

Quality and reporting of guidelines on the diagnosis and management of dystonia

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Background and purpose: The quality of clinical practice guidelines on dystonia has not yet been assessed. Our aim was to appraise the methodological quality of guidelines worldwide and to analyze the consistency of their recommendations.

Methods: We searched for clinical practice guidelines on dystonia diagnosis/treatment in the National Guideline Clearinghouse, PubMed, National Institute for Health and Care Excellence, Guidelines International Network and Web of Science databases. We also searched for guidelines on homepages of international neurological societies. We asked for guidelines from every Management Committee member of the BM1101 Action of the Cooperation between Science and Technology European framework and every member of the International Parkinson and Movement Disorders Society with special interest in dystonia.

Results: Fifteen guidelines were evaluated. Among guidelines on treatment, only one from the American Academy of Neurology could be considered as high quality. Among guidelines on diagnosis and therapy, the guideline from the European Federation of Neurological Societies was recommended by the appraisers. Clinical applicability and reports of editorial independence were the greatest shortcomings. The rigor of development was poor and stakeholder involvement was also incomplete in most guidelines. Discrepancies among recommendations may result from the weight given to consensus statements and expert opinions due to the lack of evidence, as well as inaccuracy of disease classification.

Conclusions: The quality of appraised guidelines was low. It is necessary to improve the quality of guidelines on dystonia, and the applied terminology of dystonia also needs to be standardized.

Introduction

The European Network for the Study of Dystonia Syndromes was an Action (BM1101) of the Cooperation between Science and Technology (COST)

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European framework, and had the mission of joining different national research activities together and increasing standards in the diagnosis and treatment of dystonia across Europe. As part of this comprehensive work, we evaluated the quality of available guidelines for the diagnosis and management of dystonia. We also compared the published recommendations for the diagnostic and therapeutic algorithms.

Methods

Clinical practice guidelines were searched for in the following databases: National Guideline Clearinghouse, PubMed, National Institute for Health and Care Excellence, Guidelines International Network and Web of Science (Fig. 1). The searches were conducted using the following terms: 'dystonia guideline' and 'dystonia recommendation'. We also searched homepages of international neurological societies. We contacted every Management Committee member of the COST Action BM1101, representing 24 European countries, and every member of the International Parkinson and Movement Disorders Society with special interest in dystonia, in 103 countries. The guidelines inclusion criteria were: (i) national or international clinical practice guidelines developed by medical associations or government bodies; (ii) focused on the diagnosis and/or treatment of dystonia syndromes; (iii) published between January 2000 and May 2015; and (iv) full texts available. If different versions of a guideline existed, the most recent was assessed.

Ethical approval was not required for this study as applied clinical care was analyzed.

The guidelines were evaluated with the Appraisal of Guidelines for Research and Evaluation (AGREE) II tool [1]. This instrument contains 23 items organized in six domains (Table S1). Each item is rated on a 7-point scale from 1 (strongly disagree) to 7 (strongly agree). It is followed by an Overall Guideline Assessment about the overall quality of the guideline (percentage of the maximum 7 points) and whether it should be recommended for use in clinical practice (possible answers: yes, yes with modifications and no).

Four appraisers conducted the evaluation independently, having been trained beforehand utilizing the user manual of the AGREE II and the training tools on the www.agreetrust.org webpage. In case of larger inter-appraiser differences (>2 points) between individual scores for each item, consensus was reached through discussion. An item was considered as appropriately addressed if its mean score across appraisers was >4.2 (60% of the maximum 7-point score).

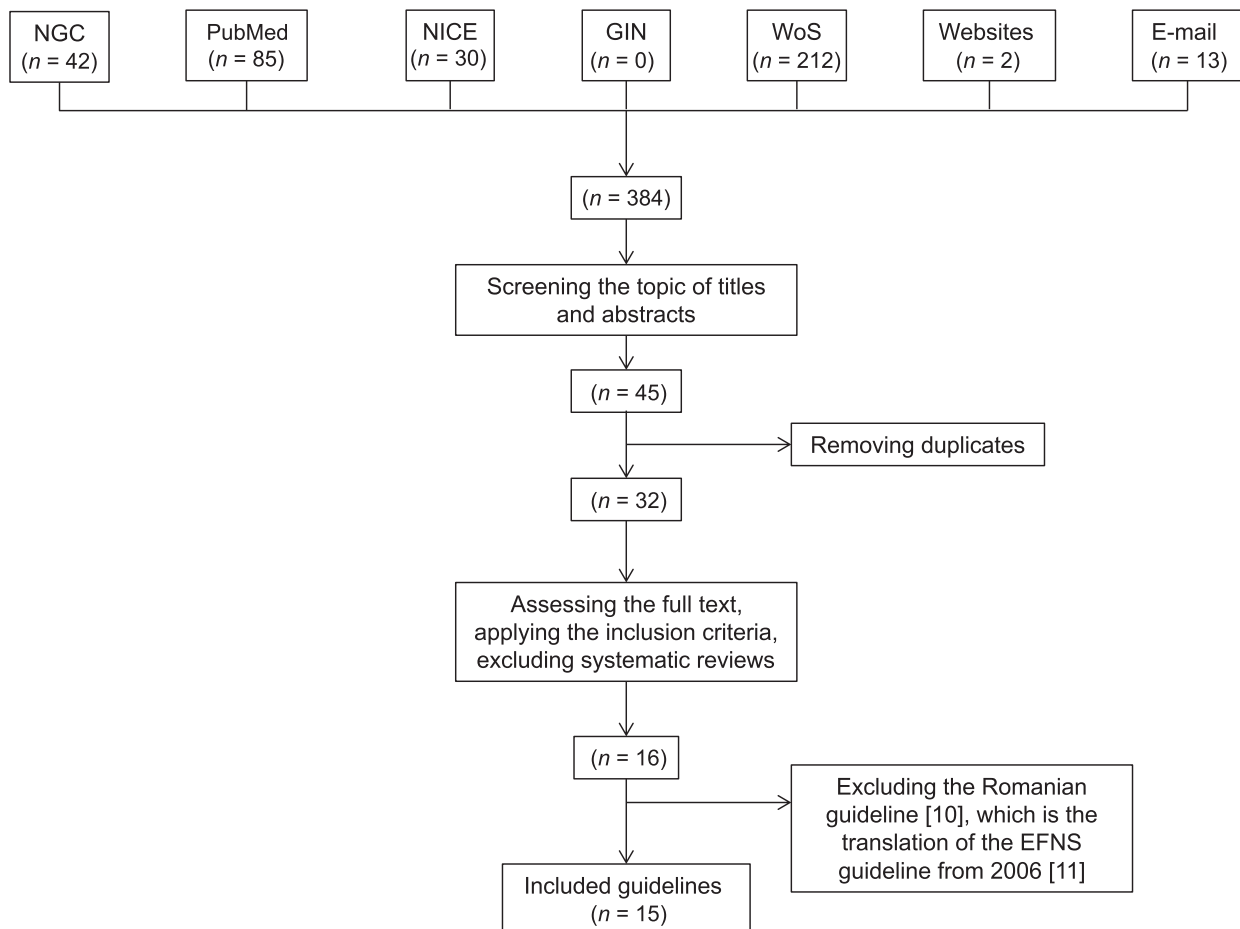


Figure 1 Literature search strategy. EFNS, European Federation of Neurological Societies; GIN, Guidelines International Network; NGC, National Guideline Clearinghouse; NICE, National Institute for Health and Care Excellence; WoS, Web of Science database.

The domain scores were subsequently calculated using the following equation: (obtained score – minimum possible score)/(maximum possible score – minimum possible score) × 100. Finally, we applied the following evaluation method from the AGREE I: high-quality guidelines need to have at least three effectively addressed domains (scores ≥ 60%) including Domain III (rigor of development) [2]. The overall quality score was calculated as the percentage of the maximum score of 7.

Data collection and descriptive statistics were performed using Statistica (StatSoft Inc., Tulsa, OK, USA) software.

We collected and compared the recommendations based on evidence, consensus statements and expert opinions. The old terminology was used in guidelines that came into operation before the new phenomenology and classification were introduced [3]; the terminology was extracted and documented it in its original form. We used the effectiveness categorization published by the British Medical Journal Clinical Evidence [4] to standardize the levels of recommendations across

guidelines (Fig. 2). We also present good practice points (GPPs) [7–9] and labeled further non-evidence-based recommendations as ‘no rating of recommendation’ (NRR).

Results

After searching the electronic databases and having received e-mail responses from 79 countries, we identified 384 documents. Forty-five publications were found after screening titles and abstracts according to the inclusion criteria. We excluded systematic reviews and duplicates, resulting in the final inclusion of 16 guidelines (Fig. 1). We did not appraise the Romanian guideline [10], which was the English translation of the European Federation of Neurological Societies (EFNS) guideline from 2006 [11].

Four guidelines [7,8,12,13] were considered evidence-based as the literature search strategy, quality of evidence and strength of recommendations were all reported [14] (Table 1).

Guideline				Effectiveness categories (BMJ Clinical Evidence) [4]
EFNS [7] Hungarian [8] Catalan [9]	Brazil [12] AAN [13]	Spanish [15]	Colombian [23]	
Rating criteria				
EFNS [5]	AAN [6]	Not named	Centre for Evidence-Based Medicine	
Rating of recommendation				
Level A One class I study or two class II studies	Level A One class I study or two class II studies	Grade A One class I study	Grade A Class I studies	Beneficial (B)
Level B One class II study or overwhelming class III evidence	Level B One class II study or overwhelming class III evidence	Grade B Class II-III studies or extrapolation from class I studies	Grade B One class II study	Likely to be beneficial (LB)
Level C Two convincing class III studies	Level C Two convincing class III studies	Grade C Class IV studies or extrapolation from class II-III studies	Grade C Class III or IV studies	Trade-off between benefits and harms (TBBH)
	Level U Data inadequate or conflicting		Grade D Class V studies	Unknown effectiveness (UE)
Not recommended				Not recommended (NR)
Good practice point (GPP) Experience of the guideline development group				
No rating of recommendation (NRR)				

Figure 2 Standardization of recommendation levels according to effectiveness categorization as established by British Medical Journal (BMJ) Clinical Evidence; AAN, American Academy of Neurology; EFNS, European Federation of Neurological Societies.

Table 1 General characteristics of the included guidelines

Guideline organization	Region; language	Year	Focus	Funding	Target users	Contains		
						Literature research strategy	Level of evidence	Level of recommendation
EFNS [7]	Europe; English	2011	D+T	NS	NS	X	X	X
Ministry of Health, Hungary [8]	Hungary; Hungarian	2009	BoNT T	NS	Botox centers, neurologists, pediatric neurologists, ophthalmologists, psychiatrists, insurance companies, Ministry of Health	X	X	X
Ministry of Health, Brazil [12]	Brazil; Portuguese	2009	BoNT T	NS	NS	X	X	X
American Academy of Neurology [13]	USA; English	2008	BoNT T	No	NS	X	X	X
Spanish Neurological Society [15]	Spain; Spanish	2012	D+T	NS	NS		X	X
Catalan Society of Neurology [9]	Spain; Spanish	2013	D+T	NS	Medical specialists, psychologists or other professionals		X	X
German Society of Neurology (DGN) [16]	Germany; German	2012	D+T	DGN	NS	X		
Austrian Society of Parkinson's Disease [17]	Austria; German	2006	D+T	NS	Neurologists and non-neurologists			
Colombian Institute of Neurology [23]	Colombia; Spanish	2014	D+T	NS	Medical staff at the Colombian Institute of Neurology		X	X
The Dystonia Society, GB [20]	GB; English	2014	D+T	Medtronic UK Ltd	Health/social care professionals, managers responsible for configuring health services			
Chilean Expert Group [18]	Chile; Spanish	2013	BoNT T	NS	NS	X		
NICE [22]	England; English	2006	DBS T	NS	Members of the Interventional Procedures Advisory Committee	X		
NICE [24]	England; English	2002	Selective peripheral denervation T	NS	Members of the Interventional Procedures Advisory Committee	X		
Ministry of Health Romania [10] (translation [11])	Romania; Romanian	2010	D+T	NS	NS	X	X	X
Chinese Academy of Medical Sciences [19]	China; Chinese	2008	D+T	NS	NS		X	
Ministry of Health and Care, Norway [21]	Norway; Norwegian	2012	D+T	NS	Politicians, decision makers, people interested in dystonia			

BoNT, botulinum toxin; D, diagnosis; DBS, deep brain stimulation; DGN, Deutsche Gesellschaft für Neurologie; EFNS, European Federation of Neurological Societies; GB, Great Britain; NICE, National Institute for Health and Care Excellence; NS, not stated; T, Treatment.

Table 2 Domain scores for each guideline and results of overall guideline assessment

Guideline	Domain score (%)						Overall guideline assessment	
	I. Scope and purpose	II. Stakeholder involvement	III. Rigor of development	IV. Clarity of presentation	V. Applicability	VI. Editorial independence	Overall quality score (%)	Recommendation of most appraisers
EFNS [7]	73.6	34.7	57.8	88.9	2.1	0	75	Y
Hungarian [8]	85.2	23.6	45.8	51.8	11.5	33.3	66.7	Ym
Brazilian [12]	50	20.8	28.6	45.8	36.4	58.3	53.6	Ym
AAN [13]	79.2	37.5	71.9	63.9	5.2	91.7	89.3	Y
Spanish [15]	31.9	2.8	20.3	91.7	20.8	0	60.7	Ym
Catalan [9]	80.5	68.05	14.6	83.3	7.3	2.1	57.1	Ym
German [16]	52.8	30.5	12.5	68.1	2.1	54.2	53.6	Ym
Austrian [17]	59.7	26.4	10.9	37.5	3.1	0	39.3	Ym/N
Colombian [23]	75	20.8	28.1	75	25	47.9	57.1	Ym
British [20]	66.7	68.05	8.3	63.9	16.7	20.8	42.9	Ym
Chilean [18]	56.9	20.8	26.6	30.5	4.2	0	42.9	Ym
NICE [22]	79.2	44.4	54.7	11.1	15.6	12.5	42.9	Ym
NICE [24]	70.8	45.8	29.7	18.1	5.2	8.3	39.3	N
Chinese [19]	20.4	3.7	4.8	20.4	2.8	0	18.6	N
Norwegian [21]	74	61	16	66.7	52.8	0	52.4	Ym

AAN, American Academy of Neurology; EFNS, European Federation of Neurological Societies; N, no; NICE, National Institute for Health and Care Excellence; Y, yes; Ym, yes, with modifications.

Quality assessment

The quality domain scores, overall quality scores and appraisers' subjective recommendations about the use of the guidelines are summarized in Table 2.

In Domain I (scope and purpose) six guidelines had a score <60% [12,15–19].

In Domain II (stakeholder involvement) only three guidelines had a score >60% [9,20,21]. The rigor of development was considered poor in Domain III; only one guideline [13] had a domain score >60%. The search for evidence was appropriate in six guidelines [7,8,12,13,18,22] and the criteria for selecting the evidence were well described in four guidelines [7,8,13,22]. The strength and limitations of the body of evidence were discussed in three guidelines [7,13,22], whereas the methods for formulating the recommendations were clearly described in two [7,13]. The health benefits and risks within the different therapeutic options were described in seven guidelines [7,8,12,13,22–24]. There was an explicit link between the recommendations and the evidence in four guidelines [7,8,13,15]. Only the American guideline [13] was externally reviewed. Only the Colombian guideline [23] mentioned an updating plan. Regarding the clarity of presentation (Domain IV), the domain score of seven guidelines [8,12,17–19,22,24] did not reach 60%. The average score of applicability in Domain V was the least among the domains. Only three guidelines [8,12,21] described facilitators and barriers to their application. Four of them [15,20,21,23] provided tools supporting their clinical use. None of them considered

the potential resource implication or formulated monitoring criteria. In Domain VI, scoring editorial independence, one guideline [13] had a domain score >60%. Only two guidelines [13,16] stated that the funding body had no influence on the content. The conflict of interest of the developers was documented in four guidelines [8,12,13,23].

The overall quality score was >60% for four guidelines [7,8,13,15]. Only the guidelines developed by the EFNS [7] and American Academy of Neurology [13] were recommended for clinical use by at least three appraisers; only the latter reached the requirements to be considered as a high-quality guideline. A difference between the two is that the EFNS guideline deals with diagnosis and treatment, whereas the American Academy of Neurology guideline deals with treatment only.

Recommendations on the diagnosis of dystonia

General recommendations about clinical diagnosis of dystonia syndromes were published in the EFNS [7], Catalan [9] and Norwegian [21] guidelines. Use of validated rating scales was encouraged in several guidelines (GPP [7,9] and NRR [15,20,21,23]).

Genetic testing was suggested after establishing the clinical diagnosis (level B) [7,9]. Recommended criteria for DYT1 mutation testing were presented in eight guidelines [7,9,15,16,19–21,23]; it was supported by evidence-based recommendations in three guidelines [7,9,15]. Indications for testing of other mutations were published as follows: DYT6 (GPP [7,9], NRR

[16,20,21,23]), DYT11 (GPP [7], NRR [16,19–21,23]), DYT8 (GPP [7], NRR [19–21]), GLUT1 (GPP [7]), DYT5 (NRR [16,21,23]), dystonia–Parkinsonism and paroxysmal dystonias (NRR [7,16,21]).

Neurophysiological tests were not routinely recommended for diagnosis and classification; however, it was stated that electromyography recordings might support the diagnosis of dystonia (GPP [7,9], NRR [15,19–21,23]).

Levodopa trial was advised in early-onset dystonia (GPP [7,9], level C [15], NRR [16,17,19–21,23]).

Brain imaging

Structural brain imaging was not routinely recommended for diagnosis of primary dystonia in adults in many guidelines (GPP [7,9], NRR [19,20]), but it was suggested in two guidelines (NRR [15,21]). It was proposed for screening of secondary forms (GPP [7,9], level A [15,23], NRR [19,20]). Computer tomography was recommended for differentiation between calcium

and iron accumulation (NRR [7,15,23], GPP [9]). Pre-synaptic dopaminergic scan was also advocated in dopa-responsive dystonia (GPP [7,9,15], NRR [21]) and dystonic tremor (GPP [7,9]).

Transcranial sonography was proposed in the Colombian guideline (NRR [23]).

Detailed examination protocol as a consensus statement (NRR) was published in four guidelines [16,17,21,23].

Recommendations on the treatment of dystonia

Effectiveness categorization of treatment options based on the recommendations is presented in Tables 3 and 4. The following additional statements were made in the guidelines.

Botulinum toxin

According to three guidelines, botulinum toxin (BoNT) can be associated with benzodiazepines or anticholinergic drugs to optimize the effect (NRR

Table 3 Effectiveness categorization of medication and physical therapy based on the recommendations

Treatment	Recommendations in the different indications of D
Anticholinergic agents	No recommendation could be made (GPP ^{7,a}); torsion D in children (NRR ¹⁶); idiopathic D in children (TBBH ^{9,15}); generalized D in children (TBBH ²³ , NRR ^{19,21}); adult therapy-resistant D (TBBH ^{9,15} , NRR ^{21,23}); acute D (TBBH ¹⁵); cervical D (NRR ¹⁶); generalized and segmental D (NRR ¹⁷); tardive D (NRR ¹⁹)
1. Trihexyphenidyl	Primary and secondary D in children (NRR ^{9,20})
Benzodiazepines	Tremor components (NRR ¹⁷); D (TBBH ^{15,23}); acute D (TBBH ¹⁵); paroxysmal/secondary forms (NRR ²³); myoclonus D (NRR ^{16,17,23}); focal, segmental and generalized D (NRR ²¹)
1. Diazepam	1. D in children (NRR ²⁰)
2. Clonazepam	2. Cervical D (NRR ²¹); myoclonus D (NRR ²¹)
Antiepileptic drugs	No recommendation could be made in D (GPP ^{7,a}); D (NRR ¹⁶); only in paroxysmal kinesiogenic D (NRR ^{16,19}); myoclonus D (NRR ²¹)
1. Valproic acid, vigabatrin	Not effective in D (TBBH ¹⁵)
2. Gabapentin	D in children (NRR ²⁰)
Antidopaminergic drugs	No recommendation could be made (GPP ^{7,a} , NRR ^{19,21})
1. Tetraabenazine	D (TBBH ^{15,23} , NRR ^{16,17}); tardive D (TBBH ¹⁵); status dystonicus in children (NRR ²⁰)
2. Neuroleptics	D (TBBH ^{15,23} , NRR ¹⁷)
2a. Clozapine	D (NRR ¹⁶)
Levodopa	After a positive diagnostic trial (GPP ^{7,a} , TBBH ^{15,23} , NRR ^{16,17,19–21}); no recommendation could be made (NRR ^{15,23})
Dopamine agonist	No recommendation could be made (NRR ¹⁵)
Baclofen	No recommendation could be made (NRR ^{15–17,19,23}); D in children (NRR ²⁰)
Lithium	Not effective in D (TBBH ¹⁵)
Mexiletine	Alternative treatment (TBBH ¹⁵)
Nabilone	Not effective in D (LB ¹⁵)
Triple Marsden cocktail	Very severe and therapy resistant, generalized D (TBBH ^{15,23})
Clonidine	Status dystonicus in children (NRR ²⁰)
Physical therapy and rehabilitation	
Physiotherapy, psychotherapy, speech therapy	D (NRR ^{9,20,21} , TBBH ^{15,23})
Transcutaneous electrical nerve stimulation	Writer's cramp (LB ^{7,9})

^aRetained from Ref. [11]. The abbreviations of the categories are followed by superscripts indicating the reference numbers of the guidelines. D, dystonia; GPP, good practice point; LB, likely to be beneficial; NRR, no rating of recommendation; TBBH, trade-off between benefits and harms; triple Marsden cocktail, a combination of tetraabenazine + pimozide + anticholinergic drug.

Table 4 Effectiveness categorization for botulinum toxin (BoNT) and surgical therapy based on recommendations

Treatment	Recommendations in different indications of D
BoNT-A or BoNT-B	Primary cranial D* (B ^{7,9}); cervical D (B ^{7,9,13} , NRR ^{19–21}); focal D (NRR ^{16,17,21}); more effective in cervical D than trihexyphenidyl (LB ¹³); blepharospasm (LB ^{12,13} , NRR ^{20,21}); focal in tardive D (TBBH ¹⁵); writer's cramp LB ¹³ (NRR ²¹); other type of upper limb D (LB ¹³ , NRR ²¹); laryngeal D (LB ¹³ , NRR ²¹); adductor LD (LB ¹³); lower limb D (UE ¹³ , NRR ²¹); abductor LD (UE ¹³); Meige syndrome (NRR ²¹)
BoNT-A	Cervical D (B ^{8,12,15,23} , NRR ¹⁸); lower limb D (TBBH ¹⁵); writer's cramp (B ^{7,9,15} , TBBH ⁸ , LB ¹² , NRR ²⁰); upper limb D (GPP ^{7,9} , TBBH ¹⁵ , NRR ²⁰); blepharospasm (B ^{8,15} , NRR ¹⁸); no evidence for blepharospasm (NRR ¹⁹); segmental D (NRR ¹²); primary generalized D (B ²³); D in cerebral palsy (LB ⁸); laryngeal D (TBBH ⁸); adductor LD (GPP ⁷ , LB ^{9,15} , NRR ²⁰); abductor LD (NRR ²⁰); it could not be recommended for abductor LD (GPP ⁹); oromandibular (NRR ¹² , TBBH ¹⁵); preparations have equal effect (TBBH ¹⁵); focal D (NRR ^{12,18} , B ¹⁵)
onaBoNT-A	Oromandibular D (TBBH ²³); limb D (LB ²³); cervical D (B ²³); blepharospasm (B ²³); adductor LD (TBBH ²³)
aboBoNT-A	Oromandibular D (TBBH ²³); limb D (LB ²³); cervical D (B ²³); blepharospasm (LB ²³); adductor LD (UE ²³)
incoBoNT-A	Oromandibular D (UE ²³); limb D (UE ²³); cervical D (B ²³); blepharospasm (B ²³); adductor LD (UE ²³)
BoNT-B	Oromandibular D (UE ²³); cervical D (B ^{15,23}); limb D (UE ²³); blepharospasm (UE ²³); adductor LD (UE ²³)
i.m. alcohol and phenol	Focal D resistant to BoNT (TBBH ¹⁵)
Intrathecal baclofen	No recommendation could be made (GPP ⁷); D (NRR ^{9,19}); primary generalized D (NRR ²³); therapy-resistant D with spasticity (GPP ^{7,a} , TBBH ^{15,23} , NRR ^{16,19,21}); truncal D (NRR ²¹)
GPi deep brain stimulation (if medication or BoNT therapy is not effective)	Primary generalized D (B ^{7,9} , LB ¹⁵ , NRR ^{16,17,19–21,23}); primary segmental D (B ^{7,9} , NRR ^{16,17,19,21,23}); cervical D (LB ^{7,9} , TBBH ¹⁵ , NRR ^{16,17,19–21,23}); status dystonicus (TBBH ¹⁵ , NRR ¹⁶); dystonic tremor (NRR ²⁰); tardive D ^b (TBBH ^{7,9,15} , NRR ^{16,17,20,23}); cases of PKAN (NRR ^{16,23}); cases of cerebral palsy (NRR ¹⁶); truncal D (NRR ²¹)
Ablative surgery	Thalamotomy/pallidotomy could not be recommended for D (NRR ¹⁶); it was stated that they may have only temporary benefit (NRR ²²); bilateral lesions are discouraged (GPP ^{7,a} , NRR ¹⁹)
Thalamotomy (Voa/Vop)	Certain D cases in centers with wide experience in stereotactic surgery interventions for movement disorders (TBBH ¹⁵)
Pallidotomy	Status dystonicus (TBBH ¹⁵)
Selective peripheral denervation	Medically refractory cervical D, perhaps with myectomy (NRR ^{16,19,20}); it is safe in therapy-resistant cervical D (TBBH ^{7,a}); careful patient selection; known side effects: infections, hemorrhage and swallowing difficulty (NRR ²⁴)
Intradural rhizotomy	Cervical D (NR ^{7,a})
Microvascular decompression	Cervical D (NR ^{7,a})

*Except for oromandibular dystonia. ^aRetained from Ref [11]. ^bIt is less effective in other secondary dystonias. The abbreviations of categories are presented as in Figure 2. The reference numbers of guidelines are presented in superscript. B, beneficial; D, dystonia; GPi, globus pallidus internus; i.m., intramuscular; LB, likely to be beneficial; LD, laryngeal dystonia; NR, not recommended; NRR, no rating of recommendation; PKAN, pantothenate kinase-associated neurodegeneration; TBBH, trade-off between benefits and harms; UE, unknown effectiveness; Voa/Vop, nucleus ventralis oris anterior/posterior.

[9,16,21]). It was stated that repeated BoNT treatments are safe and efficacious (GPP [7], NRR [20]), but cumulative doses can be dangerous in children (GPP [7]; BoNT-A: NRR [20]). Electromyography or ultrasound guidance for injections was found to improve the clinical outcome (GPP [7], NRR [20]). Other ascertainments were that BoNT should not be used in cases of abnormal neuromuscular transmission or local infection at the injection site; the recommended dosage should not be exceeded (GPP [7], NRR [8,20,23]); it is contraindicated in pregnancy (NRR [23]); and nurses or physiotherapists can assist with BoNT injections (NRR [20]).

Deep brain stimulation

It was stated in the guidelines that patient selection for the procedure is important (NRR [22]); the therapy needs specialized expertise and a multidisciplinary team (GPP [7]); potential side-effects should be

considered (GPP [7], NRR [20,22]); and life-long follow-up is required (NRR [20]).

Detailed protocols for the treatment of status dystonicus were published in only two guidelines (NRR [16,23]).

Physical therapy and rehabilitation

Additional possibilities for rehabilitation included: psychiatric care (NRR [9,21]), social support (NRR [9,21]), occupational therapy (NRR [9,20,21]), pain treatment (NRR [9,20,21]), nutritional support (NRR [9,21]) and podiatry (NRR [20]). Hydrotherapy was also proposed to support the care of dystonia, especially of cervical dystonia (NRR [9]).

Discussion

In our study, the global quality of the majority of guidelines was low. Of the 15 guidelines evaluated,

only one guideline on therapy published by the American Academy of Neurology [13] was considered to be of high quality. The EFNS [7] guideline was close to the high-quality rating and was also recommended for use by the appraisers as it provides the most diagnostic and therapeutic algorithms.

Clinical applicability is the greatest shortcoming of guidelines, enhancing the fact that guidelines do not aid the main target population, i.e. clinicians, to easily integrate recommendations into their clinical practice. Reports of editorial independence are also lacking in most guidelines. This does not inevitably mean that the recommendations were biased by competing interests but rather that higher priority was placed on other domains and focuses. This especially pertains to guidelines, which provided not only therapeutic but also detailed diagnostic recommendations [7,9,15–17,19–21,23]. Furthermore, the requirement of the different journals and platforms about editorial independence might also differ. The rigor of development was above the acceptable 60% in only one guideline [13]. The weakest items in this domain were the absence of external reviews prior to publication and the plan to update the guideline. Furthermore, the strength and limitations of the body of evidence, and the methods for formulating the recommendations were not clearly described. Stakeholder involvement was also incomplete in most of the guidelines; in particular, they did not pay attention to the views and preferences of the target populations (i.e. patients, public, etc.).

A limitation of this study was the subjectivity of the AGREE II appraisals. To increase the reliability, we recruited four appraisers as suggested by the AGREE Next Step Consortium [1].

We explored the discrepancies between the recommendations in different guidelines, and used the British Medical Journal Clinical Evidence [4] effectiveness categorization in order to resettle the various grading systems into a single one (Fig. 2).

The EFNS guideline gave the widest spectrum of diagnostic and therapeutic recommendations. In general, inconsistencies were the result of the inaccurate disease classification used and the lack of evidence in the field. Therefore, the weight of expert opinions and consensus statements in the guidelines were excessively entrusted. However, this issue is also affected by the availability of local resources, cost, health priorities and the social environment. Unambiguous recommendations, in turn, would be especially important because the differential diagnosis and clinical management of the growing number of dystonia syndromes are time-, resource- and cost-consuming, and need special expertise.

A detailed examination protocol was advised in only three guidelines [16,17,23]; this should be encouraged for future national guidelines. Considering the high number of recognized new mutations and the high cost of genetic testing, recommendations should involve the most common genetic forms and should be renewed, as generally suggested, every 3 years [25].

Most recommendations on oral therapy were based on consensus statements and expert opinions due to the lack of evidence [26]. The applications for the different BoNT preparations should be clearly described in the guidelines to promote their practical utilization. The recommendations on deep brain stimulation in primary generalized and cervical dystonia vary, and will need to be updated in the future. The management of status dystonicus should be well documented in every treatment guideline, but was only described in two guidelines.

In conclusion, we found heterogeneity in reporting and the recommendations, which might also be influenced by regional availability of resources and cultural differences. Some guidelines incorporated the recommendations from the EFNS guideline [9,10,15,19,20]. As high-quality studies for therapeutic options are still missing in the field, the development of internationally unified clinical guidelines, which involve common expert opinions, is helpful and should be put in place. Translations into different languages could propagate the use of standards in dystonia care across countries. However, local obstacles need to be addressed with implementation in different countries, as the availability of specialist training, diagnostic and treatment options vary across European countries [27]. The guidelines should be propagated directly to the clinicians with educational programs. Publication of a 'consumer' version of the guidelines in magazines or on the Internet could also be useful in assisting the therapy choices of patients [28].

Further development of clinical practice guidelines should be consistent with the AGREE II criteria to promote the high quality of patient care.

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Disclosure of conflicts of interest

The authors declare no financial or other conflicts of interest.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1 Items and domains for assessment in the Appraisal of Guidelines for Research and Evaluation II instrument [1].

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