Table 15: Review protocol for interventions for dystonia

Field (based on PRISMA-P)	Content
Key area in the scope	A. Management of abnormal muscle tone in adults aged 19 and over with cerebral palsy, including spasticity and associated movement disorders such as dystonia.
Draft review question from the scope (to be deleted in the final version)	A3 Which treatments (for example, levodopa, anticholinergic drugs, and botulinum toxin injections) are most effective for managing dystonia in adults with cerebral palsy?
Actual review question	A3 Which treatments (pharmacological treatment (levodopa, anticholinergic drugs, and botulinum toxin injections), neurosurgical procedure (deep brain stimulation, ITB) are most effective for managing dystonia in adults with cerebral palsy where dystonia is the predominant abnormality of tone?
Type of review question	Intervention
Objective of the review	The aim of this review is to determine the relative effectiveness of pharmacological treatments and neurosurgical procedures for managing dystonia in adults with cerebral palsy
Eligibility criteria – **population**/disease/condition/issue/domain	Adults aged 19 and over with predominantly dystonic cerebral palsy (Study median of age 18 years or more)
Eligibility criteria – **intervention**(s)/exposure(s)/prognostic factor(s)	Pharmacological: • Levodopa • Anticholinergic drugs (trihexyphenidyl) • Botulinum toxin injections with adjunct treatments such as lycra and splint casting • Botulinum toxin injections without adjunct treatments • Gabapentin/ pregabalin

Field (based on PRISMA-P)	Content
	• Intrathecal baclofen ITB • Tetrabenazine Non-pharmacological: • Deep brain stimulation • Orthotics for physical function (dynamithorthotics [lycra])
Eligibility criteria – **comparator(s)**/control or reference (gold) standard	• Each other • Placebo • Usual care

Outcomes and prioritisation	**Critical outcomes**
	• Health related quality of life
	• Dystonia rating scales
	  ○ DMFRS
	  ○ Fahn-Marsden Rating Scale
	• Patient or carer reported satisfaction
	Important outcomes
	• Motor function using functional measures
	• Goal attainment scores
	• Adverse events
	• Pain
	
	Minimally important differences
	• Goal Attainment Scale: 7 units
	• Modified Ashworth Scale: 1 unit
	• Quality of Upper Extremities Test: 5 units
	• ICF - Measure of Participation and Activities Screener: 2 units
	• Community Balance and Mobility Scale: 10 units

Field (based on PRISMA-P)	Content
	• Five Times Sit to Stand Test: 2.5 seconds • Seated Shot-Put: 40cm • Timed Up and Go: 5 seconds • Pain: 30% reduction – corresponding to "much improved" or "very much improved" on a global impression of change, or 2 points on a 0 to 11 pain intensity numerical rating scale • Other dichotomous outcomes will use default MIDs [RR thresholds of 0.80 and 1.2] • Other continuous outcomes will use default MIDs [0.5 times the SD of the control group]
Eligibility criteria – **study design**	• Systematic reviews of RCTs • RCTs • Comparative cohort studies (only if RCTs unavailable or limited data to inform decision making) Will consider conference abstracts only if related to RCTs
Other inclusion **exclusion criteria**	Community, residential, primary and secondary care. UK and non-UK studies. (Non UK studies from high income countries according to WHO/ World Bank criteria)
Proposed sensitivity/**sub-group analysis**, or meta-regression	No groups will be reviewed and analysed separately from the outset. In the presence of heterogeneity, the following subgroups will be considered for sensitivity analysis: • Population subgroups (e.g. age groups, presentation, severity: ○ Ambulant vs. non-ambulant • Intervention subgroups (e.g. route of administration, drugs within drug classes, high/low dose): ○ Drug dosage Important confounders (when comparative observational studies are included for interventional reviews) • Degree/severity of dystonia
Selection process – duplicate screening/selection/analysis	A random sample of the references identified in the search will be sifted by a second reviewer. This sample size will be 10% of the total, or 100 studies if the search identifies fewer than 1000 studies. All disagreements in study inclusion will be discussed and resolved between the two reviewers. The

Field (based on PRISMA-P)	Content
	senior systematic reviewer or guideline lead will be involved if discrepancies cannot be resolved between the two reviewers
Data management (software)	STAR was used to sift through the references identified by the search, and for data extraction Pairwise meta-analyses and production of forest plots was done using Cochrane Review Manager (RevMan5). 'GRADEpro' was used to assess the quality of evidence for each outcome.
Information sources – databases and dates	Database(s): Embase 1974 to Present, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present; Cochrane Library; WEB OF SCIENCE
Identify if an update	Not an update
Author contacts	For details please see the guideline in development web site.
Highlight if amendment to previous protocol	For details please see section 4.5 of Developing NICE guidelines: the manual 2014.
Search strategy – for one database	For details please see appendix B.
Data collection process – forms/duplicate	A standardised evidence table format will be used, and published as appendix D (clinical evidence tables) or H (economic evidence tables).
Data items – define all variables to be collected	For details please see evidence tables in appendix D (clinical evidence tables) or H (economic evidence tables).
Methods for assessing bias at outcome/study level	Standard study checklists were used to critically appraise individual studies. For details please see section 6.2 of Developing NICE guidelines: the manual The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/
Criteria for quantitative synthesis	For details please see section 6.4 of Developing NICE guidelines: the manual 2014.
Methods for quantitative analysis – combining studies and exploring (in)consistency	For details please see the methods see supplementary document C.
Meta-bias assessment – publication bias, selective reporting bias	For details please see section 6.2 of Developing NICE guidelines: the manual 2014.
Confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual 2014.
Rationale/context – what is known	For details please see the introduction to the evidence review.

Field (based on PRISMA-P)	Content
Describe contributions of authors and guarantor	A multidisciplinary committee developed the evidence review. The committee was convened by the National Guideline Alliance (NGA) and chaired by Dr Paul Eunson in line with section 3 of Developing NICE guidelines: the manual 2014. Staff from the NGA undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost effectiveness analysis where appropriate, and drafted the guideline in collaboration with the committee. For details please see the methods chapter of the full guideline.
Sources of funding/support	The NGA is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists.
Name of sponsor	The NGA is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists.
Roles of sponsor	NICE funds NGA to develop guidelines for those working in the NHS, public health and social care in England.
PROSPERO registration number	Not applicable

CDSR: Cochrane Database of Systematic Reviews; CENTRAL: Cochrane Central Register of Controlled Trials; CSF, cerebrospinal fluid; DARE: Database of Abstracts of Reviews of Effects; GRADE: Grading of Recommendations Assessment, Development and Evaluation; GMFCS, gross motor function classification system; HTA: Health Technology Assessment; ICF: International Classification of Functioning, Disability and Health; MID: minimally important difference; NICE: National Institute for Health and Care Excellence; NGA: National Guideline Alliance; RCT: randomised controlled trial; RoB: risk of bias; SD: standard deviation