Treatment Preferences of Adult Patients with Attention-Deficit/Hyperactivity Disorder in Canada: A Discrete Choice Experiment (DCE)

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Background

- Attention-deficit/hyperactivity disorder (ADHD) is one of the most commonly diagnosed neurodevelopmental disorders[1]
- Treatment options for adults with ADHD, including stimulants and non-stimulants, are associated with different levels of efficacy and safety[2]
- While several real-world studies have examined treatment patterns among adult patients with ADHD in Canada, there is limited information on the factors influencing treatment decisions in this population[3]

Objectives

To assess and quantify the extent to which different attributes of ADHD treatments (i.e., efficacy and safety) impact treatment preferences among adult patients in Canada

To estimate overall preferences for treatment profiles that approximate centanafadine and three selected treatments for ADHD (i.e., lisdexamfetamine dimesylate [lisdexamfetamine], atomoxetine hydrochloride [atomoxetine], and viloxazine extended release [viloxazine]) among adult patients in Canada

Methods

- An online DCE survey offered in both French and English was conducted from August 24th, 2023 to November 4th, 2023 among adult patients with ADHD recruited via an existing panel of geographically and demographically diverse individuals in Canada
- Eligible participants were adults (≥18 years) residing in Canada who had been diagnosed with ADHD and had received ≥1 pharmacological treatment for ADHD at any time

DCE and survey design

- The survey included questions about participant demographic and clinical characteristics, and a DCE portion with 13 choice tasks (including 4 tasks to assess internal validity)
  - Each choice task displayed a pair of hypothetical treatment profiles, and participants were asked to select the profile that best reflected their preference between the two profiles (**Figure 1**)
    - The hypothetical treatment profiles displayed six attributes: improvement in ADHD symptoms, and risks of 5 adverse events (AEs; anxiety, dry mouth, feeling jittery, insomnia, and nausea)
    - These attributes were selected based on published clinical trials and clinical inputs (i.e., selected AEs had an incidence of ≥5% and twice that of the placebo rate in the active arm of the respective clinical trials and a statistically significant risk difference between centanafadine and other treatments in a recent matching-adjusted indirect comparison [MAIC])[2]

Statistical analyses

- A conditional logistic regression model was used to assess patient preferences for different treatment attributes, including willingness to trade-off between attributes and the relative importance of each attribute
- A sensitivity analysis was conducted excluding participants who failed internal validity tests, including stability and transitivity
- A subgroup analysis was conducted based on treatment status, comparing currently treated patients with currently untreated patients
- Overall preferences for treatment profiles approximating centanafadine, and comparators were estimated using adjusted total utilities
- Utility scores were calculated based on the coefficients obtained from the conditional logistic regression models and the symptom improvement and AEs rates derived from a recent MAIC[2]
- The adjusted total utilities were anchored to the placebo arm of each treatment and represented the incremental utility between each treatment profile and its corresponding placebo profile

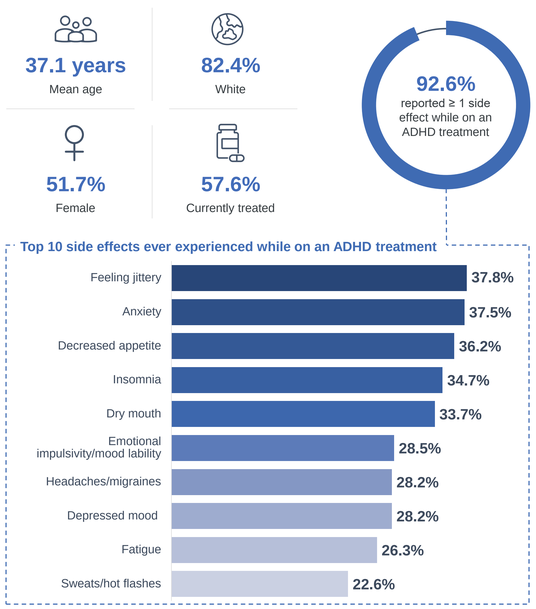
Figure 1. Example choice card

Treatment Features	Treatment A	Treatment B
Improvement in **ADHD symptoms**	25% improvement in symptoms	45% improvement in symptoms
Risk of **anxiety**	10% (10 out of 100 patients)	25% (25 out of 100 patients)
Risk of **dry mouth**	5% (5 out of 100 patients)	25% (25 out of 100 patients)
Risk of **feeling jittery**	25% (25 out of 100 patients)	5% (5 out of 100 patients)
Risk of **insomnia**	25% (25 out of 100 patients)	10% (10 out of 100 patients)
Risk of **nausea**	10% (10 out of 100 patients)	5% (5 out of 100 patients)
Which treatment do you prefer?	○	○

Results

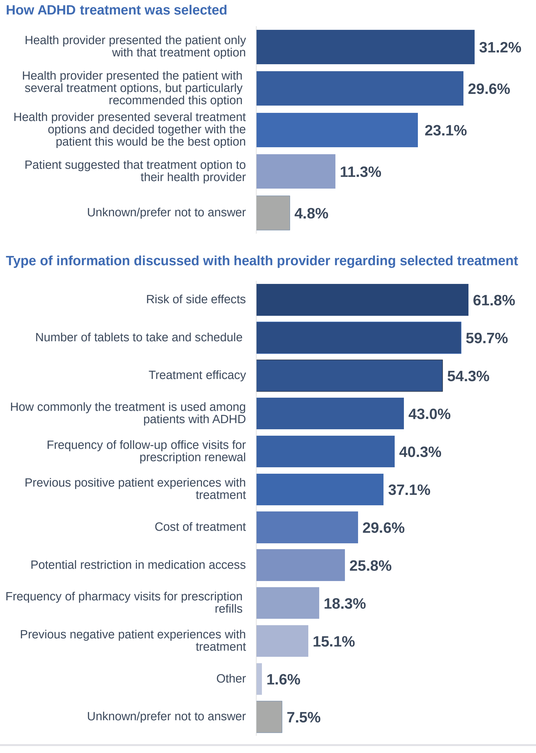
- A total of N=323 participants completed the survey, 92.6% of which experienced side effects while on an ADHD treatment at any time (**Figure 2**)

Figure 2. Participant characteristics



- About half of the patients reported that physicians discussed treatment options with them prior to initiation, but about one third of patients were only presented with one treatment option
- Efficacy and safety considerations were only discussed among 54.3% and 61.8% of patients, respectively, at the time of treatment selection (**Figure 3**)

Figure 3. Selection of current treatment



Preference for treatment attributes

- Findings from the DCE showed that participants preferred treatments providing better improvement in ADHD symptoms, and lower risks of AEs (all p <0.001, **Table 1**)
- Participants were willing to trade off varying levels of improvement in ADHD symptoms to reduce the risk of each AE
- An average patient would be willing to forego 0.96, 0.91, 0.81, 0.57, and 0.30 percentage points of improvement in ADHD symptoms to reduce their risks of insomnia, nausea, anxiety, feeling jittery, and dry mouth, respectively, by 1 percentage point (**Table 1**)

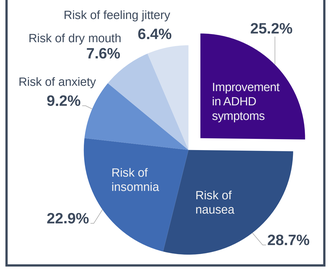
Table 1. DCE regression analyses

Attributes	Coefficient[1]	(95% CI)	P-value	Willingness to trade off[2]
Main analysis (N=323)				
Improvement in ADHD symptoms (per percentage point)	0.075	(0.069; 0.081)	<0.001*	–
Risk of anxiety (per percentage point)	-0.061	(-0.074; -0.047)	<0.001*	0.81
Risk of dry mouth (per percentage point)	-0.022	(-0.028; -0.016)	<0.001*	0.30
Risk of feeling jittery (per percentage point)	-0.042	(-0.056; -0.029)	<0.001*	0.57
Risk of insomnia (per percentage point)	-0.071	(-0.077; -0.065)	<0.001*	0.96
Risk of nausea (per percentage point)	-0.068	(-0.073; -0.063)	<0.001*	0.91
Sensitivity analysis excluding participants who failed internal validity tests (N=280)				
Improvement in ADHD symptoms (per percentage point)	0.090	(0.083; 0.097)	<0.001*	–
Risk of anxiety (per percentage point)	-0.088	(-0.103; -0.073)	<0.001*	0.98
Risk of dry mouth (per percentage point)	-0.028	(-0.035; -0.021)	<0.001*	0.31
Risk of feeling jittery (per percentage point)	-0.050	(-0.066; -0.035)	<0.001*	0.56
Risk of insomnia (per percentage point)	-0.088	(-0.095; -0.081)	<0.001*	0.98
Risk of nausea (per percentage point)	-0.080	(-0.085; -0.074)	<0.001*	0.88

[1] Regression coefficients from a conditional logistic model regressing patients' preference choice between the treatment options presented in the choice card on the difference in the attribute's levels between these options
[2] Willingness to trade-off was calculated using formula $-(\beta_{AE}/\beta_{ADHD\ symptoms})$. The number indicates the percentage points of improvement of ADHD symptoms an average patient would be willing to trade-off to achieve a 1 percentage point reduction in the risk of a particular AE

Figure 4. Part-worth utility associated with each attribute level

Figure 5. Relative importance of efficacy vs. safety attributes



- The part-worth utility figure demonstrates the utility associated with each attribute level (**Figure 4**)
  - Greater improvement in ADHD symptoms was associated with greater utility; the utility associated with 25%, 35% and 45% of symptom improvement was 1.9, 2.6, and 3.4, respectively
  - Higher risks of AEs were associated with disutility; for instance, the disutility associated with 5%, 10%, and 30% risk of nausea was -0.3, -0.6, and -2.0, respectively
- Overall, the relative importance of all AEs taken together was greater than the relative importance of improvement in ADHD symptoms (**Figure 5**)
- Findings from the sensitivity analyses (N=280), excluding participants failing the validity tests, were consistent with the results generated from the full sample, indicating robustness of the findings (**Table 1**)
- In subgroup analyses, currently untreated (but previously treated) patients valued improvement in ADHD symptoms less than currently treated patients (relative importance: 19.2% vs. 29.6%; respectively)

Reconstruction of treatment profiles

- The profile resembling centanafadine had consistently higher adjusted total utilities than lisdexamfetamine, atomoxetine, and viloxazine, in both the overall sample and the subgroups (**Figure 6**)

Figure 6. Reconstruction of treatment profiles and comparisons of adjusted total utilities[1,2]

[1] A negative adjusted total utility indicated that an average participant would prefer the placebo profile to the treatment profile
[2] The adjusted total utility of centanafadine (0.2 vs. lisdexamfetamine, 0.1 vs. atomoxetine, and 0.2 vs. viloxazine) varies across comparisons because the outcomes were measured at different time points and in different populations across MAICs

Conclusions

In Canadian patients, risk of nausea was the most important treatment attribute while efficacy, as measured by improvement in ADHD symptoms, was the second most important attribute when making treatment decisions

Patients were willing to trade off efficacy for a lower risk of adverse events, and the willingness-to-trade-off was highest for nausea, insomnia, and anxiety

In the currently untreated (but previously treated) subgroup, improvement in symptoms had a lower relative importance compared to currently treated subgroup; risk of AEs may explain why some patients decide to remain untreated

Across subgroups, a profile similar to that of centanafadine would be a preferred option for an average patient compared to that of key competitors (i.e., lisdexamfetamine, atomoxetine, and viloxazine) due to its favorable safety profile

Overall, this study helps better understand patients' preferences and their willingness to trade-off efficacy for safety, with the potential to improve treatment decision making, enhance treatment satisfaction, and foster adherence to treatments

Limitations

The current study included only respondents accessible through the survey panel vendor who wished to participate in this study. As a result, the sample may not be representative of the Canadian adult population with ADHD. Selection bias may exist in the resulting sample of respondents due to the use of convenience sampling.

To be considerate of the response burden, only a limited number of key attributes were included in the DCE questions. Additional attributes may have been important for patients' preferences.

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Disclosures

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