Title

Tardive Dyskinesia versus Tardive Syndrome. What is in a name?

Authors

Frei, Karen

Scott, Alicia

Caroff, Stanley N

et al.

Publication Date

2025

DOI

10.1016/j.parkreldis.2025.107295

Parkinsonism and Related Disorders xxx (xxxx) xxx

Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

journal homepage: www.elsevier.com/locate/parkreldis

Tardive dyskinesia versus tardive syndrome. What is in a name?

Karen Frei [a,*], Alicia Scott [b], Stanley N. Caroff [c], Joseph Jankovic [d], William Ondo [e], Leslie Citrome [f], Robert Hauser [g], Joseph H. Friedman [h], Roongroj Bhidayasiri [i], Martha Sajatovic [j], Dennis Alters [k], Jonathan Meyer [l], Stuart Factor [m], E.K. Tan [n], G. Remington [o], Ira Glick [p], Hubert Fernandez [q], Cynthia Comella [r], John Kane [s], Joseph McEvoy [t], Delwyn Miller [u], Clement C. Zai [o], J.P. Lindenmayer [v], Richard Trosch [w], Daniel D. Truong [k,x]

[a] *Loma Linda University School of Medicine, USA*
[b] *The Truong Neuroscience Institute, USA*
[c] *University of Pennsylvania, USA*
[d] *Baylor College of Medicine, USA*
[e] *Houston Methodist Neurological Institute, USA*
[f] *New York Medical College, USA*
[g] *University of South Florida, USA*
[h] *Brown University, USA*
[i] *Chulalongkorn University, Thailand; Chulalongkorn Centre of Excellence for Parkinson's Disease & Related Disorders*
[j] *Case Western Reserve University, USA*
[k] *University of California, Riverside, USA*
[l] *University of California, San Diego, USA*
[m] *Emory University, USA*
[n] *National Neuroscience Institute Singapore, Singapore*
[o] *University of Toronto, Canada*
[p] *Stanford University, USA*
[q] *Cleveland Clinic, USA*
[r] *Rush University, USA*
[s] *Zucker School of Medicine at Hofstra/Northwell, USA*
[t] *Duke University, USA*
[u] *University of Iowa, USA*
[v] *New York University, USA*
[w] *The Parkinson's and Movement Disorders Center, USA*
[x] *The Truong Neuroscience Institute, University of California, Riverside, USA*

ARTICLE INFO

Keywords:
Tardive syndrome
Tardive dyskinesia
Dopamine receptor blocking agents
Antipsychotics

1. Introduction

Chlorpromazine was introduced in 1952 [1]. Five years later, Schoneker reported involuntary oral buccal lingual (OBL) movements after prolonged treatment with chlorpromazine [2]. Faurbye et al. (1964) coined the term "tardive dyskinesia" (TD) to describe these movements emphasizing the delay in onset of the condition following antipsychotic initiation [3]. Subsequently, the phenomenologies of TD expanded to include many other abnormal movements besides OBL dyskinesia namely other stereotypies, (repetitive, coordinated,

* Corresponding author.
E-mail addresses: kfrei@llu.edu (K. Frei), danieltr@ucr.edu (D.D. Truong).

https://doi.org/10.1016/j.parkreldis.2025.107295
Received 9 October 2024; Received in revised form 20 December 2024; Accepted 15 January 2025
Available online 20 January 2025
1353-8020/

purposeless movements that are drawn from our repertoire of normal movements (e.g. chewing, lip puckering, rocking, hand tapping)), chorea, (dancelike, purposeless movements that randomly involve various body parts), dystonia, and a variety of other hyperkinetic movement disorders as adverse effects from antipsychotic agents. Furthermore, other dopamine receptor blocking agents (DRBA) besides antipsychotics, such as metoclopramide used to treat a variety of gastrointestinal disorders, soon became recognized causes of TD [4–8]. Nearly all DRBAs have been associated with the development of TD.

From that time forward, the term TD was used to describe not only OBL stereotypies, but all later onset abnormal movements we currently think of under this rubric. The term "tardive syndrome" was introduced in 1973 by Freedman in an editorial describing characteristic features of TD [9]. The term gained general acceptance in the medical literature and continued to be used in parallel with TD. In 2018 the term "tardive syndrome" was proposed as the umbrella term for all tardive phenomenologies while maintaining the term TD to denote the specific classical OBL stereotypy with chorea of the extremities as it was initially described and still is described in the DSM V-TR positioning it as a subtype among several tardive conditions [10] (See Fig. 1 for a timeline of events surrounding these disorders).

However, differences in the usage of the two terms remain to be reconciled. Some prefer the term TD while others prefer "tardive syndrome" as the umbrella term to encompass the range of phenomenologies manifested by DRBA-induced tardive disorders. Alternatively, the two terms have been used interchangeably. In each case, it is beholden upon the author to define the use of the terms in their publication.

The phenomenology of TD may overlap with that of other hyperkinetic disorders that occur spontaneously without prior history of exposure to DRBAs. These include spontaneous oral dyskinesia (SD), (involuntary repetitive stereotypical movements of the face, tongue and jaw), occurring in the normal elderly population, stereotypy in untreated individuals with autism or schizophrenia and peripherally induced dyskinesias, such as edentulous dyskinesia or oromandibular

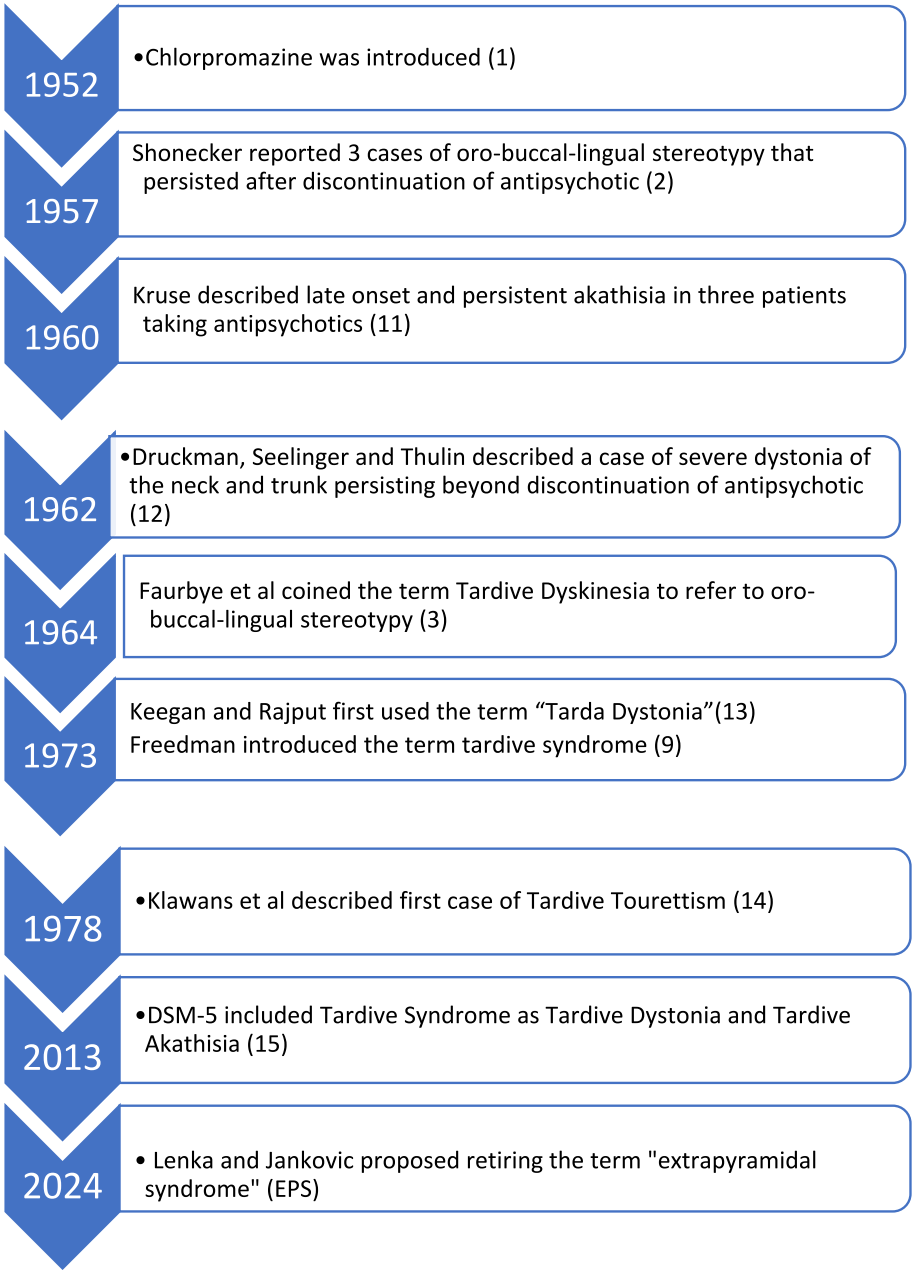

Fig. 1. Timeline of events surrounding tardive syndrome [11–16].

dystonia following dental procedure [16]. Extensive literature of the early 20th century described similar types of movements in the pre-antipsychotic era [17]. Three main differences separating TD from SD include 1) a broader range of phenomenology in TD 2) TD occurs substantially more often than SD in susceptible populations and 3) patients with TD are not always at risk for SD. They are not always elderly or afflicted with schizophrenia [18].

Although initially the occurrence of TD was thought to be related to prolonged exposure to a DRBA, it was later observed that TD may occur after a brief exposure, especially in the elderly. While symptoms of TD typically tend to develop after taking a DRBA for at least two weeks, acute dystonic reaction which may evolve into tardive dystonia can occur after only few doses of the offending drug [19]. In other cases, TD may start while patients are receiving the DRBA or even several months after discontinuation of the medication.

A unique characteristic of TD includes worsening of symptoms after stopping the DRBA and improvement with dosage increase. Although in some cases, the involuntary movements spontaneously resolved, in others the movement disorder persisted indefinitely, long after the offending drug was discontinued. Diagnosis of a tardive disorder requires DRBA exposure [10].

Additional phenomenologies apart from classic TD include tardive dystonia (T dystonia), tardive akathisia (T akathisia), tardive myoclonus (T myoclonus),tardive tourettism or tics (T tics) and tardive tremor (T tremor),. Tardive pain (T pain) is an extremely rare nonmotor tardive disorder which may include burning sensations in the oral or genital area (See Table 1 for a description of current tardive phenomenologies.).

Drug induced parkinsonism (DIP), while generally abating with discontinuation of the DRBA, may also persist. In those instances, some have thought of it as an additional form of tardive syndrome. However, this concept is controversial. While isolated cases of autopsy-proven normal substantia nigra morphology have been reported in patients with both schizophrenia and presumed idiopathic PD suggestive of tardive parkinsonism [20], dopamine transporter SPECT (Datscan) studies on patients with DIP have shown presynaptic dopaminergic deficits, implying an unmasking of subclinical idiopathic parkinsonism [21]. Moreover, cases of delayed (ie more than 6 months post DRBA discontinuation) but eventual resolution of parkinsonism have been reported in patients with normal Datscan [22]. Therefore, tardive parkinsonism is by and large not thought to be a true tardive disorder.

The tardive conditions are recognized as a group of chronic disorders induced by DRBAs that differ not only by phenomenology but also in response to medical treatment. For example, classical TD usually improves with dopamine depleting drugs and can be exacerbated by anticholinergics, whereas T dystonia oftentimes does not respond to dopamine depleting drugs but is improved with anticholinergics [19].

Table 1
Description of tardive phenomenology.

Tardive Dyskinesia	OBL stereotypy like mastication or chewing movements, sometimes with tongue protrusion and chorea involving extremities and trunk. Sometimes respiration can be involved.
Tardive Dystonia	*Repetitive muscle contractions which produce sustained or phasic abnormal involuntary postures involving face, neck, trunk or extremities. Similar to idiopathic dystonia eg. blepharospasm, cervical dystonia and truncal dystonia.*
Tardive Akathisia	*Internal restlessness accompanied by stereotypic movements such as crossing and uncrossing legs or marching in place*
Tardive Myoclonus	*Involuntary quick brief muscle contraction resulting in a jerk-like movement*
Tardive Tourettism	*Semi-involuntary movements in response to internal sensation (premonitory urge) with release following completion of movement. Can be simple or complex and motor or phonic.*
Tardive Tremor	*Mixed action greater than resting tremor, is not present prior to taking DRBA's and without family history of tremor. Worsens with DRBA discontinuation*
Tardive Pain	Pain involving mouth or tongue and or genital regions. Tends to be severe and results in obsession over the pain.

They may be separate disorders from a pathophysiological standpoint.

Although thought to be a potentially permanent condition, two longitudinal studies of TD found that a minority of patients spontaneously improve or may undergo complete resolution of symptoms over time [23,24].

The natural history and epidemiology of these disorders is not fully established with most reports consisting of case series and without distinction between phenomenology. "Tardive syndromes" are thought to be potentially permanent conditions. Most patients require continuance of antipsychotic medications, which is expected to perpetuate the condition.

One large meta-analysis found the annual incidence of TD to be 6.5 % for first-generation antipsychotics and 2.6 % for second-generation antipsychotics [25]. The incidence has been found to be similar to that reported in the 1980's and 1990's with the absolute number of new cases increasing as a result of greater use of antipsychotics for treatment of conditions other than psychosis [26]. Fortunately, the last decade has seen the development of specific and effective treatment for TD.

Despite the growing burden of TD and development of evidence-based therapies, there is still no clear consensus on terminology. In 2013 the DSM-5 recognized TD as a separate disorder from the other tardive phenomenology and recognizing T dystonia and T akathisia in the category of "tardive syndrome". All other tardive disorders were also considered to be under the category of "tardive syndrome". In 2022, the DSM-5 underwent a text revision (DSM-5TR) which maintained the terms but updated the language regarding TD specifically reflecting the advances made in the therapeutic options now available in the form of FDA-approved medications specifically indicated for TD. In summary, the nosology and the terminology have not been agreed upon. Use of the terms TD and "tardive syndrome" remain inconsistent which could lead to misinterpretation and miscommunication between clinical studies and treatment trials. More problematically, TD has been used interchangeably with "tardive syndrome" and without definition in individual publications. Further research is needed to provide clinicians with tools that will help to standardize assessment and inform treatment/care management. We sought to establish terminology of the umbrella term for these disorders through mixed classical e Delphi methodology under the auspices of the International Association of Parkinsonism and Related Disorders (IAPRD). The Delphi method is a form of expert opinion research often used in healthcare to generate consensus, develop, describe and evaluate clinical guidelines or tools. The Delphi method is appropriate in situations in which there is a lack of agreement, incomplete knowledge or uncertainty or lack of evidence [30]. The result is a manifestation of expert opinion developed via consensus This paper focuses on nomenclature consensus, specifically, to clarify the most appropriate nomenclature to refer to 1) the umbrella term that represents the specific set of involuntary movements that results from DBRA use, and 2) to further clarify the nomenclature appropriate for differentiating the phenomenologies that belong under the umbrella syndrome.

2. Materials and methods

2.1. Study design

The Delphi method is widely used across health-related studies [27–39]. Published reviews examining Delphi methodology report numerous healthcare studies but lack detailed information regarding how the Delphi technique was conducted, establishing a-priori consensus criteria, reporting stability of responses and covariation considerations [27,29,29,30,30,31,31–33]. A specific modified Delphi, one that includes a steering committee to facilitate the group communication process [30,36,37] along with an expert panel [30–32,36–38], is suitable for achieving a homogenous and specifically focused consensus outcome [34–36]. For this study, the assumption that agreement over the proposed umbrella term *can be achieved* [29,31,33,34,41,

42], governs the a-priori consensus criteria to include arriving at a conclusive term to be used as an umbrella term that is distinctive from the differing conditions associated with it.

This study borrows from the literature and operationally defines *consensus* as the extent panelists concur with other panelists, *agreement* as the proportion (%) panelists agreeing with the statements presented, and *stability* as the trend or consistency panelists respond with similar responses across all three rounds [31,33,34,36–39]. The nomenclature specific a-priori consensus criteria is $\geq$ 70 % of agreement responses for a conclusive umbrella term. Solidarity toward definitional alignment is reported as a proportion (% extent) that panelists agree, as a whole group of medical experts and the proportion that panelists agree, within their representative professional group.

Three rounds were determined as sufficient for this study: [29,31,34,36,37,40,42,47]. Questionnaire 1 (Q1) for item generation, Questionnaire 2 (Q2) for iteration and variance observance, and Questionnaire 3 (Q3) outcomes [29,31,34,36,42,47]. Prior to developing and administering questionnaires, electronic communications were provided to explain the structured group communication process, state the goal of the study, and the aggregated results from each round (ensuring anonymity protection) presented to the group [27,29–32,34–37,42]. See Fig. 2 for a flow diagram of the study design.

Q1 generated several terms which were presented along with the primary terms ("tardive syndrome" and TD) in Q2 and rated according to a 6-point agree/disagree Likert type scale. On the final questionnaire (Q3), items were presented as confirmatory binary options that required decision between the top two terms from responses received from Q2. Thus, Q3 served as the confirmation phase focused distinctly on nomenclature use. The summary of responses from Q3 would then reflect the iterative multistage consensus-based process to achieve an expert group consensus [27,31,33,36–38,40,42,46–48].

Additionally, both Q2 and Q3 included strategic practical application vignettes and case study items. These outcomes were compared to the responses on definitional rules and terminology related survey items to demonstrate variation, if any, between practical application of the concepts and nomenclature rules surrounding the TD/tardive Syndrome terminology. Three cases were posed in Q2: 1) a description of classic TD, 2) a description of a combination of classic TD and T dystonia and 3)

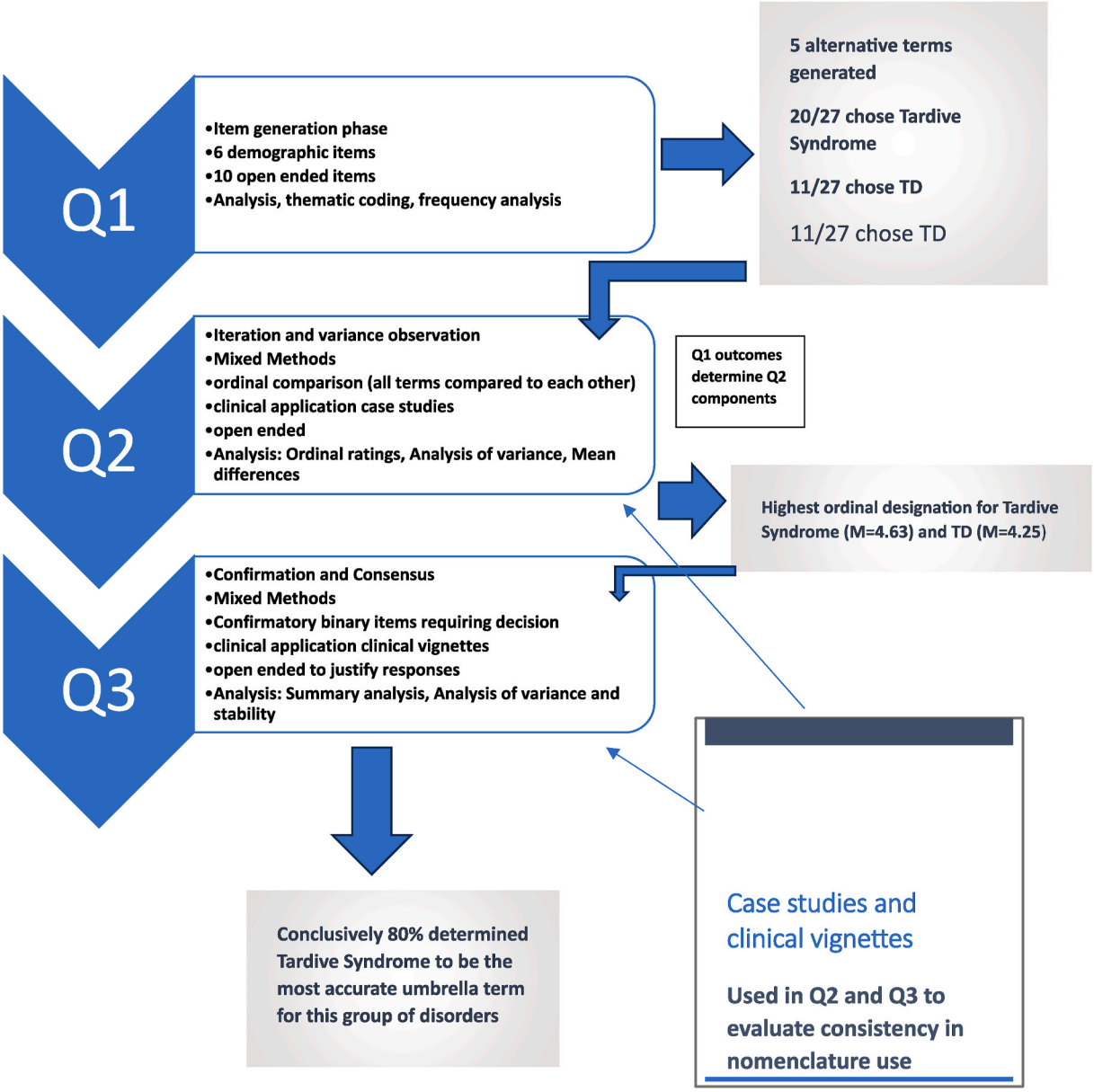

Fig. 2. Flow diagram of eDelphi study design.

a case of acute-onset dystonia, oculogyric crisis. The three vignettes in Q3 included 1) application of terminology in the setting of giving a talk, educating others on the topic, 2) a description of Huntington's disease and 3) a description of a combination of classic TD and T dystonia. Each vignette was followed by multiple choice questions of the best description of the patients' conditions and how they would handle the situation educating others on this topic.

2.2. Panelists

A panel with 27 members: movement disorder neurologists (n = 13), psychiatrists (n = 13) and a clinical researcher was assembled. Responses from the researcher were observed separately, included for whole group analysis only and parsed from consideration for analysis of group variance [41,46–48]. (See Appendix A for panel member details). Another important sample characteristic is that one of the responding experts (neurologist) was the study administrator. To protect anonymity and integrity in data collection a biostatistician was employed to ethically manage all aspects of data collection, analysis, and reporting [29–32,34,36–38,40]. Of the 27 panelists agreeing to participate, a subset was recruited to serve as steering committee members (n = 8). These members served as additional validation as they were asked to judge the appropriateness of each round's objectives, and review documents and surveys developed across the entirety of the study [30,36,37].

2.3. Participation

All panel members responded to Q1; 26 (13 psychiatrists, 12 neurologists, 1 researcher) responded to Q2, and 22 (11 psychiatrists, 10 neurologists, 1 researcher) responded to Q3. Across all three surveys members were explicitly asked to answer all questions yet several chose to skip questions. This participation trend reflects selective contribution efforts across a majority of the panel members and is commonly experienced across Delphi studies in healthcare [35–37].

To facilitate participation, communication was electronic including emails and electronic surveys. Standard edited Word docs were used as an alternative to the electronic platform format to ensure the highest response rate [32,35–37,39]. Careful considerations were made to protect against attrition and opinion inflation; all panelists were invited to contribute to all rounds regardless of whether they completed 100 % of the previous rounds' questionnaires, and summaries of whole group responses were distributed to all panel members [30,35,36,38,39].

2.4. Data analysis

This study used mixed methods statistical analyses aimed at reducing subjectivity, scrutinize validity, and observe variance via disagreement and participation, as required by the a-priori consensus, agreement, stability measures operationally defined above. Outcomes reported include item generation for preferred nomenclature from Q1, mean differences and proportional agreement from Q2, and concludes with confirmatory decision-specific, binary responses from Q3 (Term 1 vs Term 2).

3. Results

Five alternative terms, apart from TD or "tardive syndrome" were generated from Q1(See Table 2). Of the 27 panelists, 20 (9 psychiatry, 10 neurology and 1 researcher) preferred "tardive syndrome", 11 (6 psychiatry, 5 neurology) preferred TD for all tardive movement disorders, 2 responded with preference for both terms with TD denoting all chorea syndromes and 1 panelist preferred to use TD for in-clinic practice and "tardive syndrome" for research purposes.

In Q2 panel members were asked to independently rate, using 6-point Likert type scale, the 7 terms generated from Q1 according to the following statement: *I would use this term regularly in my practice as an umbrella term to describe all the tardive conditions*. Higher mean scores reflect more agreement. Responses (n = 24) indicate slightly higher agreement for *tardive syndrome* (M = 4.63, SD = 1.663) over *TD* (M = 4.25 SD = 1.824). In comparison to the other 5 terms rated, responses indicate agreement with regular use of both "tardive syndrome" and TD. (See Table 2).

Separate analysis of sums and means between only the top two terms was further parsed by profession and results indicate no statistically significant differences between professional groups. The responses result in agreement to using "tardive syndrome" as the umbrella term (M = 4.86, Sum = 107 out of 132 possible) over the use of TD (M = 4.45, Sum = 98 out of 132). Though no statistically significant differences between groups exists, it is interesting that neurologists report higher agreement toward using "tardive syndrome" regularly over psychiatrists (neurology M = 5.30, SD = 1.337; psychiatry M = 4.50, SD = 1.567), whereas responses indicate psychiatrists reporting higher agreement for using TD (psychiatry M = 4.69, SD = 1.975; neurology M = 4.11, SD = 1.364).

Measures of independent proportional agreement indicate that out of 25 responses 81.8 % of the panel agree with "tardive syndrome" as opposed to 18.2 % disagree with its use. Also, out of those 25 responses, proportional agreement indicates 68.2 % agree to use TD whereas a larger 31.8 % disagree with its use. Similar to the Q1 thematic frequency analysis, both the mean and proportion of agreement results of Q2 favored the use of "tardive syndrome" over TD. Regarding the a-priori consensus criteria, only responses to "tardive syndrome" met and exceeded the a-priori consensus criteria of >70 % agreement. Responses for the use of TD fell just below criteria for agreement resulting in higher proportional disagreement overall.

Q3 was structured to reach confirmation in nomenclature in two different approaches. In the first section, panelists were provided 2 authoritative texts, and the second section presented a non-authoritative, simple pros/cons table of each term. The first question was prefaced by a summary of the findings from Q2 (authority = panel's collective knowledge) and a passage from the DSM 5 (authority = established publication knowledge). Response options required panel members to select between "tardive syndrome", TD, or "prefer not to make a selection". Of the 20 responses received 80 % (16 of 20) determined "tardive syndrome" as the term "that most accurately represents all of the tardive conditions overall" with 10 % (2 of 20) still preferring to use TD. These results met and exceeded the a-priori consensus criteria of ≥70 % agreement. Interestingly, 10 % (2 of 20) preferred not to make a selection between the terms.

Between group results indicate 88.9 % of the neurologists that

Table 2
Open response terms generated from Q1 surveyed in Q2 across whole group.

	Tardive Syndrome	Tardive Dyskinesia	Tardive Movement Disorders	Tardive Disorder	Tardive Movement Syndrome	Tardive Motor and Nonmotor Disorder	Dopamine Antagonist Delayed Hyperkinesia
N	24	24	25	25	25	23	25
Missing	3	3	2	2	2	4	2
Mean	4.63	4.25	3.36	3.12	2.88	2.17	2.00
SD	1.663	1.824	1.89	1.453	1.641	1.267	1.19

responded (n = 9) selected "tardive syndrome", along with 72.7 % of the psychiatrists that responded (n = 11). Both group's responses met the a-priori consensus criteria of ≥70 % agreement. One neurologist and one psychiatrist were among the responses that chose *not to make a selection*. Finally, the only responses selecting TD were the responses received by the psychiatrist group.

The second question presented panelists with a standard pros/cons table listing each of the terms side-by-side. Panelists were asked to "select which term most accurately describes the group of disorders resulting from DRBA exposure which can persist even when the DRBA has been discontinued". The response options available required panelists to select one term or the other. Of the 20 responses included in the analysis, 90 % (18 of 20) of the panel experts selected "tardive syndrome" as the term "that most accurately represents all of the tardive conditions". These responses far exceed the a-priori consensus criteria of ≥70 % agreement. Responses still indicated that 10 % (2 of 20) of the experts still preferred to use TD. Between groups analysis confirms that the responses selecting TD belong to the psychiatrist group. Between groups analysis also revealed that 100 % of the neurologists (n = 9) in the panel selected "tardive syndrome" when responding to the pros/cons table question.

Q3 findings lend to solidarity toward alignment with 80 % and 90 % of panelists agreeing that "tardive syndrome" is most appropriate term, rather than TD, as a whole group of medical experts. This is also reflected within their respective professional groups (though with some variance within psychiatrists) as neurologists responded with 88.9 % and 100 % selecting "tardive syndrome" concurring with 72.7 % and 81.8 % of psychiatrists that agree, within their representative professional group.

Analysis of the case studies and vignettes showed a different response. Case 1 describing TD, 74 % (84.2 %) rated the patient as having TD and "tardive syndrome" with equal numbers of psychiatrists and neurologists. 88.9 % recognized acute onset dystonia – oculogyric crisis. 78.3 % recognized Huntington's disease – both cases were not tardive disorders. Two cases: one in Q2 and one in Q3 described TD and T dystonia. In Q2 59.3 % rated the patient as having TD, T dystonia and "tardive syndrome" showing recognition of "tardive syndrome" as the umbrella term in use. However, in Q3, 40.7 % rated the patient as having TD, T dystonia and "tardive syndrome". 25.9 % responded with "tardive syndrome" only, not differentiating between phenomenologies and 18.5 % rated TD alone showing recognition of TD as the umbrella term.

Using a more direct approach the Delphi panel was asked to rate how they would describe these disorders when teaching this subject. 87 % rated "tardive syndrome" with an explanation of the different tardive disorders, 3.7 % rated TD without distinction between phenomenologies, 3.7 % rated TD with an explanation of the different disorders using a different term for the condition TD and 3.7 % rated TD with an explanation of the different disorders using the same term TD for the classic condition. Despite the majority using "tardive syndrome" as the umbrella term with distinction between phenomenology, there were a few who maintained use of TD as both umbrella term and as the name for the condition described as OBL stereotypy with chorea.

4. Discussion

The findings of this Delphi study reflect consensus, according to the a-priori definition for this study. Specifically, the panel members agree with the use of the term "tardive syndrome", as the umbrella term to describe all the tardive phenomenologies reserving the term TD for the specific phenomenology of OBL stereotypy with or without chorea of the extremities. Consensus from the Delphi panel agreed that there should be no abbreviation of "tardive syndrome", as TS can be confused with Tourette's syndrome.

Although this study looked at more than a single proportional consensus, the addition of agreement analysis and analysis of the stability of responses across rounds lends to successfully defining the umbrella term as well as exposing that the response of experts vary (both within and between groups) across declarative statement responses (agreement variance) and practical application items in different ways. Interestingly, the changes in responses to direct questions suggests some remaining uncertainty regarding terminology.

The case studies and vignettes provide evidence for this. There were individuals who held on to the term TD as the umbrella term without changing the name of the well described TD phenomenology. So, while recognizing the term "tardive syndrome" there was disagreement regarding use of this term which could prolong the confusion of terminology in the future.

There may be some disagreement whether to accept differing phenomenologies as part of "tardive syndrome" without distinguishing between the umbrella term and the different phenomenologies but rather to lump all the movement disorders in one group as a "dyskinesia". This highlights the difficulty professionals have with changing terminology and possibly to distinguishing patients' movements which represents a potential challenge for the revision of the AIMS and its adoption. Although "tardive syndrome" was the preferred umbrella term, consensus was not 100 % and a minority of panelists continued to choose TD despite the conflict between the phenomenology associated with that name. This may represent a reluctance to accept and/or diagnose the range of phenomenologies seen in tardive syndrome. The differing phenomenologies need further study and more education regarding diagnosis of these conditions is required.

With these findings we offer a few possibilities of what not achieving 100 % agreement might mean for this Delphi study:

1. Consistently observed variation across responses warrants additional analysis that may contribute to understanding the decision process for this panel.
2. There are still aspects of involuntary movement phenomenologies that require further identification and classification.
3. The text-based definitions do not represent the clinical phenomenologies accurately.
4. The assumption that an agreement at 100 % is not achievable.

Considering the limitations and complications experienced throughout this study it is important to note that this specific sample of physicians chose to participate during a global pandemic. In cases in which responses or participation may be questioned, it is worthy to note that several alternative approaches in administering meetings and survey distribution had to be adapted to facilitate 'at-convenience' participation during this time.

The pandemic also resulted in the Delphi process taking longer than originally anticipated. Despite the complexities of the time, it was observed that the participation of the panel members regarded the topic and charge of the study as valuable and continued to participate where feasible.

Additional limitations include panel members with predetermined ideas regarding the nomenclature possibly skewing the consensus. All efforts were made to have a balanced panel with equal numbers of movement disorder neurologists and psychiatrists. All members were knowledgeable regarding the area of research, and many were well published in this area.

5. Conclusion

The finding of "tardive syndrome" as the umbrella term for the group of disorders sharing the characteristics of DRBA exposure and persistence beyond discontinuation of the drug, is a result of this study's iterative multistage consensus-based process for achieving an expert group consensus [30,34,36,39–41,43–45,48]. Thus, "tardive syndrome" is recommended to be adopted from this point forward, as the umbrella term when reported in literature, clinical practice notes and diagnostic materials. No abbreviation should be used for this term as TS can be

confused with Tourette's syndrome.

There is more to this question of nosology than semantics. Much more research into tardive syndrome including pathophysiology is needed. There may be a greater number of conditions and/or phenomenologies which need to be more clearly identified. At this time, using the term "tardive syndrome" as the umbrella term and retaining the term TD for the subtype of tardive syndrome with OBL stereotypy and chorea can enhance communication and standardization in the literature.

CRediT authorship contribution statement

Karen Frei: Writing – review & editing, Writing – original draft, Project administration, Investigation, Conceptualization. **Alicia Scott:** Supervision, Project administration, Methodology, Formal analysis. **Stanley N. Caroff:** Writing – review & editing, Writing – original draft, Investigation. **Joseph Jankovic:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Conceptualization. **William Ondo:** Writing – review & editing, Writing – original draft, Investigation. **Leslie Citrome:** Writing – review & editing, Writing – original draft, Investigation. **Robert Hauser:** Writing – review & editing, Writing – original draft, Methodology, Investigation. **Joseph H. Friedman:** Writing – review & editing, Writing – original draft, Investigation. **Roongroj Bhidayasiri:** Writing – review & editing, Writing – original draft, Investigation. **Martha Sajatovic:** Writing – review & editing, Writing – original draft, Investigation. **Dennis Alters:** Writing – review & editing, Writing – original draft, Investigation. **Jonathan Meyer:** Writing – review & editing, Writing – original draft, Investigation. **Stuart Factor:** Writing – review & editing, Writing – original draft, Investigation. **E.K. Tan:** Writing – review & editing, Writing – original draft, Investigation. **G. Remington:** Writing – review & editing, Writing – original draft, Investigation. **Ira Glick:** Writing – review & editing, Writing – original draft, Investigation. **Hubert Fernandez:** Writing – review & editing, Writing – original draft, Investigation. **Cynthia Comella:** Writing – review & editing, Writing – original draft, Investigation. **John Kane:** Writing – review & editing, Writing – original draft, Investigation. **Joseph McEvoy:** Writing – review & editing, Writing – original draft, Investigation. **Delwyn Miller:** Writing – review & editing, Writing – original draft, Investigation. **Clement C. Zai:** Writing – review & editing, Writing – original draft, Investigation. **J.P. Lindenmayer:** Writing – review & editing, Writing – original draft, Investigation. **Richard Trosch:** Writing – review & editing, Writing – original draft, Investigation. **Daniel D. Truong:** Writing – review & editing, Writing – original draft, Resources, Investigation, Funding acquisition.

Funding

Funding for this research was provided by the Christian Truong Foundation under the auspices of the International Association of Parkinsonism and Related Disorders.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests.

Acknowledgements

The following Delphi panel members participated in part of the study:

Stanley Fahn, M.D.
Gerald Maguire, M.D.
Jamie Woods, M.D.

Appendix A

Delphi Panel Demographics

			Type of Practice	N	Years in Practice	N
Psychiatry	CA	n = 13				
	Canada		Academic	9	≤24 yrs	0
	GA		Government	0	25–34 yrs	6
	IA		Private	1	35–44 yrs	3
	NY		Academic/Private	2	45–52 yrs	3
	OH		Academic/Government	1	–	1
	PA		Academic/Govt/Private	0	–	
Neurology	CA	n = 13				
	FL		Academic	8	≤24 yrs	0
	GA		Government	1	25–34 yrs	7
	IL		Private	0	35–44 yrs	2
	MI		Academic/Private	3	45–52 yrs	3
	NY		Academic/Government	1	–	0
	OH		Academic/Govt/Private	1	–	
	RI					
	Singapore					
	Thailand					
	TX					
Research/Other	Canada	n = 1	–	1	–	1
Total		27		27		24

	Google Scholar		Scopus		Web of Science		PubMed	
	#Publications/Documents	#Cites	#Publications/Documents	#Cites	#Publications/Documents	#Cites	#Publications/Documents	##Cites
Psychiatry	6525	99,196	2775	148,993	1333	31,260	5296	*NA*
Neurology	5363	294,711	5241	348,047	905	28,972	7712	*NA*
	11,888	393,907	8016	497,040	2238	60,232	13,008	*NA*

Search terms included panel member name + "movement disorders". All results were publicly available.

References

[1] T.A. Ban, Fifty years chlorpromazine: a historical perspective, Neuropsychiatry. Dis. Treat. 3 (4) (2007) 495–500.
[2] M. Schoneker, Ein Eigentumliches syndrome in oralen bereich bei metaphen application {An unusual syndrome in the oral region caused by administration of megaphen], Nervenarzt 28 (1957) 35.
[3] A. Faurbye, P.K. Rasch, P.B. Petersen, G. Brandborg, H. Pakkenbers, Neurological symptoms in pharmacotherapy of psychosis, Acta Psychiatr. Scand. 40 (1964) 10–27.
[4] H.L. Klawans, D. Bergen, G.W. Bruyn, Neuroleptic-induced tardive dyskinesias in nonpsychotic patients, Arch. Neurol. 30 (1970) 338–339.
[5] S. Lavy, E. Melamed, S. Penchas, Tardive dyskinesia associated with metoclopramide, Br. Med. J. 14 (1978) 77–78.
[6] R.E. Wiholm, O. Mortimer, G. Boethius, J.E. Haggstrom, Tardive dyskinesia associated with metoclopramide, Br. Med. J. 268 (1984) 545–547.
[7] M.L.'E. Orme, R.C. Tallis, Metoclopramde and tardive dyskinesia in the elderly, Br. Med. J. 289 (1984) 397–398.
[8] D.D. Sewell, D.V. Jeste, Metoclopramide-associated tardive dyskinesia. An analysis of 67 cases, Arch. Fam. Med. 1 (2) (1992) 271–278.
[9] D.X. Freedman, Neurological syndromes associated with antipsychotic drug use. A special report, Arch. Gen. Psychiatr. 28 (1973) 463–467.
[10] K. Frei, D.D. Truong, S. Fahn, J. Jankovic, R.A. Hauser, The nosology of tardive syndromes, J. Neurol. Sci. 389 (2018) 10–16.
[11] W. Kruse, Persistent muscular restlessness after phenothiazine treatment: report of 3 cases, Am. J. Psychiatr. 117 (1960) 152–153.
[12] R. Druckman, D. Seelinger, B. Thulin, Chronic involuntary movements induced by phenothiazines, J. Nerv. Ment, Dis. 135 (1962) 69–76.
[13] D.L. Keegan, A.H. Rajput, Drug-induced dystonia tarda: treatment with L-Dopa, Dis. Nerv, Sustainability 38 (1973) 167–169.
[14] H.L. Klawans, D.K. Falk, P.A. Nausieda, W.J. Weiner, Gilles de la, Tourette syndrome after long-term chlorpromazine therapy, Neurol. Now. 28 (1978) 1064–1068.
[15] American Psychiatric Association, Diagnostic and Statistical Manual of Mental Disorders, fifth ed., 2013.
[16] A. Lenka, J. Jankovic, Peripherally-induced movement disorders: an update, Tremor Other Hyperkinet Mov 13 (2023) 8.
[17] J.H. Friedman, Historical perspective on movement disorers, J. Clin. Psychiatry 65 (Suppl 9) (2004) 3–8.
[18] S.N. Caroff, G.S. Ungvari, D.G. Cummingham Owens, Historical perspectives on tardive dyskinesia, J. Neurol. Sci. 389 (2018) 4–9.
[19] R.E. Burke, S. Fahn, J. Jankovic, C.D. Marsden, A.E. Lang, S. Gollomp, J. Ilson, Tardive dystonia: late-onset and persistent dystonia caused by antipsychotic drugs, Neurol. Now. 32 (12) (1982 Dec) 1335–1346.
[20] J.H. Friedman, H.H. Fernandez, Autopsy follow-up of a patient with schizophrenia and presumed idiopathic Parkinson's disease, Clin. Neuropharmacol. 24 (2001) 120–121.
[21] M. Lorberboym, T.A. Treves, E. Melamid, Y. Lampl, M. Hellman, R. Djaldetti, [123I]-FP/CIT SPECT imaging for distinguishing drug-induced parkinsonism from Parkinson's disease, Mov. Disord. 21 (4) (2006) 510–514.
[22] T. Lim, A. Ahmed, I. Itin, M. Gostkowski, J. Rudolph, S. Cooper, H.H. Fernandez, Is 6 months of neuroleptic withdrawal sufficient to distinguish drug-induced parkinsonism from Parkinson's disease? Int. J. Neurosci. 123 (3) (2013) 170–174.
[23] G. Gardos, J.O. Cole, D. Haskell, D. Marby, S. Schniebolk Paine, P. Moore, The natural history of tardive dyskinesia, J. Clin. Psychopharmacol. 8 (4) (1988) 31S–37S.
[24] D. Zutshi, L.J. Cloud, S.A. Factor, Tardive syndromes are rarely reversible after continuing dopamine receptor blocking agents: experience from a university- based movement disorders clinic, Tremor and Other Hyperkinetic Disorders 4 (2014) 1–9.
[25] M. Carbon, J.M. Kane, S. Leucht, C.U. Correll, Tardive dyskinesia risk with first- and second-generation antipsychotics in comparative randomized controlled trials: a meta-analysis, World Psychiatr. 17 (3) (2018) 330–340.
[26] S.A. Factor, Management of tardive syndrome: medications and surgical treatments, Neurotherapeutics 17 (2020) 1694–1712.
[27] B. Graham, G. Regehr, J.G. Wright, Delphi as a method to establish consensus for diagnostic criteria, J. Clin. Epidemiol. 56 (2003) 1150–1156.
[28] E. A Holey, J.L. Feeley, J. Dixon, V.J. Whittaker, An exploration of the use of simple statistics to measure consensus and stability in Delphi studies, BMC Med. Res. Methodol. 7 (2007 Nov 29) 52, https://doi.org/10.1186/1471-2288-7-52. PMID: 18045508; PMCID: PMC2216026.
[29] I.R. Diamond, R.C. Grant, B.M. Feldman, P.B. Pencharz, S.C. Ling, A.M. Moore, P. W. Wales, Defining consensus: a systematic review recommends methodologic criteria for reporting of Delphi studies, J. Clin. Epidemiol. 67 (4) (2014) 401–409, https://doi.org/10.1016/j.jclinepi.2013.12.002. ISSN 0895-4356, https://www.sciencedirect.com/science/article/pii/S0895435613005076.
[30] E.G. Trevelyan, N. Robinson, Delphi methodology in health research: how to do it? European Journal of Integrative Medicine 7 (2015) 423–428, https://doi.org/10.1016/j.eujim.2015.07.002. ISSN 1876-3820, https://www.sciencedirect.com/science/article/pii/S1876382015300160.
[31] S. Humphrey-Murto, M. de Wit, The Delphi method-more research please, J. Clin. Epidemiol. 106 (2019) 136–139, https://doi.org/10.1016/j.jclinepi.2018.10.011. Epub 2018 Oct 21. PMID: 30352274, https://pubmed.ncbi.nlm.nih.gov/30352274/.
[32] R. Veugelers, M.I. Gaakeer, P. Patka, R. Huijsman, Improving design choices in Delphi studies in medicine: the case of an exemplary physician multi-round panel study with 100% response, BMC Med. Res. Methodol. 20 (2020) 156, https://doi.org/10.1186/s12874-020-01029-4.
[33] T. Lange, C. Kopkow, J. Lützner, K.-P. Gunther, S. Gravius, H.-P. Scharf, J. Stove R. Wagner, J. Schmitt, Comparison of different rating scales for the use in Delphi studies: different scales lead to different consensus and show different test-retest reliability, BMC Med. Res. Methodol. 20 (2020) 28. https://doi-org.ezproxy.lib.ou.edu/10.1186/s12874-020-0912-8.
[34] Masahiro Banno, Yasushi Tsujimoto, Yuki Kataoka, The majority of reporting guidelines are not developed with the Delphi method: a systematic review of reporting guidelines, J. Clin. Epidemiol. 124 (2020) 50–57, https://doi.org/10.1016/j.jclinepi.2020.04.010. ISSN 0895-4356, https://www.sciencedirect.com/science/article/pii/S0895435619310996.
[35] A. Boel, V. Navarro-Compán, R. Landewé, D. van der Heijde, Two different invitation approaches for consecutive rounds of a Delphi survey led to comparable final outcome, J. Clin. Epidemiol. 129 (2021) 31–39, https://doi.org/10.1016/j.jclinepi.2020.09.034. ISSN 0895-4356, https://www.sciencedirect.com/science/article/pii/S0895435620311203.
[36] P. Nasa, R. Jain, D. Juneja, Delphi methodology in healthcare research: how to decide its appropriateness, World J. Methodol. 11 (2021) 116–129, https://doi.org/10.5662/wjm.v11.i4.116. PMID: 34322364; PMCID: PMC8299905.
[37] Z. Shang, Use of Delphi in health sciences research: a narrative review, Medicine 102 (7) (2023) e32829, https://doi.org/10.1097/MD.0000000000032829.
[38] X. Yang, Z. Xu, J. Xu, Large-scale group Delphi method with heterogeneous decision information and dynamic weights, Expert Syst. Appl. 213 (A) (2023) 118782, https://doi.org/10.1016/j.eswa.2022.118782. ISSN 0957-4174, https://www.sciencedirect.com/science/article/pii/S0957417422018000.
[39] M. Niederberger, A. Homberg, Argument-based QUalitative Analysis strategy (AQUA) for analyzing free-text responses in health sciences Delphi studies, MethodsX 10 (2023) 102156, https://doi.org/10.1016/j.mex.2023.102156. ISSN 2215-0161, https://www.sciencedirect.com/science/article/pii/S2215016123001565.
[40] R. Jandhyala, Delphi, non-RAND modified Delphi, RAND/UCLA appropriateness method and a novel group awareness and consensus methodology for consensus measurement: a systematic literature review, Curr. Med. Res. Opin. 36 (2020) 1873–1887, https://doi.org/10.1080/03007995.2020.1816946. Epub 2020 Sep 15. PMID: 32866051.
[41] S. Bolboacă, Medical diagnostic tests: a review of test anatomy, phases, and atatistical treatment of data, Comput. Math. Methods Med. 28 (2019 May) 1891569, https://doi.org/10.1155/2019/1891569, 2019:PMID: 31275427; PMCID: PMC6558629.
[42] K.A. McKenzie, J.D. Mahnken, Simulating and estimating agreement in the presence of multiple raters and covariates, Stat. Med. 42 (2023) 1687–1698, https://doi.org/10.1002/sim.9694. Epub 2023 Mar 5. PMID: 36872574.
[43] W. Guy, ECDEU Assessment Manual for Psychopharmacology: Revised (DHEW Publication Number ADM 76-338), US Department of Health, Education and NIMH Psychopharmacology Research Branch, Division of Extramural Research Programs, Welfare, Public Health Service, Alcohol, Drug Abuse and Mental Health Administration, Rockville,MD, 1976.
[44] S.N. Caroff, S.H. Leong, C.B. Roberts, R.M. Berkowitz, E.C. Campbell, Correlates of the abnormal involuntary movement scale in veterans with tardive dyskinesia, J. Clin. Psychopharmacol. 40 (2020) 373–380, https://doi.org/10.1097/JCP.0000000000001229. PMID: 32639290.
[45] D. Martino, V. Karnik, R. Bhidayasiri, D. Hall, R. Hauser, A. Macerollo, T. Pringsheim, D. Truong, S. Factor, M. Skorvanek, A. Schrag, Scales for antipsychotic-associated movement disorders: systematic review, critique, and recommendations, Mov. Disord. 20 (2020), https://doi.org/10.1002/mds.29392. Online ahead of print.
[46] U. Taksh, A Critical Review of Rating Scales in the Assessment of Movement Disorders in Schizophrenia, 7, 2006, pp. 1225–1229, https://doi.org/10.2174/13894500677822658 (2006), PMID: 17017898.
[47] A.A. Mitani, P.E. Freer, K.P. Nelson, Summary measures of agreement and association between many raters' ordinal classifications, Ann. Epidemiol. 10 (2017) 677–685.e4, https://doi.org/10.1016/j.annepidem.2017.09.001. Epub 2017 Sep 22. PMID: 29029991; PMCID: PMC5687310.
[48] W. Wang, N. Lin, J.D. Oberhaus, M.S. Avidan, Assessing method agreement for paired repeated binary measurements administered by multiple raters, Stat. Med. 10 (2020) 279–293, https://doi.org/10.1002/sim.8398. Epub 2019 Dec 1. PMID: 31788847; PMCID: PMC7233794.