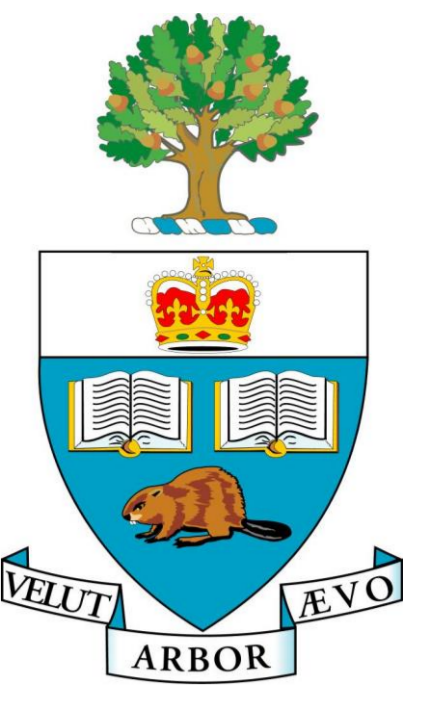


Incidence of Antipsychotic-Associated Side Effects: Impact of Clinician vs. Patient Ratings and Change vs. Absolute Scores

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Background

- There are two means by which treatment-related adverse events, reflecting severity, can be reported.
- One is “absolute score”, where side effects are defined by a certain cut-off point (e.g., a score of more than mild).
- The second option represents “change in score”, where side effects are defined as a higher score on a scale when compared to baseline.
- The absolute score definition is commonly used for treatment-related adverse events in randomized controlled trials on antipsychotics in schizophrenia, whereas the change score definition is less commonly employed.
- To our knowledge, however, there have been no studies concurrently comparing the two definitions.
- The present study aimed to compare (1) detection rates of antipsychotic-associated side effects between clinician and patient ratings, and (2) concurrent detection rates of side effects for clinicians and patients using the change and absolute score definitions.

Methods

- Data from phase 1 of the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE, N=1,460) were analyzed.
- In CATIE study, 18 adverse events were systematically and concurrently assessed by both clinicians and patients using a 4-point severity scale ranging from 0 (Absent) to 3 (Severe) at baseline, 1, 3, 6, 9, 12, 15, and 18 months.
- The incidence of antipsychotic-associated side effects was calculated according to two definitions: (1) change score – a higher score on the scale rated by clinicians or patients than that at the baseline of phase 1; and (2) absolute score – a score of 2 or 3 on the scale rated by clinicians or patients during phase 1 (notably, the original CATIE publication adopted the latter approach).
- Patients whose baseline score was 3 for the change score definition and those whose baseline score was 2 or 3 for the absolute score definition were excluded since this made it impossible to detect side effects.
- If a side effect occurred at multiple time points, the first occurrence was used.
- To compare the two definitions, patient and clinician concurrent detection rates (i.e., how frequently patients and clinicians detected the side effects detected by clinicians and patients, respectively) were descriptively reported for all 18 adverse events.

Results

- The differences in incidence of antipsychotic-associated side effects between clinician and patient ratings were as small as 5.7% across the two definitions (Table 1).
- The incidence of all side effects across clinician and patient ratings was approximately two times higher when using the change vs. absolute score definition (Table 1).
- Among the side effects detected by patients, 11 side effects were identified more frequently by clinicians with 14.3%-30.2% differences when using the change vs. absolute score definition (Table 2).
- Conversely, there was no difference >10% in patient or clinician concurrent detection rate on any item when using the absolute vs. change score definition (Table 2).

Conclusion

- **(1) Patients’ detection and reporting of antipsychotic-associated side effects is comparable to that of clinicians.**
- **(2) The change score definition (i.e., a higher score on the scale than that at baseline) is more sensitive in detecting antipsychotic-associated side effects than the absolute score definition (i.e., a score of moderate or severe on the scale).**
- **(3) Clinicians’ detection of antipsychotic-associated side effects aligns more closely with patient reports when using the change vs. absolute score definition.**
- **These findings suggest that patient ratings are in line with clinician ratings, and that the change score definition may be superior for the assessment of antipsychotic-associated side effects in clinical studies.**

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Table 1. Differences in detection rates of antipsychotic-associated side effects between clinician and patient ratings according to change and absolute score definitions

	Change score definition ^a			Absolute score definition ^b		
	Detection rate (%)		Difference ^c (%)	Detection rate (%)		Difference ^c (%)
	Clinician rating	Patient rating		Clinician rating	Patient rating	
Akathisia	30.5	31.0	-0.5	13.3	17.5	-4.2
Akinesia	29.3	29.0	0.3	13.3	15.4	-2.1
Constipation	21.2	22.5	-1.3	9.5	11.6	-2.2
Dry mouth	35.5	36.1	-0.6	18.8	21.8	-3.0
Gynecomastia/Galactorrhea	7.5	7.7	-0.2	2.3	2.4	-0.1
Hypersomnia	25.6	24.4	1.2	14.0	15.1	-1.1
Incontinence/Nocturia	12.2	12.2	-0.1	4.8	4.8	0.0
Insomnia	37.0	36.7	0.3	23.1	23.9	-0.7
Menstrual irregularities	26.4	21.8	4.6	19.6	13.9	5.7
Orthostatic faintness	26.5	27.2	-0.6	10.8	13.5	-2.7
Sex drive problem	25.4	24.1	1.3	17.9	17.8	0.1
Sexual arousal problem	20.7	20.6	0.2	15.1	16.0	-0.8
Sexual orgasm problem	19.5	19.1	0.3	14.3	14.6	-0.3
Sialorrhea	16.8	17.7	-0.9	5.0	7.1	-2.1
Skin rash	15.1	15.4	-0.3	5.6	6.5	-0.9
Sleepiness	40.2	40.9	-0.7	24.2	26.8	-2.6
Urinary hesitancy	11.4	11.5	-0.1	3.9	4.6	-0.7
Weight gain	34.2	32.9	1.3	18.8	17.6	1.2

^aDefined as a higher score on clinician- or patient-rated adverse event severity assessment than baseline during phase 1

^bDefined as a score of 2 (moderate) or 3 (severe) on clinician- or patient-rated adverse event severity assessment during phase 1

^cDifference in detection rates of antipsychotic-associated side effects between clinician and patient ratings

Table 2. Differences in patient and clinician concurrent detection rates of antipsychotic-associated side effects between change and absolute score definitions

	Patient concurrent detection rate ^a (%)			Clinician concurrent detection rate ^b (%)		
	Change score definition ^c	Absolute score definition ^d	Difference ^e (%)	Change score definition ^c	Absolute score definition ^d	Difference ^e (%)
Akathisia	76.2	81.4	-5.2	75.7	53.3	22.4
Akinesia	83.9	84.7	-0.8	84.0	68.9	15.0
Constipation	95.0	95.2	-0.2	89.6	70.8	18.8
Dry mouth	86.8	90.7	-3.8	86.1	70.9	15.2
Gynecomastia/Galactorrhea	88.8	62.5	26.3	88.3	70.6	17.7
Hypersomnia	87.3	88.0	-0.8	91.6	84.0	7.6
Incontinence/Nocturia	92.0	81.8	10.1	93.1	78.8	14.3
Insomnia	89.0	89.1	-0.1	90.1	83.7	6.4
Menstrual irregularities	90.9	81.4	9.5	86.1	88.9	-2.8
Orthostatic faintness	89.0	82.2	6.8	88.6	61.4	27.3
Sex drive problem	85.2	86.7	-1.5	90.7	93.2	-2.5
Sexual arousal problem	88.9	91.5	-2.6	91.0	91.5	-0.5
Sexual orgasm problem	92.3	91.1	1.2	93.4	94.1	-0.7
Sialorrhea	88.1	88.6	-0.5	84.3	54.1	30.2
Skin rash	92.7	88.3	4.3	90.0	73.0	17.0
Sleepiness	86.4	87.0	-0.7	87.3	72.8	14.5
Urinary hesitancy	93.3	89.1	4.2	91.5	67.7	23.8
Weight gain	79.9	76.0	3.9	86.3	76.9	9.4

Bold number indicates a ≥10% difference in patient or clinician concurrent detection rates of antipsychotic-associated side effects between change and absolute score definitions.

^aRate of antipsychotic-associated side effects detected by clinicians and also detected by patients

^bRate of antipsychotic-associated side effects detected by patients and also detected by clinicians

^cDefined as a higher score on clinician- or patient-rated adverse event severity assessment than baseline during phase 1

^dDefined as a score of 2 (moderate) or 3 (severe) on clinician- or patient-rated adverse event severity assessment during phase 1

^eDifference in patient or clinician concurrent detection rates of antipsychotic-associated side effects between change and absolute score definitions