

Quantifying the tolerability of antipsychotic treatment-related side effects in schizophrenia: a survey study of patients and caregiver proxies

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CONCLUSIONS

- Both direct patient and proxy respondents reported that extrapyramidal symptoms – namely, pseudoparkinsonism and tardive dyskinesia – were less tolerable relative to other antipsychotic-associated side effects. The side effects reported as most tolerable were feeling tired or drowsy and dry mouth.
- Respondents expressed hesitancy to start new medications that may cause low-tolerability side effects, and high likelihood of wanting to switch medications should those side effects occur – even if the medication would help their symptoms.
- Patients find antipsychotic side effects to be highly bothersome and express that side effects greatly interfere with both physical and mental health.
- Results suggest that more tolerable antipsychotic treatment approaches are needed.

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INTRODUCTION

- Antipsychotic medications are considered mainstay treatment approaches for schizophrenia.¹ However, these medications often confer a high side effect burden – including cognitive, metabolic, and neurological effects – that can lead to reduced adherence and negative health outcomes.^{2,3}
- Previous survey research has found that side effects may affect preferences for treatment, with patients wanting to avoid high blood sugar, weight gain, and negative impacts to cognition and energy levels.^{4,6}
- Understanding how patients perceive the tolerability of various antipsychotic-associated side effects ensures that therapeutic options address patient needs and preferences and can as well as support shared decision-making.

STUDY OBJECTIVES

- To quantify tolerance for side effects associated with antipsychotics, as reported directly by patients and by caregiver proxy respondents
- To investigate the impact of patients' least tolerable side effects on patient willingness to start a new medication or to switch medications

RESULTS

SAMPLE CHARACTERISTICS

- A total of 300 patients were studied (n=200 patient respondents, n=100 caregiver proxy respondents). Patients had a mean age of 41.3 years (SD: 12.5), 44% were male, 22.7% were Black/African-American, and 22% identified as Hispanic/Latino.
- All patients were taking an oral antipsychotic medication at the time of the study. In addition, 30% were receiving a long-acting injectable (LAI) antipsychotic, and many were currently taking antidepressants, anti-anxiety medications, and mood stabilizers (Table 1).

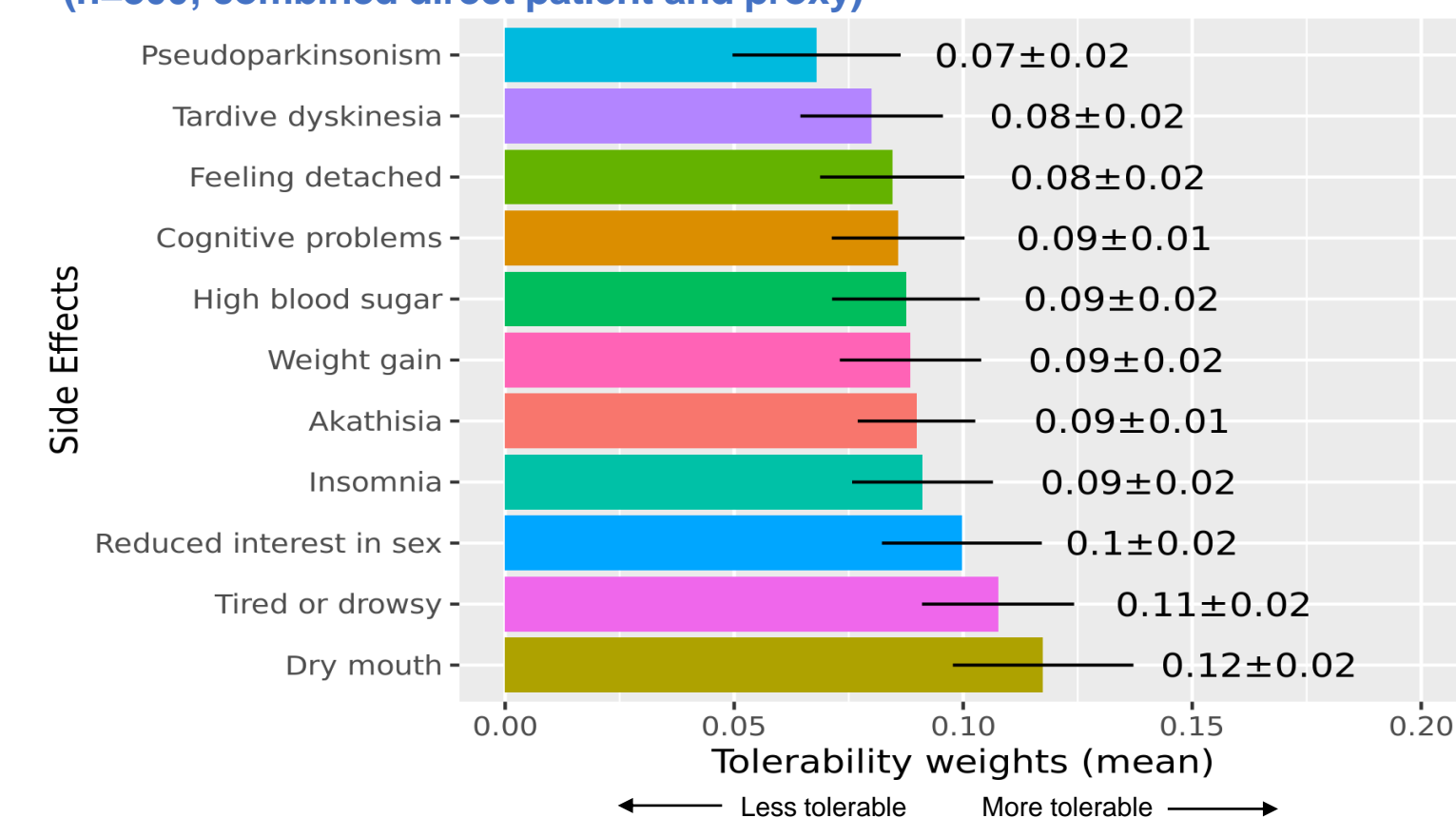
Table 1. Sample characteristics (n=300)

Characteristic	Total (n=300)
Age (mean [SD, range])	41.3 12.5, 18-96
Gender (n, %)	
Male	132 44.0%
Female	164 54.7%
Non-binary	4 1.3%
Race (n, %)*	
White	213 71.0%
Black	68 22.7%
Other	39 13.0%
Ethnicity (n, %)	
Hispanic/Latino	66 22.0%
Not Hispanic/Latino	231 77.0%
Don't know/not sure	3 1.0%
Current psychiatric medications (n, %)*	
Oral antipsychotic	300 100.0%
Long-acting injectable antipsychotic	90 30.0%
Antidepressant	153 51.0%
Antianxiety	127 42.3%
Mood stabilizer	116 38.7%
Stimulant	47 15.7%
Commonly used antipsychotics (n, %)*	
Aripiprazole (Abilify)	95 31.7%
Quetiapine (Seroquel)	72 24.0%
Risperidone (Risperdal)	53 17.7%
Haloperidol (Haldol)	49 16.3%
Time since schizophrenia diagnosis (n, %)	
Less than 3 years ago	70 23.3%
Between 3 and 7 years ago	152 50.7%
Between 7 and 10 years ago	15 5.0%
10 or more years ago	62 20.7%
Don't know/not sure	1 0.3%

SIDE EFFECT TOLERABILITY

- Results of the MaxDiff exercise showed that pseudoparkinsonism had the lowest tolerability weight, indicating that this side effect was considered least tolerable relative to all other side effects. Tardive dyskinesia and feeling like a “zombie” were the second and third most tolerable side effects, respectively. Reduced interest in or enjoyment of sex, feeling tired or drowsy, and dry mouth emerged as being more tolerable.
- While not displayed separately here, proxy responses (i.e., caregivers answering on behalf of care recipients with severe illness) were concordant with direct patient responses; the top three most and top three least tolerable side effects were the same across the two groups.

Figure 1. Side effect tolerability – results of MaxDiff choice exercise (n=300; combined direct patient and proxy)



- In the direct elicitation assessment, respondents were asked to select the three side effects (out of 11) that they felt would be least tolerable. The side effects most often selected among these top three were **pseudoparkinsonism (selected by 50% of respondents)**, **memory/cognitive problems (35%)**, and **significant weight gain (35%)**. Consistent with the MaxDiff, dry mouth was also selected as the most tolerable side effect.
- After selecting their least tolerable side effects, participants were asked about: (a) their willingness to start a medication that would help their symptoms but could potentially cause that side effect, and (b) their desire to switch to another medication if they began experiencing that side effect (Figures 2 and 3).

Nearly one-third (32%) of respondents would be “extremely unwilling” to start a medication that could potentially cause pseudoparkinsonism

Nearly half (46%) would “definitely” want to switch to another medication if they began experiencing pseudoparkinsonism

METHODS

STUDY DESIGN

- This was an observational, cross-sectional survey study of n=200 individuals with schizophrenia and=100 unpaid, informal caregivers of individuals serving as proxy respondents for individuals with severe illness.
- The survey included two methods for quantifying patient tolerance for side effects associated with antipsychotic medications, 1) Maximum Difference Scaling (MaxDiff);⁷ 2) Direct elicitation of least tolerable side effects. Side effects were selected based on a targeted literature review and collaboration with patient advocacy partners.
- The following side effects were assessed: (1) feeling tired or drowsy, (2) significant weight gain, (3) reduced interest in or enjoyment of sex, (4) insomnia or having problems falling or staying asleep, (5) high blood sugar that may lead to diabetes, (6) akathisia, (7) pseudoparkinsonism, (8) tardive dyskinesia, (9) dry mouth, (10) feeling detached or disconnected from one's surroundings, like a “zombie”, and (11) problems with memory, concentration or thinking.
- Additional survey topics included questions related to desire to start, switch, or stop medication as a result of side effects, treatment satisfaction, treatment-related side effect burden, quality of life, and sociodemographic information.

SURVEY RECRUITMENT AND FIELDING

- Prior to fielding the surveys, pilot testing was conducted with 4 patient and 4 proxy respondents to assess instructional clarity, question relevance, and cognitive burden.
- A third-party vendor supported survey programming and recruitment. All respondents were required to meet eligibility criteria and agree to informed consent before proceeding with the survey.
- Participants were recruited through the vendor's study databases, through the National Alliance on Mental Illness (NAMI) constituency, and via a community-based recruitment partner (patients only) (Savvy Cooperative).
- Upon survey completion, participants received honoraria for their time.

DATA ANALYSIS

- Survey data were analyzed based on a prespecified framework explicated in a study protocol. Data were deidentified, cleaned, and quality control checks were performed. For the main analyses, direct patient data were pooled with proxy response data.
- Data from the MaxDiff choice exercise were analyzed based on published statistical guidance for this methodology.⁸

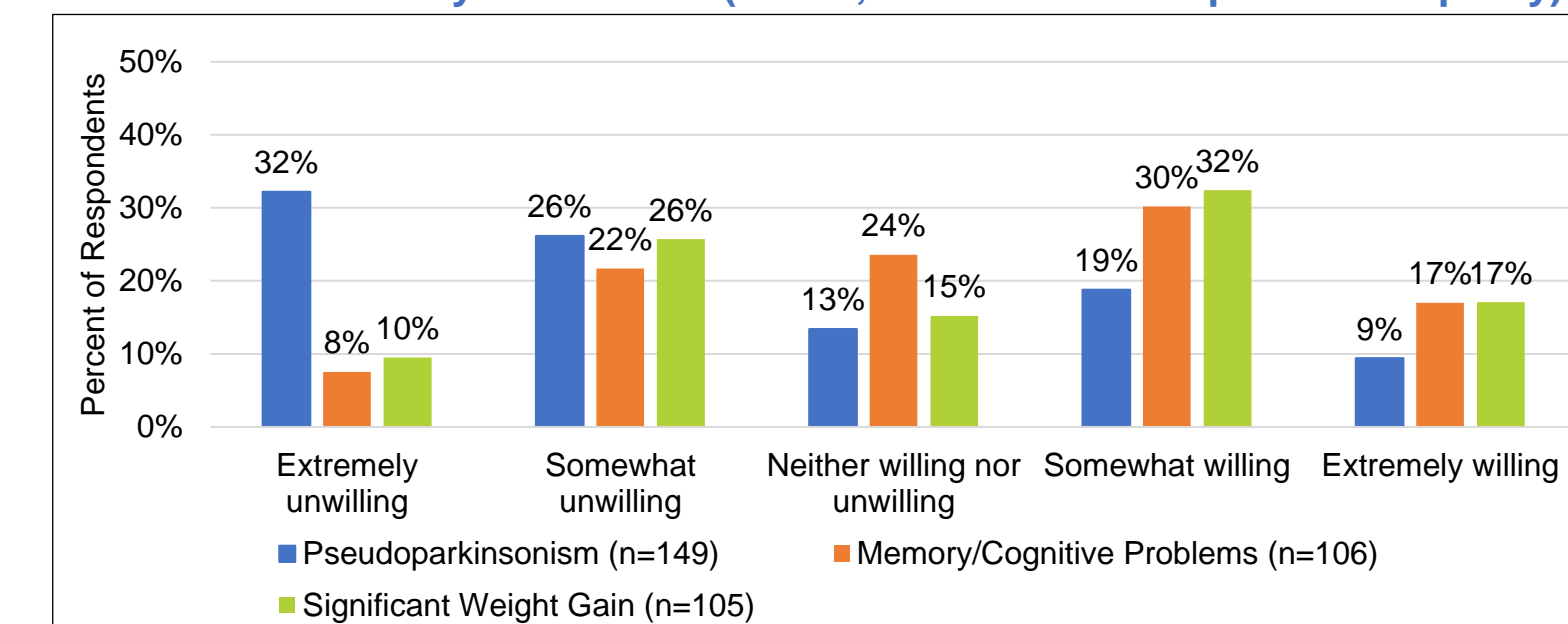
TREATMENT SATISFACTION

- Respondents were also asked selected questions from the Treatment Satisfaction Questionnaire for Medication (TSQM)⁹ to assess their level of satisfaction with their current antipsychotic medications.

Nearly one-third (32%) reported that the side effects of their antipsychotic medication were “very” or “extremely” bothersome

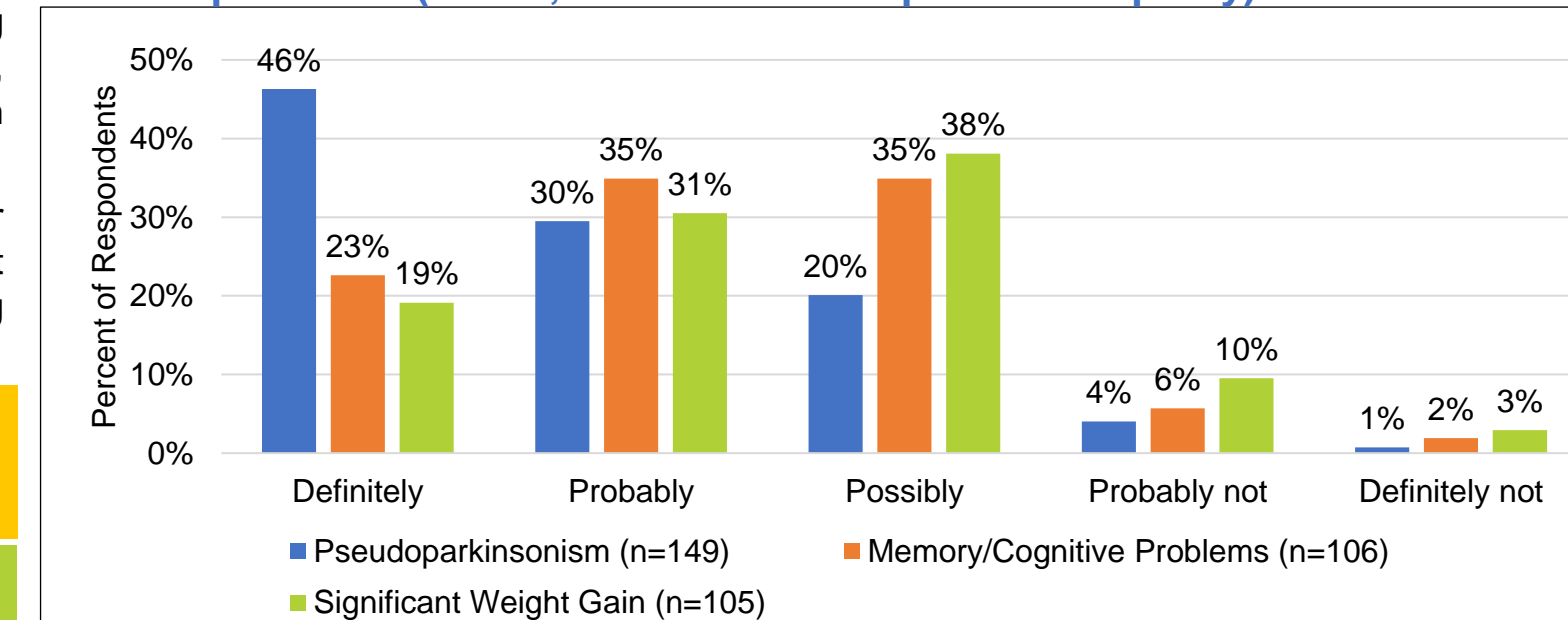
Many reported that antipsychotic side effects interfered with their mental health (45%) and/or with their physical health (42%) “quite a bit” or “a great deal”

Figure 2. Reported willingness to start an antipsychotic medications that may cause low-tolerability side effects (n=300; combined direct patient and proxy)



If your health care provider suggested that you start taking an antipsychotic medication that would help your schizophrenia symptoms, but could potentially cause [side effect], how willing would you be to start taking this medication?

Figure 3. Reported desire to switch medications if low-tolerability side effects were experienced (n=300; combined direct patient and proxy)



Imagine that you started taking an antipsychotic medication that helped to improve your schizophrenia symptoms, but you also began experiencing pseudoparkinsonism. How much would it make you want to switch to another antipsychotic medication?

*Respondents could select more than one option and thus percentages may add up to more than 100%.