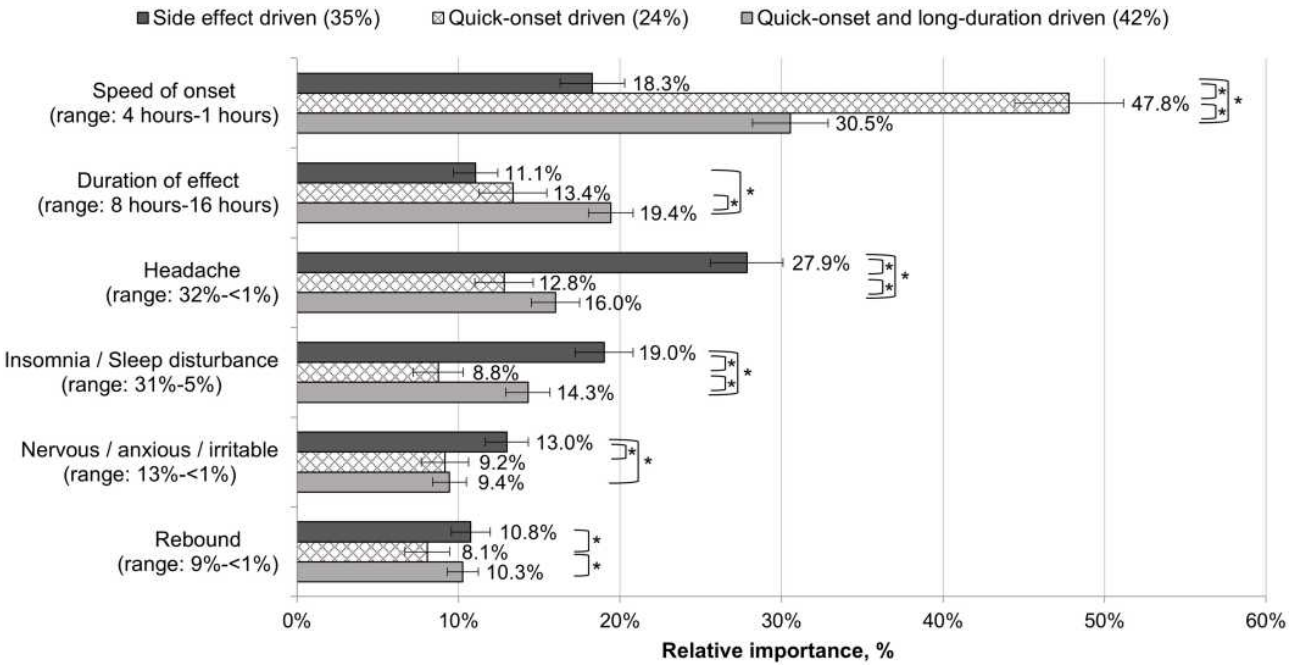

Figure 2 Mean relative attribute importance by latent class group.
Notes: Relative importance estimates are ratio data; 30% is twice as important as 15%. Error bars represent 95% confidence intervals. *Denotes significant pairwise comparisons at $P<0.05$.

preferred duration of effect among this group was 14 hours (Table 3).

The "Quick-onset and long-duration" group was the largest patient group (n=84, 42.0%) and valued reducing the speed of onset from 4 hours to 1 hour and increasing the duration of effect from 8 hours to 16 hours (Figure 2). A duration of effect of 16 hours was the most preferred length of duration in this group (Table 3).

Patient Characteristics by Latent Class Group

Tables 1 and 2; Supplemental Table 1 report patient characteristics by latent class group. Among employed patients, a higher proportion of "Quick onset and long duration" patients reported ≥4 work burdens (44.8% vs 30.4% and 27.0%, respectively) and night work (31.3% vs 13.0% and 18.9%, respectively) than "Side effects" and "Quick onset" patients (Table 2). "Quick onset and long duration" patients also had a higher proportion identifying as Hispanic (45.2%) compared with 27.5% and 27.7% of "Side effects" and "Quick onset" patients, respectively (Table 1).

Compared with "Side effects" patients, higher proportions of "Quick onset" and "Quick onset and long duration" patients had a college degree or higher (42.0% vs 53.2% and 51.2%, respectively), were employed (66.7% vs 78.7% and 79.8%, respectively), and had children in their household (42.0% vs 55.3% and 53.6%, respectively). Compared with "Side effects" patients, a higher proportion of "Quick onset" and "Quick onset and long duration" patients also reported taking their medication daily (66.7% vs 89.4% and 76.2%, respectively) (Table 1).

Discussion

This study reports on treatment preferences among adults with ADHD, filling an important gap in the literature as previous preference studies in ADHD primarily have focused on preferences of children or caregivers of children.[17] The results of this study demonstrated the importance of individualization of treatment choices among adults with ADHD when choosing between long-acting stimulant medications. The majority of adult patients value onset and duration attributes such that they are willing to accept increases in risks of medication side effects in exchange for reducing the time of onset from 4 hours to 1 hour or increasing the duration from 8 hours to 14 or 16 hours. When given discrete choices between a variety of variables regarding efficacy and side effect profiles, three different distinct groups of patient profiles arose, indicating that while all attributes are important, patients may prioritize these attributes differently when it comes to selecting a long-acting ADHD medication. Specifically, the largest proportion (42%) of patients

would prefer a quick onset and long duration of action, while the next largest group (35%) preferred minimizing side effects and a final group primarily desired a quick onset of action. These results are consistent with treatment guidelines that recognize the need to consider the individual patient and their unique needs when selecting a -treatment.[64,65] This underscores the need for shared decision-making, ie for health-care providers to continuously take into consideration the preferences and individual needs of each patient when discussing treatment options for ADHD, which may be of particular importance to individuals who require effective control of their ADHD symptoms through most of their waking hours. According to a review article, health-care providers tend to be most concerned with symptom control during work or school hours for patients with ADHD; as such, they may not take into consideration that symptom control at the beginning and end of the day may be very important to patients and caregivers.[66]

Patients desiring a quick onset and longer duration of effect (14–16 hours) were most likely to have stressful or burdensome work activities and have children at home, suggesting they desired quick onset and longer duration medications to meet the demands they face in the morning, during work hours and after. Conversely, patients desiring to minimize side effects were least likely to be employed, have a college degree, and to take their medication daily. Understanding patient characteristics that drive preferences may be beneficial to health-care providers to better guide discussions with their patients on tailoring treatment.

The results of this study are generally consistent with other research showing that patients prefer a medication with the most rapid onset of action and the longest duration of action.[19,20] While the importance of the duration of effect varied across the three latent class groups, it is important to note that all patients desired a duration of at least 12 hours. This aligns with the average of 11.9 hours that patients self-reported needing the effect of their medication to last. That the effect of patients' current ER treatment was perceived to last only an average of 9.1 hours in the current study points to the unmet need of patients when it comes to duration of effect of their treatment for ADHD.

To adults in this study, it was shown that reducing the risk of a rebound effect after medication wears off from 9% to <1% was the least important side effect attribute, but this reduction was still viewed as important with statistically significant preference weights for each of these levels. Rebound effects have been reported as some of the most common challenges health-care providers face with current treatment for ADHD.[67] While several laboratory classroom studies have demonstrated that this phenomenon exists,[42,68] little research has quantified the prevalence of this rebound effect. To develop the levels for this study, only two publications were identified that quantified this rebound effect.[34,39] If the rate of rebound is higher than 9%, then it can be anticipated that reducing this risk would take on greater importance. If patients have experienced rebound effect on all medications and they perceive that the actual risk is higher than 9%, they would likely be less concerned with reducing the risk from 9%.

Limitations

This study has limitations. It is possible for differences to arise between stated and actual choices as the hypothetical situations presented in the survey may not completely match actual emotional, clinical, or financial impact. To minimize these differences, the survey instrument was designed with clinical evidence and input from patients and physicians to mimic realistic health-care decisions as closely as possible, and a rigorously stated preference methodology (DCE) was used. The representation of females in this study is higher relative to the expected male-female ratio. One could hypothesize that a higher proportion of females are being treated with long-acting medications and a stimulant, which was the focus of this study. Alternatively, females may have been more likely than men to participate in this study, reflecting a known participation bias in online survey research.[69–71] This may limit the generalizability of these results to the overall adult ADHD population. However, it is noteworthy that previous studies have shown that gender is not associated with the phenotypic presentation of ADHD in adulthood, as symptoms such as inattention, impulsivity and hyperactivity were found to be present in both males and females.[72] Further, as shown in Table 1, the proportion of females did not differ across the three latent class groups identified in the current study.

Conclusion

In summary, this study shows that individual patients value medication attributes differently, which can be accounted for with respect to optimizing medication treatment of adults with ADHD. The findings of this study highlight the significant work burden and

emotional impact of adult ADHD with 75% reporting moderate or severe work-related burden and 78% reporting at least one other psychiatric comorbidity. Among the ADHD adult population, three patient groups emerged with differing importance given to various treatment attributes. Trade-offs between speed of onset, duration of effect, and risk of side effects each will vary in terms of their importance depending upon the patient and his/her characteristics. While a group of adult patients with ADHD will trade-off most attributes for a quick onset of the medication, a second group will trade-off efficacy attributes for a lower risk of side effects such as headache or insomnia. The third and largest group of adults with ADHD in this study values both a quick onset and a long duration of effect. These results provide insight into how adult patients with ADHD value and assess meaningful "benefit-risk" when making treatment decisions, which can be useful for facilitating physician-patient communication and shared decision-making. These findings also support the need for prescribers to have a strong understanding of the different attributes of long-acting stimulant products that are important to patients and to readily communicate to patients their rationale for the selection process.

Abbreviations

ADHD, attention deficit hyperactivity disorder; ASRS, Adult ADHD Self-Report Scale; DCE, discrete choice experiment; ER, extended release; HB, hierarchical Bayesian; IR, immediate release; ISPOR, International Society for Pharmacoeconomics and Outcomes Research; SD, standard deviation; US, United States.

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author, M.J.C.M., upon reasonable request.

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Author Contributions

All authors have made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, and/or analysis and interpretation, or in all these areas; have drafted or written, or substantially revised or critically reviewed the article, have agreed on the journal to which the article was submitted, have reviewed and agreed on all versions of the article before submission, during revision, the final version accepted for publication, and any significant changes introduced at the proofing stages, and agree to take responsibility and be accountable for the content of the article.

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