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of Physicians

Spasticity in adults: management using botulinum toxin

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Contents

Guideline Development Group	vi
Executive summary	vii
Summary of the recommendations	ix
Acronyms and abbreviations	xiv
1 The guidance development process	1
2 Spasticity – what is it and why does it matter?	3
2.1 Definition and pathophysiology	3
2.2 Epidemiology	3
2.3 Why is it important to treat spasticity?	3
2.4 Describing the effects of spasticity	4
3 Management and treatment of spasticity	6
3.1 Principles	6
3.2 Physical treatment	6
3.3 Pharmacological treatment	7
4 Physical interventions and concomitant therapies	9
4.1 Education	9
4.2 Self-management	9
4.3 Postural management	10
4.4 Stretching	10
4.5 Task training (practice)	11
4.6 Strength training	11
4.7 Electrical stimulation	11
4.8 Summary	12
5 Pharmaceutical interventions	13
5.1 Pharmaceutical interventions for generalised spasticity	13
5.2 Pharmaceutical interventions for regional or segmental spasticity	14
5.3 Pharmaceutical interventions for focal spasticity	14

6	Botulinum toxin in clinical practice	15
6.1	What is BoNT?	15
6.2	How does BoNT-A work?	15
6.3	Licensed products	15
6.4	Presentation, storage and reconstitution	16
6.5	Administration	16
6.6	Dosage	16
6.7	Off-label treatment	17
6.8	Duration of effect	18
6.9	Adverse effects	18
6.10	Contraindications	19
7	Using botulinum toxin to treat spasticity	20
7.1	Summary of key principles for use of BoNT-A	20
7.2	Early intervention	20
7.3	Longer-term treatment	20
7.4	Localisation and distinction of spasticity from contractures	22
7.5	Patient selection	22
7.6	Treatment goals	22
7.7	Muscle selection	22
7.8	Pre-injection patient consultation	24
7.9	Information about the treatment	25
7.10	Injection technique	25
7.11	Post-injection management	27
7.12	Clinical review	27
7.13	Documentation	28
8	Formal evaluation of effectiveness	29
8.1	Focal Spasticity Index	30
9	Prescribing, supply and administration by non-medical injectors (NMIs)	33
9.1	Supply and administration of BoNT-A	33
9.2	Prescribing of BoNT-A	35
9.3	Current practice in the UK regarding BoNT-A for spasticity management	35
10	Organisation of services	37
10.1	Requirements	37
10.2	Service evaluation	38
10.3	Training	38
11	References	40
	Appendix 1: Evaluation of evidence for these guidelines	47
	Background	47
	The GRADE process	47
	Methodology	48
	The NSF typology of evidence	49

Appendix 2: Injection sites for BoNT-A	53
Appendix 3: Tools to assess outcome	64
Structured approach to Goal Attainment Scaling	64
The Numeric Graphic Rating Scale (NGRS)	66
The SPIN Screen	67
Associated Reaction Rating Scale (ARRS)	68
Arm Activity measure (ArmA)	70
Leg Activity measure (LegA)	70
The Spasticity-related Quality of Life tool (SQoL-6D)	75
Global assessment of benefit	77
Appendix 4: Goal Attainment Scaling – how to do it	78
What is GAS and how is it rated?	78
Problems with GAS for use in routine clinical practice	79
Appendix 5: Focal Spasticity Index example proforma	80
Appendix 6: Sample Patient Information Sheet	82
Introduction	82
What are botulinum toxin injections?	82
What is focal spasticity?	82
What are the aims of botulinum toxin injections?	82
What are the alternatives to botulinum toxin injections?	83
How long do the effects last?	83
Are there side effects from botulinum toxin injections?	83
Contact details for advice during working hours	83
General trust information	83
Appendix 7: Methods for prescribing, supply and administration by non-medical injectors	84
Key definitions	84
Supply and administration of botulinum toxin	85
Prescribing of BoNT-A	86
Appendix 8: Physical interventions and physical therapies	89
Passive stretching	89
Active exercise therapies	91
Mental imagery/mental rehearsal/mirror therapy	92
Summary	93
Appendix 9: Conflicts of interest	94
Appendix 10: Summary of evidence	96

Guideline Development Group

The Guideline Development Group comprised the following members and representation:

Member	Representing
Dr Stephen Ashford (chair, editor) Consultant physiotherapist, London North West University Healthcare NHS Trust Clinical lecturer, King's College London	ACPIN CSP
Prof Lynne Turner-Stokes (co-editor) Consultant physician in rehabilitation medicine, Regional Hyperacute Rehabilitation Unit, London North West University Healthcare NHS Trust, Northwick Park; Professor of rehabilitation medicine, King's College London	BSRM RCP
Dr Rhoda Allison Consultant physiotherapist, Torbay and South Devon NHS Foundation Trust	
Ms Lynsay Duke Advanced occupational therapy practitioner, Walkergate Park, Centre for Neurological Rehabilitation and Neuro-Psychiatry, Northumberland Tyne and Wear NHS Foundation Trust	RCOT
Dr Ganesh Bavikatte Consultant physician in rehabilitation medicine, The Walton Centre, Liverpool	
Dr Stephen Kirker Consultant physician in rehabilitation medicine, Addenbrookes Hospital, Cambridge	
Dr Peter Moore Consultant neurologist, The Walton Centre, Liverpool	ABN
Prof Anthony B Ward Consultant physician in rehabilitation medicine, North Staffordshire Rehabilitation Centre, Stoke on Trent	BSRM
Prof Diana Bilton User representative	

Association of British Neurologists (ABN)

Association of Chartered Physiotherapists in Neurology (ACPIN)

British Society of Rehabilitation Medicine (BSRM)

Chartered Society of Physiotherapy (CSP)

Royal College of Occupational Therapists (RCOT)

Royal College of Physicians (RCP)

Executive summary

These national guidelines provide an update to the document published in 2009 (Royal College of Physicians, British Society of Rehabilitation Medicine *et al* 2009).

- Spasticity is involuntary muscle overactivity, which commonly follows damage to the central nervous system (brain and spinal cord). It presents in a variety of ways depending on the size, location and age of the lesion, and may have a number of harmful secondary effects such as pain, deformity and impaired function.
- Spasticity management is challenging due to the diversity of patient presentation and goals or aims of treatment. It will normally include a combination of physical and pharmacological management, often using a variety of different approaches according to the individual patient's needs.
- Local intramuscular injection of botulinum toxin (BoNT) is an established, well-tolerated treatment in the pharmacological management of focal spasticity. There is a strong body of Level I evidence for its effectiveness in the management of both upper and lower limb spasticity.
- The purpose of these guidelines is to provide clinicians with the knowledge and tools to use BoNT appropriately in this context. The principles for successful intervention are:
 - appropriate patient selection
 - establishment of clear goals for treatment
 - clear establishment of the immediate and ongoing treatment programme.
- BoNT is licensed in the UK for treatment of focal spasticity in the arm and leg. It has also become an accepted part of routine management of spasticity in other muscle groups, such as neck and jaw muscles.
- BoNT should only be injected by clinicians experienced in the assessment and management of spasticity. It should not be used in isolation, but as part of a coordinated multidisciplinary approach, involving physical management and therapy, to achieve the desired effect.
- Changes in UK legislation regarding the administration and prescribing of medication mean that, in addition to medical staff, physiotherapists and nurses (and in some instances other allied health professionals) are trained to inject and/or prescribe BoNT and other pharmacological agents used in the management of spasticity. The current arrangements for prescribing, supply and administration of BoNT by non-medical injectors is described in this document.

- The selection of appropriate patients and the definition of clear, achievable, realistic and measurable goals are crucial to the successful use of BoNT in spasticity management. Common goal areas for intervention include:
 - pain relief
 - reduction of involuntary movements (eg associated reactions, spasms)
 - prevention of contractures and deformity
 - passive function (making it easier to care for the affected limb)
 - active function (using the affected limb)
 - mobility.
- Treatment goals should be agreed between the team and the patient and/or their family, and documented.
- All BoNT injections should be accompanied by a formal assessment of outcome. Outcome measures should be relevant to the documented goals for treatment. In the last decade a substantial body of work has been undertaken to develop a consistent approach to outcome measurement that can be used internationally. This includes:
 - a structured approach to Goal Attainment Scaling (GAS) to capture achievement of the intended goals for treatment
 - a Focal Spasticity Index that applies a limited set of standardised measures alongside GAS; the choice of measures for the individual patient being determined by their priority goal areas for treatment.

The rationale for this is to combine a person-centred approach to goal setting and outcome measurement, which provides comparable information across different populations, practices and programmes of care and avoids excessive burden in data collection.

- If used according to the guidance, BoNT has the potential to reduce the overall costs of ongoing care in people with severe spasticity through the prevention of contracture and deformity, and improved ease of care and handling.
- A substantial body of evidence now exists for the overall effectiveness of BoNT in the treatment (reduction) of spasticity. Further research should focus on the totality of what is a complex intervention, and include the physical interventions often applied with pharmacological interventions such as BoNT, in the management of spasticity.

Summary of the recommendations

1 Overarching statement		Grade of evidence*	Strength
1.1	<p>Botulinum toxin type A (BoNT-A) is a safe and effective treatment for upper and lower limb spasticity, resulting in both passive and active functional gains:</p> <ul style="list-style-type: none"> Commissioning of spasticity management programmes should include provision for use of BoNT-A injection, when administered in line with the recommendations below. 	RA E1 E2	Strong

2 Principles of coordinated spasticity management		Grade of evidence	Strength
2.1	The management of spasticity should be undertaken by a coordinated multidisciplinary team (MDT), rather than by individual clinicians working in isolation.	E1 E2	Moderate
2.2	<p>Before using BoNT-A, the team must ensure that:</p> <ul style="list-style-type: none"> all remediable aggravating factors have been addressed an appropriate physical management programme is in place a suitable programme of ongoing coordinated management is planned. 	E1 E2	Strong
2.3	<p>BoNT-A must only be injected by clinicians who have:</p> <ul style="list-style-type: none"> appropriate understanding of functional anatomy experience in the assessment and management of spasticity, and the use of BoNT-A in this context knowledge of appropriate clinical dosing regimens and the ability to manage any potential complications. 	E1 E2	Strong
2.4	BoNT-A injection must be part of a rehabilitation programme involving physical management and/or rehabilitation to achieve an optimal clinical effect.	RA E1 E2	Moderate

3 BoNT-A injection		Grade of evidence	Strength
3.1	Patients should be selected for BoNT-A on the basis of: <ul style="list-style-type: none"> • focal or multi-focal problems due to spasticity • a dynamic spastic component as opposed to contracture • clearly identified goals for treatment and anticipated functional gains (taking into account the risks of any negative impact where patients rely on their spasticity for function). 	E1 E2	Strong
3.2	Patients and their families/carers should: <ul style="list-style-type: none"> • be given appropriate information • have an understanding of the realistic goals and expected treatment outcomes • agree treatment goals before any treatment, including BoNT-A, is given. 	E1 E2	Strong
3.3	Informed consent should be obtained from patients prior to injection. If the patient does not have the mental capacity to consent, current local (eg trust) policies for obtaining consent or making 'best interests' decisions should be followed with reference to the Mental Capacity Act 2005.	E1 E2	Strong
3.4	Clinicians must be aware that different BoNT-A products have different dosage schedules. The current recommended maximum doses per treatment session within licensed usage for spasticity are: <ul style="list-style-type: none"> • 200–240 units (arm); 300 units (leg) BOTOX® • 1,500 units Dysport® (total body dose arm and leg) • 500 units Xeomin® (arm). Clinicians should refer to Appendix 2 for the recommended doses for individual muscles.	A	Very strong
3.5	Electromyogram, electrical stimulation and/or ultrasound should be used to localise the BoNT-A injection, according to the site and purpose of the injection.	RC E1 E2	Moderate

4 Concomitant therapies		Grade of evidence	Strength
4.1	Individuals at risk of contracture or loss of joint range should receive interventions (eg splints, casts or positioning) to provide passive stretch of sufficient duration and intensity when there is still potential for reversibility.	RA E1 E2	Moderate
4.2	Task-practice training (repetitive practice) should be considered when improvement in activity performance and motor control are the target or goal of treatment.	RA E1 E2	Moderate

5 Prescribing, supply and administration by non-medical practitioners		Grade of evidence	Strength
5.1	<p>When provided as part of a multidisciplinary programme, prescribing and injecting of BoNT-A by non-medical practitioners is safe, effective, and potentially highly cost-efficient.</p> <ul style="list-style-type: none"> Providers should consider the development of these roles to support optimal clinical services for patients. Summaries of product characteristics for BoNT-A preparations should be updated to reflect current practice and legislation with respect to non-medical injectors in the UK. 	RB E2	Strong
5.2	<p>Processes for the administration and/or prescription of BoNT-A by non-medical practitioners (eg nurses, physiotherapists and other allied health professionals) are now well established in the UK.</p> <ul style="list-style-type: none"> As for all spasticity interventions, the administration of BoNT-A by medical and non-medical practitioners should be in the context of an MDT decision. Support must be available from a medical clinician who has the appropriate expertise and knowledge of BoNT-A injections, and may provide medical back-up in the event of any complications. Non-medical clinicians with appropriate qualifications and prescribing rights may undertake prescription in accordance with UK statutes. If the clinicians involved do not have prescribing rights, a formal system (such as a <i>Patient Specific Direction</i> or a <i>Patient Group Direction</i>) should be produced to enable the administration of BoNT-A under sound clinical governance principles. Careful attention should be given to the additional training needs of all staff involved, eg sterile intramuscular injection techniques, anatomical assessment. 	E2	Strong

6 Follow-up, documentation and outcome evaluation		Grade of evidence	Strength
6.1	<p>All injections should be followed by:</p> <ul style="list-style-type: none"> • therapy review in 7–14 days for assessment and if necessary orthotics/splinting • MDT review at 4–6 weeks to assess effect and patient status • MDT review at approximately 3–4 months to plan future management (although re-injection intervals may be longer than this, depending on the stage, trajectory and types of goal). 	E1 E2	Moderate
6.2	<p>Injections should be followed by a formal assessment of outcome that includes:</p> <ul style="list-style-type: none"> • severity of presentation at baseline • achievement of intended goals for treatment using Goal Attainment Scaling • standardised measures selected according to the goals for treatment. 	RA E1 E2	Very strong
6.3	<p>Outcome evaluation should be standardised as far as possible to support comparison for quality benchmarking and research.</p> <ul style="list-style-type: none"> • The Focal Spasticity Index described in these guidelines represents a standardised framework incorporating a limited range of widely-used validated measures, classified within the six main goal areas. 	E1 E2	Moderate
6.4	<p>Documentation for all injections should include:</p> <ul style="list-style-type: none"> • patient and carer expectations for outcome • risks of treatment discussed • a clear statement of agreed treatment goals • baseline outcome measures appropriate to those goals • BoNT-A product, batch number, dose, dilution and muscles injected • follow-up treatment plan • evaluation of outcome and repeat measures • plans for future management. 	E1 E2	Strong

7 Services		Grade of evidence	Strength
7.1	Services administering BoNT-A should have access to staff with the relevant expertise and facilities, including adequate space, therapy staff and equipment for splinting/orthotics.	E2	Strong
7.2	Clinicians should have access to facilities to aid assessment, selection and treatment planning, eg electromyography, nerve/muscle stimulation, ultrasound etc.	RC E2	Moderate
7.3	A clinical service should routinely use a single preparation to avoid confusion over dosage and to ensure knowledge of the product characteristics (see Summary of product characteristics at www.emc.medicines.org.uk).	E2	Strong

8 Training		Grade of evidence	Strength
8.1	Clinicians undertaking BoNT-A injection should be able to demonstrate that they have the appropriate competency and training. Training should take the form of supervised clinical practice, supplemented as appropriate by formal accredited courses.	E1 E2	Strong
8.2	Training programmes should be in place to ensure that all relevant disciplines are trained and up to date.	E1 E2	Strong
8.3	Formal evaluation methods should be established to ensure that the necessary knowledge, experience and skills are acquired to perform the procedures and provide a service.	E1 E2	Moderate

9 Future research		Grade of evidence	Strength
9.1	A substantial body of evidence now exists for the overall effectiveness of BoNT-A in the treatment of spasticity. Further research should focus on the gathering of 'practice-based evidence' to inform critical questions such as: <ul style="list-style-type: none"> • Which patients are most likely to respond? • What are the optimum strategies for follow-up therapy in different situations? • What are the real-life benefits for patients and to society in general? 	E1 E2	Strong
9.2	Research should incorporate a range of research methodologies to inform effective and cost-efficient practice in the application of BoNT-A for spasticity management, and should include a standardised approach to outcome evaluation using the Focal Spasticity Index.	E1 E2	Strong
9.3	An agreed framework should be developed for recording data for health economic analyses, including standardised approaches to costing treatment and outcomes, including spasticity-related quality of life for cost-utility analysis.	E1 E2	Strong
9.4	Prospective data should be systematically gathered in the course of routine clinical practice to provide an accurate description of current interventions, together with outcome evaluation.	E1 E2	Strong
9.5	A national system for collection and collation of a minimum dataset based on the information listed in 9.4 above should be developed and implemented, both for the purposes of quality benchmarking and for the assembly of practice-based evidence.	E1 E2	Strong

*The evidence to underpin these recommendations is summarised in Appendix 10.

Acronyms and abbreviations

ACPIN	Association of Chartered Physiotherapists in Neurology
AGREE	Appraisal of Guidelines Research and Evaluation
ArmA	Arm Activity measure
BI	Barthel Index
BoNT	botulinum toxin
BSRM	British Society of Rehabilitation Medicine
CMC	carpometacarpal
CNS	central nervous system
CSP	Chartered Society of Physiotherapy
DB	double blind
eMC	electronic Medicines Compendium
EMG	electromyography
FCR	flexor carpi radialis
FES	functional electrical stimulation
FSI	Focal Spasticity Index
FDA	Food and Drug Administration (United States)
FIM	Functional Independence Measure
GAS	Goal Attainment Scaling
GDG	Guideline Development Group
ICF	International Classification of Functioning, Disability and Health
IP	interphalangeal
LegA	Leg Activity measure
LASIS	Leeds Arm Spasticity Impact Scale
LL	lower limb
MAS	Modified Ashworth Scale
MC	metacarpal
MDT	multidisciplinary team
MS	multiple sclerosis
MT	metatarsal
MTP	metatarsophalangeal

NGRS	Numeric Graphic Rating Scale
NMI	non-medical injector
NMJ	neuromuscular junction
NMP	non-medical prescriber
NSF	National Service Framework
PC-RCT	placebo controlled randomised clinical trial
PGD	Patient Group Directions
PIP	proximal interphalangeal
PSD	Patient Specific Direction
RCOT	Royal College of Occupational Therapists
RCP	Royal College of Physicians
RCT	randomised controlled trial
RMA	Rivermead motor assessment
ROM	range of motion
SMART	specific, measurable, achievable, realistic, timed
SPC	summary of product characteristics
SPIN	Scale of Pain Intensity
TBI	traumatic brain injury
U	units
UL	upper limb
VAS	Visual Analogue Scale
VRS	Verbal Rating Scale
WHO	World Health Organization
WTE	whole-time equivalent

1 The guidance development process

BoNT has an established place in the pharmacological management of spasticity. There is now considerable experience of use, knowledge of its indications, effects and safety in clinical practice.

Guidance for the management of adults with spasticity was first produced in 2001 (Working Party 2001) and was published as part of the Royal College of Physicians' Concise Guidance series in 2002 (Turner-Stokes and Ward 2002). The guidelines were updated in 2009 and published by the Royal College of Physicians as *Spasticity in adults: management using botulinum toxin. National guidelines*.

This document updates the 2009 guidelines (Royal College of Physicians, British Society of Rehabilitation Medicine *et al* 2009). Its purpose is to guide clinical practice in the treatment of adults with spasticity in the correct use of BoNT-A as part of an overall patient management programme; and to provide a background understanding of this complex field of intervention, as well as some practical tools for implementation.

This guidance has been developed in accordance with the principles laid down by the AGREE Collaboration (Appraisal of Guidelines for Research and Development, www.agreecollaboration.org) (St George's Hospital Medical School 2001).

In addition to clinical experience, there is now a substantial body of trial-based evidence for the effectiveness of BoNT-A in reducing spasticity in both the upper and lower limb, which is detailed further in Appendix 10. However, as is often the case, there is little direct trial-based evidence to inform the exact process and context of BoNT-A administration and the surrounding management of spasticity, which are the main focus of this guidance.

Taking this into account, this update used a novel pragmatic methodology for assimilating evidence and grading the recommendations. We used a modified version of the GRADE process, taking a top-down approach to target our literature searches.

Evidence evaluation was conducted using the typology of evidence that was developed for the UK National Service Framework for Long Term Conditions (Department of Health 2005), which is demonstrated to be useful in the evaluation of evidence for recommendations where the literature is expected to include a broad church of research design and expert opinion (Turner-Stokes, Harding *et al* 2006; Baker, Harding *et al* 2010).

The methodology is further described in Appendix 1.

The guidance development process is summarised in Table 1.

Table 1: Summary of the guidance development process

Scope and purpose	
Overall objective of the guidance	To promote the appropriate use of BoNT-A in the management of spasticity, give guidance on its administration and the wider principles of management. This guidance updates: <i>Spasticity in adults: management using botulinum toxin. National guidelines</i> . London: Royal College of Physicians, 2009.
The patient group	Adults with spasticity due to neurological illness or injury.
Target audience	Health professionals involved in the management of spasticity, providers and purchasers of rehabilitation services.
Clinical questions covered	How should patients be selected for treatment with BoNT-A and how should it be administered? What are the principal goals for treatment and how should outcomes be measured?
Stakeholder involvement	
The Guideline Development Group (GDG)	The guidance was instigated by the British Society of Rehabilitation Medicine (BSRM), in association with: <ul style="list-style-type: none"> • Royal College of Physicians, London • Association of British Neurologists • Chartered Society of Physiotherapy • Royal College of Occupational Therapists: Specialist Section Neurological Practice • Association of Chartered Physiotherapists in Neurology In addition, the original guidance was shared widely with user representatives and professional organisations during its development.
Funding	Costs of travel and accommodation for attending meetings, and for guidance production were met by an unrestricted grant to the BSRM, funded equally by all three pharma companies that manufacture BoNT-A licensed for use in spasticity management in the UK.
Conflicts of interest	All authors and group members have declared, and provided details of, any actual or potential conflicts of interest.
Rigour of development	
Evidence gathering	Evidence for this guidance was supported by a systematic review of the clinical trials for BoNT-A in spasticity. In addition, Cochrane Library and Medline searches were conducted by individual members of the group to address specific issues according to their area of expertise.
Review process	Identified studies were reviewed by at least two members of the GDG.
Links between evidence and recommendations	The system used a pragmatic methodology to evaluate evidence and grade recommendations, based on a modified GRADE approach and using the typology that was developed for the UK National Service Framework for Long Term Conditions (2005).
Piloting and peer review	The final draft was widely circulated to all relevant parties and their comments incorporated, together with the results of a pilot exercise on patient referral.
Implementation	
Tools for application	A documentation proforma is included along with some practical examples of outcome measures.
Plans for review	Review is planned in 5 years.

2 Spasticity – what is it and why does it matter?

2.1 Definition and pathophysiology

The term ‘spasticity’ was originally defined by Lance in 1980 (Lance 1980) as a velocity-dependent increase in muscle tone resulting from hyper-excitability of the tonic stretch reflex in people with upper motor neurone (UMN) syndrome following damage to the brain or spinal cord.

If left untreated, a vicious cycle occurs, in which unopposed contraction (spastic dystonia) in the affected muscle groups leads to an abnormal limb posture, resulting in soft tissue shortening and further biomechanical changes in the contracted muscles. This in turn prevents muscle lengthening and perpetuates further stiffness (Burke, Wissel *et al* 2013).

At a clinical level, two main factors contribute to resistance to movement:

- neurogenic component: overactive muscle contraction
- biomechanical component: stiffening and shortening of the muscle and other soft tissues.

In 2005, the SPASM group therefore proposed an alternative definition which recognised spasticity as ‘*a disorder of sensory-motor control resulting from an upper motor neurone lesion, presenting as intermittent or sustained involuntary activation of muscles*’ (Burridge, Wood *et al* 2005).

2.2 Epidemiology

The prevalence of spasticity varies according to the causative pathology.

It is estimated that approximately one-third of post-stroke patients develop symptomatic spasticity (Watkins, Leathley *et al* 2002; van Kuijk, Hendricks *et al* 2007) (overall range 4–42% (Wissel, Schelosky *et al* 2010)) and 60% of patients with severe multiple sclerosis.

Approximately 75% of patients with physical disability following severe traumatic brain injury will develop spasticity requiring specific treatment. Of these, approximately one-third may require treatment with BoNT-A (Verplancke, Snape *et al* 2005).

2.3 Why is it important to treat spasticity?

Spasticity can be painful, distressing, and a potentially costly cause of disability (Ward 2003). Secondary

complications arising from spasticity include impaired movement, difficulty maintaining hygiene and self-care, poor self-esteem and body image, pain and pressure ulcers (see Table 2). These may be distressing for the patient and difficult to manage for carers and health professionals involved in care. In some cases, the secondary complications may interfere with rehabilitation and can increase the cost of both rehabilitation and longer-term care over time.

A successful treatment package, often incorporating physical and pharmacological treatments, can improve physical function and can also prevent secondary complications (Boyd, Pliatsios *et al* 2000; Turner-Stokes, Fheodoroff *et al* 2013; Ward, Wissel *et al* 2014).

It is important to remember, however, that spasticity is not always harmful – sometimes it can even be helpful. For example, patients with a combination of muscle weakness and spasticity may rely on the spasticity to maintain their posture and aid standing or walking. Thus, some patients need little or no treatment. However, spasticity may change over time and therefore requires repeated assessment and management. Treatment is indicated when spasticity causes harm or interferes with function.

2.4 Describing the effects of spasticity

The World Health Organization's International Classification of Functioning, Disability and Health (ICF) is a model to describe the impacts of the health condition on (a) the body, (b) ability to perform activity and (c) participation in society (see Fig 1) (WHO 2001).

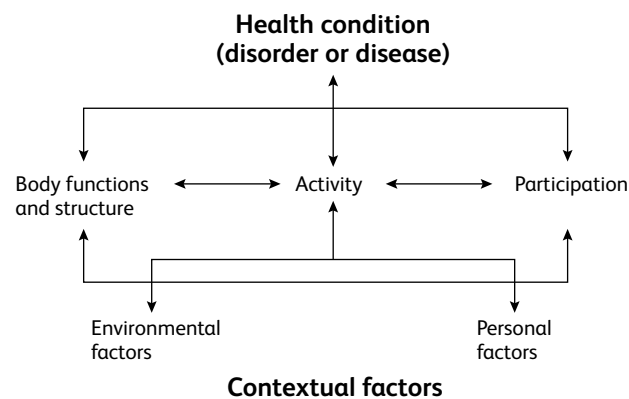


Fig 1: The International Classification of Functioning, Disability and Health

The ICF is a useful framework for describing the impact of disease and the benefits of effective treatment. Given the wide range of unwanted effects of spasticity, the goals for treatment may be highly diverse, depending on the nature of the presentation, trajectory of change (ie towards recovery or deterioration) and the individual's personal aims and aspirations.

In the context of spasticity management, the primary focus of the intervention is typically at the level of impairment (ie to reduce unwanted muscle overactivity). But wherever possible, it is important to demonstrate change at a functional level. Two categories of function have been described in this context (Ashford and Turner-Stokes 2006; Sheean 2008).

Active function	Execution of a functional task by the individual themselves .
Passive function	A task (such as a care activity) performed by a carer for the individual, or to an affected limb by the patient using an unaffected limb.

In some instances the treatment of spasticity may unmask voluntary muscle movement allowing the individual to manage active functional tasks that they were previously unable to perform. More often, however, the underlying weakness of the limb precludes the return to active function. Nevertheless, relieving spasticity may still have important benefits in terms of passive function, making it easier to care for the affected limb. This has been highlighted in both upper and lower limb spasticity (Turner-Stokes, Fheodoroff *et al* 2013; Ward, Wissel *et al* 2014; Wein, Esquenazi *et al* 2015).

Table 2: Harmful effects of spasticity classified according to the WHO ICF

ICF Level	Problem	Effect
Impairment	Muscle spasms	Pain Difficulty with seating and posture Fatigue
	Abnormal trunk and limb posture	Contractures Limb deformity Pressure ulcers/other tissue viability problems
	Pain	Distress and low mood Poor sleep patterns
Activity	Loss of active function	Reduced mobility and dexterity Difficulty with sexual intercourse Difficulty with continence
	Loss of passive function	Difficulty with care and hygiene Increased carer burden Difficulty with wheelchair seating or bed positioning
Participation	Impact of any/all of the above	Poor self-esteem / self-image Reduced social interaction Impact on family relationships Impact on work

Participation and overall quality of life are affected by a wide variety of general and external factors (which include the individual's physical environment and social context). Treatment of focal spasticity is unlikely to impact substantially at this level in most cases, but the effect on self-esteem and family relationships should not be overlooked, even though this may not be detectable by standardised generic quality of life measures.

3 Management and treatment of spasticity

3.1 Principles

Spasticity should be treated when it is causing symptoms or problems for the patient's function or care provision. As noted in Chapter 2, not all spasticity requires treatment. Intervention should be offered only where it is likely to have a meaningful benefit for the patient. Spasticity management should be part of a goal-orientated programme, centred on the patient's priority goals for treatment.

Physical management is fundamental to treatment, aimed at alleviating aggravating factors, symptom relief, improving function and preventing deterioration. BoNT-A is an adjunct to meeting the wider rehabilitation aims of the patient, carer and treating team. It should not be used in isolation, but in parallel with appropriate physical therapy and other anti-spasticity strategies and importantly, postural management programmes.

The management of spasticity is complex and requires a multidisciplinary team (MDT) working together with the patient and family/carers. The MDT clinicians may include:

- medical specialists eg rehabilitation medicine physician, neurologist, geriatrician
- nurse/professional care staff
- therapists: physiotherapist, occupational therapist
- others: rehabilitation engineer, orthotist.

3.2 Physical treatment

3.2.1 Management of aggravating factors

Because spasticity results in part from the abnormal processing of sensory input, nociceptive stimuli such as pain and discomfort will exacerbate and make it harder to treat. Initially therefore, the MDT should identify and eliminate any remedial factors, which may be aggravating spasticity. These include:

- pain or discomfort
- constipation
- infection (eg urinary or respiratory tract infection, pressure sores)
- tight clothing
- poor postural management.

3.2.2 24-hour postural management

Nurses and carers play a key role in spasticity management as they are responsible for positioning and handling of the patient throughout the 24-hour period. Other members of the MDT also play an important role in advising on positioning, providing special seating and postural support systems etc. Education and advice are important for good physical management of spasticity; it takes considerable staff time, and all caregivers need to be involved.

When planning the postural management programme, it should be recognised that the body needs to change position. There is not just one correct position, but a range of different positions that may act to vary the stretch on different muscles and body parts throughout the day. Careful positioning in bed, supported sitting in a wheelchair, periods in a standing frame and splinting/orthotics, all contribute to the maintenance of muscle length and control of spasticity. In addition, these measures reduce the risk of complications such as pressure sores, which may result from abnormal pressure points and shearing forces.

3.2.3 Physical therapy

Physical therapy refers to physical treatments or interventions that are provided by a range of clinicians rather than just those provided or overseen by a physiotherapist. The principal aims of physical therapy are to:

- maintain muscle and soft tissue length across joints
- strengthen weak muscles and facilitate neurological recovery
- facilitate care giving (passive functional improvements)
- facilitate active control of any residual movements to allow for active participation in tasks (active functional improvements).

The physical therapy programme may require input from a range of clinicians, including physiotherapists, occupational therapists and orthotists. It should be directed by professionals with experience in the management of neurological disease. More detail is given in Chapter 4.

3.3 Pharmacological treatment

Physical treatment alone may be insufficient to overcome the effect of increased muscular tone (spasticity) or its mechanical consequences, particularly in moderate to severe spasticity. Pharmacotherapy should therefore be considered early in the management of the patient.

The choice of treatment will depend to some extent on the pattern and distribution of spasticity.

- Intramuscular BoNT-A injections or (less commonly) nerve blockade with phenol in aqueous solution are the pharmacological treatments of choice for focal spasticity.
- If spasticity causes multi-focal problems, BoNT-A may again be helpful, but dose limitations may reduce its long-term effectiveness and additional strategies such as intrathecal baclofen, or a combination of BoNT-A and phenol can be considered.
- Oral anti-spasmodic agents (eg baclofen, tizanidine) may be considered for generalised or segmental spasticity but frequently carry the unwanted side effects of drowsiness and muscle weakness.

However, it is not uncommon to have a mixed pattern of spasticity with both focal and generalised elements. In practice, interventions are often combined – for example BoNT-A may be given to target a specific problem (eg difficulty maintaining hand hygiene) while baclofen is prescribed to manage a background of spasticity.

Fig 2 provides an overview of spasticity intervention incorporating physical and pharmacological intervention. More detail is given in Chapter 5.

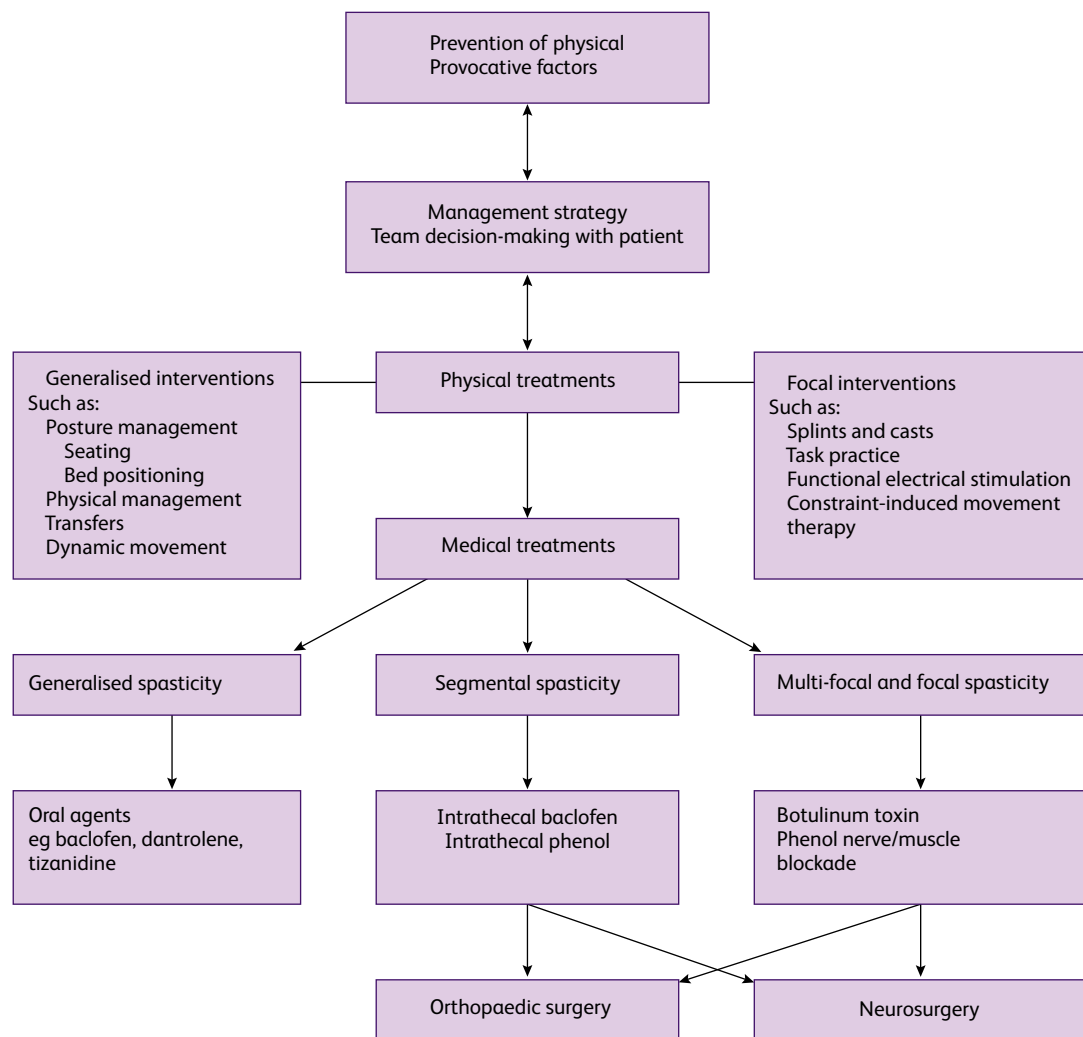


Fig 2: Management strategy for adults with spasticity

4 Physical interventions and concomitant therapies

Management of spasticity should be provided within the context of a wider rehabilitation programme and involve a range of interventions dependent upon the individual's clinical need (Watanabe 2004; Turner-Stokes 2009b; Esquenazi, Novak *et al* 2010; Olver, Esquenazi *et al* 2010; Yelnik, Simon *et al* 2010; Demetrios, Khan *et al* 2013; Sunnerhagen, Olver *et al* 2013).

Spasticity may impact on an individual's ability to use the limb to carry out active functional tasks (active function) or on their ability to care for the limb (passive function). Broadly, physical interventions will act through movement re-education where there is potential for functional use of the limb, and on prevention of adaptive muscle shortening/contracture development – particularly in a non-functional limb.

The evidence for effectiveness of different physical interventions is summarised briefly in Appendix 8. The diversity of presentation and individual goals for treatment present a challenge for randomised controlled studies and other experimental research designs. Although the trial-based evidence for enhanced benefit through a combination of BoNT-A and physical intervention is limited, the benefits of a combined approach are well-accepted in clinical practice.

Spasticity is a long-term condition, and the majority of patients are based in the community. Whether interventions involve movement re-education or passive stretching, most of the actual work is done by the patient and/or their carers, with professionals acting in an advisory capacity. Their engagement is therefore essential, and this can be achieved through communication and discussion to help them choose from the possible options for intervention, and through techniques such as education, self-rehabilitation and goal management training.

4.1 Education

Clear explanation about the physical presentation and the options available for management of spasticity should be provided to patients and/or their carers, as applicable. This should include information about triggers of spasticity, aggravating factors, the impact of medications (including botulinum toxin), and advice about how spasticity can be best managed.

4.2 Self-management

Individual patients and their carers may be able to follow self-management programmes, including positioning, stretching and self-exercise. A clear plan detailing the elements of the programme should be

provided to support individuals in line with their negotiated and agreed goals. Some authors advocate the use of contracts and diaries to maintain motivation (Gracies 2016). These programmes may include postural management, the wearing of splints or orthoses, stretching or strengthening exercises and task training exercises.

4.3 Postural management

Postural management can enhance not only physical comfort, respiration, communication and visual abilities, but help to prevent or limit the development of secondary complications such as adaptive muscle shortening, exacerbation of spasticity, pain, and pressure areas.

A 24-hour approach to postural management requires a planned approach encompassing all activities and interventions that impact on an individual's posture and function (Gericke 2006).

- For immobile patients this typically involves the use of profiling beds, sleep systems, wedges, T rolls, wheelchairs and seating to optimise the position of the head, pelvis, trunk and limbs.
- For ambulant patients, mobility equipment (walking sticks/frames) should be selected carefully and set at the correct height.

4.4 Stretching

Stretching is widely advocated to combat muscle shortening and prevent the development of contractures. However, the limited evidence that exists suggests that to be effective stretch must be applied for several hours per day over a prolonged period – and ongoing in chronic spasticity (Moseley, Hassett *et al* 2008; Katalinic, Harvey *et al* 2010). Debate continues regarding the optimal methods of application and the manner in which improvements may be maintained.

4.4.1 Orthoses – splinting and casting

It is rarely possible to deliver hands-on stretching over a sufficient period of time, so splinting and/or casting are often used to provide a more prolonged stretch.

An 'orthosis' is the general term for all externally applied devices used to modify the structural and functional characteristics of the neuromuscular and skeletal systems by applying forces to the body (College of Occupational Therapists and Association of Chartered Physiotherapists in Neurology 2015). However, in clinical practice the term is commonly used to describe devices provided by orthotists, usually for long-term management.

'Splinting' in spasticity management

- Splints are typically removable devices and can be bespoke or generic and commercially manufactured. They are usually made of moulded plastic or resin and applied to the limb using 'Velcro' straps.
- Casts are bespoke cylindrical devices that enclose the limb circumferentially and are usually made of plaster or fibreglass. Once in place they are typically left on for a period of days or weeks to produce a more consistent stretch. In some cases they may be divided ('bi-valved') to form a removable cast that can be reapplied with strapping.

Despite the paucity of research evidence, splinting and casting continue to be used in clinical practice (Adrienne and Manigandan 2011; Andringa, van de Port *et al* 2013) and are frequently advocated following focal spasticity intervention with BoNT-A. Appendix 8 provides a brief summary of the current evidence, which is explored in more detail in the splinting practice guidelines (College of Occupational Therapists and Association of Chartered Physiotherapists in Neurology 2015).

4.5 Task training (practice)

If an individual has some volitional selective motor control, then more active movement re-education may be indicated. Most interventions to support the recovery of active function involve a form of task practice exercise therapy.

Two Cochrane reviews provide evidence for modest functional improvement from repetitive task training (French, Thomas *et al* 2010; Pollock, Farmer *et al* 2014), and NICE (National Institute of Health and Care Excellence 2013b) found sufficient evidence to recommend that it should be offered to stroke patients. However, the training is intensive, requiring at least 20 hours of practice per week for maximal effect (Pollock, Farmer *et al* 2014), which may limit its uptake in practice.

There is no evidence that people with spasticity suffer adverse consequences following these interventions. It is important to note that exercise therapy does not improve active function in those with no (or very limited) motor control, resulting in weakness. In this instance, goals may be better tailored to passive function (Parry, Lincoln *et al* 1999).

4.6 Strength training

Strength training involves exercise against resistance. Maintaining or improving the underlying strength of muscles through strength training has not been widely researched in brain injury and stroke. Although there was initial caution in using strength training in neurological disorders due to the belief that it may exacerbate spasticity, this is now known not to be the case.

There is now moderate evidence from systematic reviews that progressive strength training in the early phase post stroke can be effective in improving active function and core stability (Ada, Dorsch *et al* 2006; Pollock, Farmer *et al* 2014), but this requires fairly intensive work of approximately 60 minutes of strengthening exercise per week to be effective, as demonstrated in people with multiple sclerosis (Jolk, Alcantara *et al* 2012). Nevertheless, it is recommended by NICE for stroke patients (National Institute of Health and Care Excellence 2013b).

4.7 Electrical stimulation

Electrical stimulation of muscles may be applied for reducing pain, for exercise therapy or as an orthotic in initiation of movement in the upper and lower limb (for example functional electrical stimulation for foot-drop).

One systematic review (Stein, Fritsch *et al* 2015) found sufficient evidence for reduction in spasticity and improved range of movement, to recommend neuromuscular electrical stimulation for patients with post-stroke spasticity, when combined with other treatments.

In addition to its use as an adjunct to physical therapies, there is limited evidence that electrical stimulation of muscle may increase uptake of BoNT-A if used around the time of injection (Hesse S, Reiter F *et al* 1998). The muscle should be stimulated via its motor nerve, which increases turnover and re-uptake of neuronal vesicles to increase uptake of BoNT-A.

4.8 Summary

Management of spasticity should be provided within the context of a wider rehabilitation programme and involve a range of specific physical interventions dependent upon the individual's clinical need. A variety of therapeutic physical interventions may also help to specifically improve the uptake or effectiveness of BoNT-A, including the provision of stretch, electrical stimulation and repetitive task training, and these should be considered as part of the overall programme.

The choice of intervention will depend on the stage of each individual's rehabilitation journey, their retained abilities and presenting impairments. Clinicians should consider the likelihood of achieving active or passive functional outcomes, and take an evidence-based approach to identify the most appropriate intervention to achieve the intended goals for treatment.

5 Pharmaceutical interventions

While the focus of these guidelines is on treatment of focal spasticity with BoNT-A, this is in the context of wider rehabilitation and other options for managing spasticity should also be considered when appropriate (see Fig 2).

5.1 Pharmaceutical interventions for generalised spasticity

Oral antispasmodic medication may be used to provide a systemic effect for generalised spasticity. The agents currently licensed for treating spasticity in the UK are baclofen, tizanidine, dantrolene and diazepam. These are most useful for more widespread spasticity of modest severity, but their maximum effect may be limited by sedation, muscle weakness or occasional liver toxicity.

Off-label, gabapentin is also recommended as first or second line treatment for spasticity in UK National Guidelines for Multiple Sclerosis (National Institute of Health and Care Excellence 2014) based on evidence of randomised controlled trials (Cutter, Scott *et al* 2000). There is also anecdotal evidence for pregabalin and levetiracetam in spasticity (Hawker, Frohman *et al* 2003; Braid, Kirker *et al* 2013). While they cannot be recommended for off-label use, these medications are in very common usage respectively for neuropathic pain and epilepsy in the context of acquired brain injury, and so patients may still benefit from their dual effects.

Clonidine is widely discussed in American literature (Brashear and Elovic 2010), but is currently little used in the UK to treat spasticity. Like tizanidine, it is an imidazoline, acting on alpha 2 noradrenergic receptors, but unlike tizanidine, a transdermal preparation is available, for which there is some evidence of efficacy in spasticity (Weingarden and Belen 1992; Yablon and Sipski 1993). It may provide an option for patients with generalised spasticity, who are unable to take an effective dose of oral medication.

Sativex (delta-9-tetrahydrocannabinol, cannabidiol) is the first new drug to be licensed for treating spasticity since tizanidine in 1997, as an add-on therapy, in patients with refractory spasticity caused by multiple sclerosis (Novotna, Mares *et al* 2011). In a meta-analysis of the efficacy and safety of Sativex on spasticity in people with multiple sclerosis (Wade, Collin *et al* 2010), a minority of patients were shown to have a very useful and sustained response. However, many showed no benefit, and NICE have not supported its use in England. It is sprayed onto the lining of the cheek, limiting its use to patients who can participate and tolerate the very unpleasant taste.

All off-label use of systemic medications may be considered as a last resort in refractory spasticity but, as always, clinicians should follow relevant guidance for off-label prescribing (General Medical Council 2013), taking full responsibility for the decision. Informed consent should be obtained and documented.

5.2 Pharmaceutical interventions for regional or segmental spasticity

Patients with regional or segmental spasticity may benefit from intrathecal administration. This offers the advantage of delivering the medication directly to where it is needed, and reducing the unwanted side effects – particularly drowsiness and impaired cognition, which can be dose-limiting factors for oral medication.

Intrathecal baclofen therapy has been available for 30 years, and is now routinely commissioned by NHS England. It is very effective for regional spasticity in the lower limbs and trunk (Furr-Stimming, Boyle *et al* 2014). Implantable pumps have become more sophisticated, and can now be programmed to deliver a variable dose to manage changing needs over the 24-hour period. The dose and degree of muscle weakening can be adjusted to permit some patients with residual strength to walk more easily, once their spasticity has been reduced. Intrathecal baclofen can reduce autonomic storming in people with brain and spinal cord injury, but helps only a few people with severe dystonia (Furr-Stimming, Boyle *et al* 2014).

Significant disadvantages of intrathecal pumps include the risk of infection and the need to attend clinics every 3 months or so to have the pump refilled. For patients with troublesome spasticity who have lost voluntary control of lower limbs, bladder and bowel, intrathecal phenol in glycerol solution may represent a simpler alternative (Jarrett and Thompson 2002; Gaid 2012), which avoids the risk of surgery and the burden of frequent trips to the hospital.

5.3 Pharmaceutical interventions for focal spasticity

Although their popularity has waned in favour of intramuscular BoNT-A, peripheral nerve blocks with phenol (6% in aqueous solution) still represent an alternative solution for some patients. They offer the advantage over BoNT-A of causing a greater degree of muscle relaxation for much longer and at much less expense, although they also produce more profound weakness.

Phenol may cause neurogenic pain or paraesthesia if applied to a mixed motor/sensory nerve, so it is safer and most useful for pure motor nerves, such as posterior tibial and obturator nerve blocks in the lower limb, or musculocutaneous blocks in the upper limb.

Careful localisation is required using a nerve stimulator, so phenol nerve blocks should only be used in experienced hands. However, they may have a place in the treatment of patients with troublesome spasticity and dystonia of hip adductors and calf muscles, especially for non-ambulant patients or ‘walkers’ who are already dependent on an ankle–foot orthosis (AFO) (Gaid 2012). They are particularly appropriate for patients in nursing homes in the palliative stage of their disease.

Phenol may also be used to target muscles innervated by mixed nerves, by injecting at the motor point: this is most often used for hamstrings, but can also be used in the upper limb (Roy 2012).

6 Botulinum toxin in clinical practice

6.1 What is BoNT?

BoNT is produced by the bacterium *Clostridium botulinum*. Various strains have been found to produce seven antigenically distinct protein neurotoxins labelled types A–G (Hambleton and Moore 1995). BoNT type A is a powerful neurotoxin that has been developed into a therapeutic agent.

6.2 How does BoNT-A work?

The botulinum neurotoxins all exhibit similar pharmacological activity. They prevent the release of acetylcholine from the pre-synaptic nerve terminal, thus blocking peripheral cholinergic transmission at the neuromuscular junction (NMJ). This results in a reduction in muscle contraction, and a dose-dependent reversible reduction in muscle power. Active NMJs take up BoNT-A more avidly than NMJs at rest. BoNT-A also blocks gamma-efferent fibre NMJs in muscle spindles and thus probably reduces reflex sensitivity.

The clinical effects are temporary, lasting for 3–4 months. The toxin degrades and becomes inactive within the nerve terminal (Hambleton and Moore 1995; Hambleton, Pickett *et al* 2007). The NMJ atrophies and then regenerates with re-sprouting. The muscle weakness resolves over 3–4 months.

6.3 Licensed products

A **licensed medicine** is a medicine with a valid marketing authorisation (product licence) in the UK. Licences apply to a particular product and indications, which are summarised in the ‘Summary of product characteristics’ (SPC). Use of a medicine outside its licensed indications (as contained within the SPC) is described as ‘off-label’. Off-label use only applies to medicines that are already licensed, ie hold a valid marketing authorisation.

This guidance refers to the use of BoNT-A for skeletal muscle spasticity in general, and not to a particular product. Product-specific advice is given only in relation to those products currently licensed for spasticity management in the UK.

BOTOX®, Dysport®, and Xeomin® are type-A toxins that are all licensed for the treatment of adult focal spasticity in the UK. In the USA, the Food and Drug Administration (FDA) has allocated generic names (given in brackets below) to each product as they are considered to be distinct biological agents. In the UK:

- BOTOX® (OnabotulinumtoxinA) is licensed for the treatment of focal spasticity, including wrist, hand and ankle disability due to stroke in adults.
- Dysport® (AbobotulinumtoxinA) is licensed for the treatment of focal spasticity of the arm, and for leg spasticity affecting the ankle in stroke and traumatic brain injury.
- Xeomin® (IncobotulinumtoxinA) is licensed for treatment of spasticity of the arm in adults.

All three products covered by these guidelines are licensed for treatment of spasticity in the UK. However, it is evident from the information above that the current UK licensing arrangements vary between products. They are quite narrow, being restricted to certain muscle groups and in some cases to certain conditions (eg stroke). However, there is evidence to indicate that BoNT injection, which is technically outside the defined terms of the licence, may be clinically effective and safe (Turner-Stokes, Fheodoroff *et al* 2013; Ward, Wissel *et al* 2014; Wissel, Bensmail *et al* 2017). Nevertheless, the use of products in these situations is still not covered by the terms of the licence and is classified as off-label.

6.4 Presentation, storage and reconstitution

BOTOX® and Xeomin® are currently available in vials of 50, 100 and 200 units, and Dysport® in vials of 300 and 500 units.

Unopened vials of BOTOX® and Dysport® should be stored at temperatures between 2–8°C.

- BOTOX® can be stored at or below -5°C.
- Dysport® should not be frozen.
- Unopened vials of Xeomin® can be stored and transported at room temperature, but not above 25°C.

Vials of toxin should be reconstituted using normal saline. Vigorous shaking and flushing through needles should be avoided.

Once reconstituted, BOTOX®, Dysport® and Xeomin® are stable for up to 24 hours if kept in a refrigerator at 2–8°C, but care is required to avoid microbacteriological contamination. If used in the community, appropriate measures must be taken to keep these products within the correct temperature range.

6.5 Administration

BoNT-A is injected intramuscularly into selected muscles. Although it can diffuse through muscle fascial barriers, its effect is concentrated in the injected muscles so that it is possible to generate highly focal weakness (Aoki 1999). The injections do not have to be placed precisely in the motor end-plate zone as BoNT-A diffuses to some extent within the muscle. (See Chapter 7 for further details on injection technique). However, injections placed close to motor end-plate zones may be more effective. See Appendix 2 for information on injection of specific muscles.

6.6 Dosage

BoNT-A doses are measured in units (U) intended to standardise doses (Hatherway and Deng 1994). Nevertheless, the various BoNT-A preparations that are commercially available have different dose schedules. The doses are **not interchangeable** with each other (see summary of product characteristics on

www.emc.medicines.org.uk) (eMC). Individual manufacturer's guidance should be followed. There is no agreed consistent dose conversion ratio between preparations.

It is essential to select the correct dose schedule (see Appendix 2). Early reports of BoNT-A trials commonly did not specify the preparation used. One report used the term 'Botox' as a generic word when in fact the study used Dysport® (Dengler, Neyer *et al* 1992). Some studies have combined results from patients using different preparations. It is the responsibility of the clinician administering the botulinum toxin to ensure that the name of the botulinum toxin preparation used is correctly documented in the clinical notes.

In general, larger doses carry increasing risk of systemic adverse effects, but in addition there is potential concern about causing local weakness in muscles required for vital function – in particular swallowing and respiration, especially when using BoNT-A in the neck or proximal upper limb muscles.

The maximum recommended dose in limb spasticity is 1500 units Dysport® for the arm and leg in a single adult injection session (leg or arm, or arm and leg treated together). For Xeomin® the maximum recommended dose in arm spasticity is 500 units in a single adult injection session, and no more than 250 units should be administered to the shoulder muscles. For BOTOX® the maximum recommended dose is 200 to 240 units in the arm or 300 units in the leg in a single adult injection session. There are reported instances of higher doses being used without adverse effects, especially in non-naïve patients, but clinicians should be aware that larger doses carry increasing risk of systemic adverse effects and make sure that appropriate arrangements are in place for monitoring and managing any adverse effects. There is one report of patients occasionally developing systemic symptoms at moderate doses after many previous injections of similar doses (Bhatia, Munchau *et al* 1999). However, this is rare.

Experience has generated 'standard' doses which are generally well-tolerated, and which work for most patients. Generally, large, hypertrophied or highly active muscles need larger doses, and smaller, less active muscles or lightweight patients need smaller doses. The degree, and to some extent duration of weakness, are dose-dependent.

The dose should be reduced if the target muscles are already weak, or if there is an increased risk of side effects in an individual patient. Pre-existing local tissue disruption (recent trauma or infections) or conditions causing systemic weakness (such as myopathy, myasthenia gravis, motor neurone disease, or neuropathy) should provoke extreme caution, but are not absolute contraindications (Moore and Naumann 2003).

6.7 Off-label treatment

Because of the diversity of presentation and individual goals for treatment, it has been noted in several large observational cohort studies that many treatments with BoNT-A are 'off-label', in that they do not follow the SPC precisely (Esquenazi, Mayer *et al* 2012; Turner-Stokes, Fheodoroff *et al* 2013).

SPCs are more up to date for some products than others, but have generally failed to keep up with clinical practice. This is not surprising as it takes a substantial evidence base (typically of randomised controlled trials (RCTs)) to change an SPC and it is neither practical nor feasible to conduct RCTs in all the situations in which BoNT-A is applied. **Therefore, off-label usage should be permitted in the interests of progression in clinical understanding of the effective uses of BoNT.** However, clinicians

should be aware when they are using the products off-label, and ensure that the justification for this is discussed with the patient and is documented.

6.8 Duration of effect

BoNT-A is taken up by the NMJ within 12 hours (Schiavo, Benfenati *et al* 1992), and its clinical effect occurs gradually over 4–7 days, occasionally longer. It interferes with neuromuscular synaptic transmission for 12–20 weeks, and causes clinically detectable weakness for 3–4 months in most situations (Aoki 1999; Simpson, Hallett *et al* 2016). The weakened muscles recover their activity after cessation of the BoNT-A activity. This recovery can be an advantage when a BoNT-A injection gives an unexpectedly poor result, but has the disadvantage that the injection may need to be repeated for prolonged effect (Ward and Barnes 2007). The clinical benefit can persist for many months (particularly when accompanied by an appropriate physical management regimen) and wears off gradually. Repeat injections generally follow a similar course.

Experience in other neurological conditions has demonstrated that patients may become biologically resistant to BoNT-A as a result of antibody formation, especially with frequent, large dose injections (Greene and Fahn 1992; Greene and Fahn 1993; Hambleton and Moore 1995). This has led to the general advice to avoid repeated injection at less than 3-monthly intervals. However, modern preparations of toxins may be less immunogenic, for example the current preparation of BOTOX® is potentially less immunogenic than the original preparation of BOTOX® for clinical use.

Although secondary non-response is theoretically an issue for the use of BoNT-A in spasticity, it is rarely reported in practice. This may be because spasticity is often self-limiting in the course of natural recovery, eg following stroke or brain injury, so that long-term repeated injections are required for only a minority of patients. Advice regarding repeat injections may therefore be different for the post-acute situation, as opposed to chronic spasticity management, and is further discussed in Chapter 7.

6.9 Adverse effects

Serious adverse events are rare, but mild and transient adverse effects may occur; for a full list clinicians should refer to the product SPC at: www.emc.medicines.org.uk (eMC). However, they may include:

- **Local muscle weakness** from toxin spread to nearby muscles. This may cause temporary functional loss. Local muscle atrophy may occur. Rarely, more generalised muscle weakness may be seen, particularly if high doses are given in multiple muscles (Bakheit, Ward *et al* 1997).
- **Dysphagia** occurs mainly when high doses are used around the neck or proximal upper limb. Nevertheless, it should be remembered that patients with brain injury or stroke may have impaired swallowing reflexes. Care should be taken when injecting larger doses of BoNT-A in patients with a history of dysphagia, especially if they do not have percutaneous gastrostomy (PEG) feeding tubes. Some patients with spastic or dystonic dysphagia may improve.
- **Respiratory failure** has not been reported in adults, although there have been isolated case reports in children with cerebral palsy. Nevertheless, it remains a theoretical risk for higher dose treatments, and should be considered when planning injections for patients with profound neuromuscular compromise.

- **Autonomic dysfunction**, if it occurs, is almost always sub-clinical. Once again, however, it is something to bear in mind in patients who may already have a degree of autonomic dysfunction, eg some patients with Parkinson's disease or diabetes.
- **'Flu-like' symptoms** for up to a week, at some point in the month after injection. These are transient and mild.
- **Other rarely reported side effects** are rashes, altered taste, and brachial neuritis (very rare) following local injections.

These adverse effects are self-limiting and do not appear to affect the activity of BoNT.

The peak period for adverse effects is usually at 2–4 weeks post-injection. The same dose and pattern of injections can produce variable results in different cycles, with adverse effects occurring even after several apparently identical and successful injections. Similarly, subsequent exposure to BoNT-A does not always reproduce side effects seen on earlier occasions, but it may be prudent to adjust the dose and pattern of injections.

Clinicians should inform patients and family practitioners of the possible adverse effects and should take steps to minimise or avoid them by modifying the subsequent injections. Where BoNT-A is administered or prescribed by non-medical injectors, specific arrangements must be in place for medical back-up in case a significant adverse event occurs, however unlikely this may be.

6.10 Contraindications

For a full list of contraindications and special warnings and precautions for the use of BoNT, clinicians should refer to the product SPC at: www.emc.medicines.org.uk (eMC).

7 Using botulinum toxin to treat spasticity

7.1 Summary of key principles for use of BoNT-A

- BoNT-A is useful in the management of focal spasticity, whether of cerebral or spinal origin (Jankovic and Schwartz 1995), but it should be used as part of an integrated multidisciplinary approach and accompanied by a rehabilitation programme.
- BoNT-A should be used to address specific functional limitations resulting from focal spasticity (ie muscle overactivity confined to one or a group of muscles that contribute to a specific functional problem).
- BoNT-A will not recover lost function, except where that function has been lost due to antagonist muscle overactivity.

7.2 Early intervention

BoNT-A has been shown to provide a sustained reduction in post-stroke upper-limb spasticity when combined with rehabilitation in patients as early as 2–12 weeks after the stroke (Rosales, Kong *et al* 2012). Functional use of the arm and hand was not adversely affected.

BoNT-A can result in long-term gains in people with sudden onset neurological conditions such as stroke. If used appropriately in the early phases of rehabilitation, it may prevent soft tissue shortening arising from the combined effect of spasticity and limb immobility. This may potentially help to avoid learned disuse and facilitate neurological recovery. For example, in some patients with regional spasticity (eg a paretic upper limb), a one-off serial approach with injections into several different muscle groups over a relatively short time window (6–12 weeks) has been reported to be successful in curtailing upper limb spasticity, and has led to a good functional recovery in a small number of cases (Turner-Stokes and Ashford 2007).

7.3 Longer-term treatment

In people with severe and long-standing spasticity, the focus will be more on symptom control or passive function outcomes such as pain relief or wearing of splints (Ashford and Turner-Stokes 2006; Turner-Stokes, Kheodoroff *et al* 2013). For example, severe flexion deformity of the fingers as a result of spasticity may cause pain, affect hand hygiene and cause skin breakdown. In these people, repeated BoNT-A treatments may be required over several years. Careful attention to physical management in between injections can help to reduce the frequency of BoNT-A treatments, and reduce the likelihood of secondary non-response. Here the general advice of avoiding repeat injections within 3 months should be adhered to.

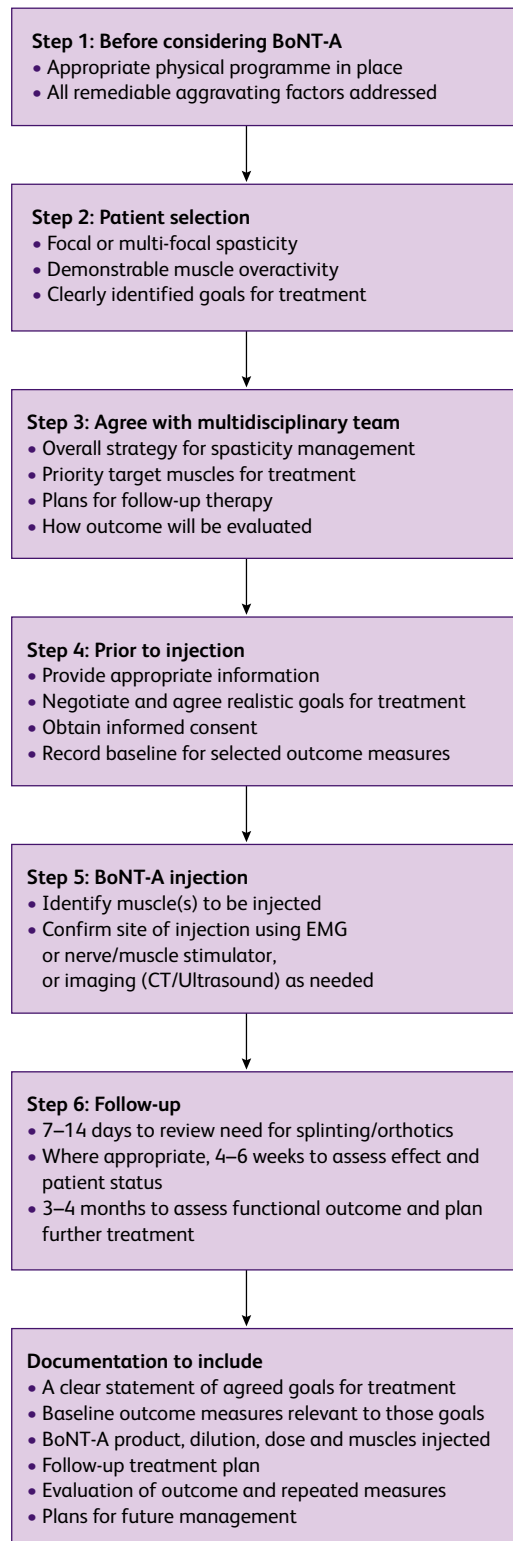


Fig 3 Key steps to treatment of spasticity with BoNT-A

7.4 Localisation and distinction of spasticity from contractures

Severe spasticity is often difficult to differentiate from contracture. Electromyography (EMG) may be useful to identify the presence of unwanted muscle activity during passive and active movement as well as during effortful activity to identify associated reactions. EMG may also be very useful to differentiate spasticity from contracture. Examination under anaesthesia or sedation may be useful to assess the presence of contracture, for which other interventions may be more appropriate.

Fig 3 summarises the key steps to treatment of spasticity with BoNT-A.

7.5 Patient selection

Appropriate patient selection is crucial to the successful treatment of spasticity. Patients must have focal or multi-focal spasticity with demonstrable evidence of muscle overactivity and there must be clearly agreed goals for treatment. Table 3 provides a checklist for selection.

Table 3: Patient selection checklist

What is the problem and is it amenable to treatment with BoNT-A?
Is the problem a result of focal spasticity; if so, which muscles are involved?
Is BoNT-A the most appropriate treatment?
Are there any contraindications to BoNT-A injection?
Have treatment goals been identified and agreed with the patient and treating MDT?
Who will provide the ongoing physical treatment and monitoring?
How will treatment outcomes be evaluated and will the measures used be appropriate?
Has the patient consented to treatment, or does the family assent on their behalf?

7.6 Treatment goals

The first step is to consider the likely outcomes from treatment. In some cases, active functional goals may be appropriate, but there may also be important gains to be made in terms of passive function or avoiding progression of impairment. Goals analysis from four large studies have identified six common categories for treatment goals (Ashford, Fheodoroff *et al* 2016). These are shown in Table 4.

7.7 Muscle selection

Identifying the cause of the problem is fundamental to planning treatment. It is important to distinguish between spasticity and weakness because, although both cause limb deformity, their treatment differs considerably (Richardson, Greenwood *et al* 2000). Spasticity usually involves several muscles and may occur in common postural patterns. The MDT will need to consider the predominant active muscles in relation to the intended goals for treatment (see Table 5).

Knowledge of functional anatomy and the action of muscles is essential. Muscle selection and the order/priority of treatment should be agreed between the treating clinician and the MDT.

Table 4: Treatment goals

Principal ICF domains	Key goal areas (ICF codes)
Domain 1: Symptoms and impairment	1. Pain/discomfort/stiffness (b280, b780, b134) 2. Involuntary movements (b760, b765) 3. Impairment (prevention of contractures) (b710, b735)
Domain 2: Activities (active and passive function)	4. Passive function (caring for the affected limb), (d520) 5. Active function (using the affected limb in some motor task) (d430, d440, d445) 6. Mobility (d415, d450)
Other	<ul style="list-style-type: none"> • Cosmesis (improving body image) • Facilitation of therapy

ICF= International Classification of Functioning, Disability and Health

Table 5: Common patterns of spasticity and treatment benefits

Pattern	Muscle involved	Benefits
Upper limb		
Shoulder adduction, internal rotation and retraction¹	<ul style="list-style-type: none"> • Pectoralis major • Latissimus dorsi • Teres muscle group • Subscapularis • Rhomboids and interscapular muscles 	<ul style="list-style-type: none"> • Sitting posture • Ease of dressing • Axillary hygiene • Improve balance and symmetry of gait and can sometimes help to reduce unwanted spasticity in the elbow and hand
Elbow flexion²	<ul style="list-style-type: none"> • Biceps brachii • Brachialis • Brachioradialis 	<ul style="list-style-type: none"> • Improve flexion deformity • Improve reach/retrieve
Pronation of the forearm³	<ul style="list-style-type: none"> • Pronator teres • Pronator quadratus 	<ul style="list-style-type: none"> • Hand function
Flexed wrist and clenched hand⁴	<ul style="list-style-type: none"> • Flexor carpi ulnaris and radialis • Flexor digitorum superficialis and profundus • Flexor pollicis longus 	<ul style="list-style-type: none"> • Maintain palmar skin hygiene • Improve grasp release

1 Turner-Stokes and Ashford 2007; Esquenazi, Albanese *et al* 2012; Turner-Stokes, Fheodoroff *et al* 2013; Ward, Wissel *et al* 2014; O'Dell, Brashear *et al* 2017; Simpson, Patel *et al* 2017

2 Simpson, Gracies *et al* 2009; Shaw, Rodgers *et al* 2010; Turner-Stokes, Baguley *et al* 2010; Shaw, Price *et al* 2011; Esquenazi, Albanese *et al* 2012; Rosales, Kong *et al* 2012; Turner-Stokes, Fheodoroff *et al* 2013; Ward, Wissel *et al* 2014; Simpson, Patel *et al* 2017

3 Turner-Stokes, Baguley *et al* 2010; Esquenazi, Albanese *et al* 2012; Turner-Stokes, Fheodoroff *et al* 2013; Ward, Wissel *et al* 2014; Simpson, Patel *et al* 2017

4 Simpson, Gracies *et al* 2009; Shaw, Rodgers *et al* 2010; Turner-Stokes, Baguley *et al* 2010; Shaw, Price *et al* 2011; Esquenazi, Albanese *et al* 2012; Rosales, Kong *et al* 2012; Turner-Stokes, Fheodoroff *et al* 2013; Ward, Wissel *et al* 2014; Simpson, Patel *et al* 2017)

Table 5 – continued

Pattern	Muscle involved	Benefits
Lower limb		
Thumb in palm, intrinsic muscles⁵	<ul style="list-style-type: none"> • Opponens pollicis, adductor pollicis, flexor pollicis brevis, lumbricals, interossei 	<ul style="list-style-type: none"> • Improve grasp and hand opening
Hip adductor⁶	<ul style="list-style-type: none"> • Adductor magnus, longus and brevis 	<ul style="list-style-type: none"> • Improve 'scissor gait' • Ease of perineal hygiene and urinary catheterisation • Easier sexual intercourse
Hip and knee flexion⁷	<ul style="list-style-type: none"> • Psoas major, iliacus, medial hamstring group (gracilis, semi-tendinosus, semi-membranosus), biceps femoris 	<ul style="list-style-type: none"> • Improve weight bearing • Improve gait pattern and seating posture
Knee extension⁸	<ul style="list-style-type: none"> • Quadriceps group 	<ul style="list-style-type: none"> • Seating posture (note potential to worsen sit to stand and standing)
Plantar flexed and inverted foot⁹	<ul style="list-style-type: none"> • Gastrocnemius, soleus and posterior tibialis 	<ul style="list-style-type: none"> • Correct equinus deformity, and foot inversion to allow heel strike
Toe clawing¹⁰	<ul style="list-style-type: none"> • Flexor hallucis longus, flexor digitorum longus 	<ul style="list-style-type: none"> • Ease of donning footwear and comfort
Hyperextension of great toe¹¹	<ul style="list-style-type: none"> • Flexor hallucis longus • Extensor hallucis longus 	<ul style="list-style-type: none"> • Ease of donning footwear and comfort

5 Simpson, Gracies *et al* 2009; Esquenazi, Albanese *et al* 2012; Turner-Stokes, Fheodoroff *et al* 2013; Ward, Wissel *et al* 2014; Simpson, Patel *et al* 2017

6 Snow, Tsui *et al* 1990; Hyman, Barnes *et al* 2000; Olver, Esquenazi *et al* 2010; Esquenazi, Albanese *et al* 2012

7 Olver, Esquenazi *et al* 2010; Esquenazi, Albanese *et al* 2012; Ward, Wissel *et al* 2014; Wein, Esquenazi *et al* 2015

8 Olver, Esquenazi *et al* 2010; Esquenazi, Albanese *et al* 2012; Ward, Wissel *et al* 2014; Wein, Esquenazi *et al* 2015

9 Das and Park 1989; Burbaud, Wiart *et al* 1996; Kaji, Osako *et al* 2010; Olver, Esquenazi *et al* 2010; Esquenazi, Albanese *et al* 2012; Wein, Esquenazi *et al* 2015

10 Olver, Esquenazi *et al* 2010; Esquenazi, Albanese *et al* 2012

11 Olver, Esquenazi *et al* 2010; Esquenazi, Albanese *et al* 2012

7.8 Pre-injection patient consultation

7.8.1 Agreed goals for treatment

Patients often have high expectations of functional gain. Before treating with BoNT-A, the treatment goals and expected outcomes should be negotiated and agreed with the patient and their family to ensure that the expected outcome is realistic and worthwhile. All parties should be clear about what is involved, and the need for compliance and commitment to the subsequent therapy. The procedure for Goal Attainment Scaling (GAS) described in Appendix 4 can be a helpful step in the negotiation of realistic goals.

7.9 Information about the treatment

The clinician should explain to the patient, their family or carers what the treatment will entail; which muscles, the number of injections, the potential benefits and adverse effects, and the importance of following the advice from the MDT. Liaison is required with the local team if the patient is being treated by a team other than the injecting centre. Written information given to patients should be in an accessible format.

7.9.1 Consent

The treating clinician must obtain informed consent from the patient prior to the injection and take account of appropriate ethical issues including those relating to the Mental Capacity Act (England & Wales) 2005, Mental Capacity Act (Northern Ireland) 2016 or Adults with Incapacity (Scotland) Act 2000.

It is advised, wherever possible, to inform patients and/or their carers when the planned treatment is ‘off-label’ for the product used. However, this information is highly technical and patients with cognitive/communicative problems may simply find the information confusing and be none the wiser. In practice, the amount of information to give is a matter for clinical judgement, weighing up the likely risks of the treatment.

An example of a Patient Information Sheet is included in Appendix 6.

7.9.2 Anti-coagulation

Many patients who have had a stroke may be on medications to treat or prevent thromboembolism. All anticoagulants (including aspirin, clopidogrel, other antiplatelet medication, warfarin, low molecular weight heparin or newer oral anticoagulants (novel oral anticoagulants – NOACs)) can increase the risk of bruising and bleeding at the injection site.

BoNT-A injections can often be given safely to patients on thromboembolic prophylaxis but may require modification of the injection technique such as using the smallest needle possible, and avoiding multiple pass injections or excessive exploration with electromyography (EMG) needles.

For patients on full anticoagulation regimens (such as treatment doses of heparin, warfarin or NOACs), caution should be exercised when considering injection. It may be appropriate to consider temporarily stopping these medications, but the risk of doing this needs to be carefully weighed against the benefits likely from the injection. For warfarin, many clinicians would suggest not injecting in patients with an INR >3, especially for deeper muscles, due to the increased risk of intramuscular bleeding. For this group of patients, case-by-case risk analysis is required to weigh up the need and likely benefits of injection against the risks of lowering the INR or stopping anticoagulation for that particular individual.

7.10 Injection technique

The BoNT-A injection must be prepared according to the manufacturer’s instructions and the appropriate disposal facilities should be available for unused BoNT-A.

7.10.1 Planning and siting of injections

The planning and siting of the injections should be undertaken by the clinician in consultation with the rest of the MDT. A variety of localisation techniques is available to assist correct placement of the injection, including EMG, nerve or muscle stimulation and imaging, using ultrasound or occasionally, CT scanning.

Even though some of the larger superficial muscles may be identified with knowledge of surface anatomy, localisation techniques may still be helpful – especially in the presence of adipose tissue, or where normal anatomy is distorted. For smaller, less accessible muscles, localisation techniques are essential to ensure correct placement of the injection.

The choice of localisation technique is dependent to some extent on operator choice.

- EMG can be used to confirm placement within the muscle and the presence of muscle activity (Keenan, Haider *et al* 1990). This can be particularly useful where there is doubt about which muscles are the most active.
- Nerve or muscle stimulation can be used to confirm placement by producing a ‘twitch’ in the target muscle. This can be particularly useful for pinpointing specific muscles when these are targeted for rebalancing, for example to improve fine motor function in the hand.
- Imaging can be used to visualise muscle and needle placement, and to avoid other structures such as nerves or blood vessels. It is particularly useful for distorted anatomy and is painless (unlike the other localising techniques). However, the equipment costs are considerable.

The best sites for injection are theoretically the nerve end-plate zones deep in the muscle bulk. The patterns of end-plate zones are not yet clearly mapped, but it is not necessary to make multiple passes using needle EMG looking for their subtle, characteristic electrical signature. In most cases, BoNT-A diffuses sufficiently from the site of injection to make this unnecessary.

Small and moderate-sized muscles will usually respond to BoNT-A injected simply into the belly of the muscle. Injection location is often not critical perhaps because BoNT-A tends to ‘seek out’ the active NMJ. Although there is some diffusion through muscle fascia (Shaari, George *et al* 1991; Shaari and Sanders 1993), muscles with well-delineated separate components such as quadriceps need separate injections for each major section. Conversely, unwanted muscle weakness can occur in adjacent muscles because of this diffusion. This needs to be explained to the patient. Muscles with fibres arrayed in parallel may be more effectively weakened by multiple injections transversely across the muscle belly, while muscles with fibres arranged longitudinally may require a spread of injections along their length (Moore 2002).

Some authorities recommend multiple scattered smaller injections to spread the toxin even in medium-sized muscles. The justification for multiple injections within a single muscle partly depends on the theoretical concept of BoNT-A saturation of a volume of muscle (50U BOTOX® or 200U Dysport® has been suggested as a maximum dose per site). However, multiple injections may be uncomfortable particularly at higher dilution volumes, and may lead to temporary pain-induced increase in muscle tone.

It is important to document the dose and dilution of BoNT-A, the type of BoNT-A, the location of BoNT-A and the number of injection sites per muscle. A sample proforma is given in Appendix 4.

7.11 Post-injection management

Post-injection management is as important as the injection itself, and the same team members who were involved in pre-injection assessment should also be involved in the post-injection treatment – including measurement of outcome, reassessment and review of goal achievement. It should be confirmed that appropriate post-injection management is available and scheduled prior to the injection taking place.

Post-injection management should include as appropriate:

- assessment of the need for orthotics/splinting or review of existing orthoses, once the clinical effect of muscle weakening is observed (usually 7–14 days post-injection), and to establish a plan for further review/revision of orthoses as required
- assessment of patient and carer engagement and education on stretching regimes and guidance on task practice activities
- provision of therapy to increase muscle strength of the opposing muscle groups, when indicated
- consideration of other treatments that may enhance the effects of BoNT-A such as constraint therapy or electrical stimulation as appropriate:
 - active NMJs take up BoNT-A more avidly than NMJs at rest, and there is some evidence that electrical stimulation of the **injected muscle** may enhance the anti-spastic effects of BoNT-A (Hesse, Reiter *et al* 1998). However, it is necessary to stimulate the motor point or the nerve to the muscle, in order to activate the NMJs to achieve this effect
 - functional electrical stimulation of the **antagonist muscle** may help to build up muscle strength and so enhance functional benefits (Hesse, Reiter *et al* 1998).

7.12 Clinical review

The effect of BoNT-A and its duration varies between individuals. The effects of BoNT-A should be monitored over time, and standardised assessment and evaluation should be performed at realistic intervals.

7.12.1 7–14 day review

This review is normally undertaken by the therapy team to assess the need for splinting/orthotics and other therapy interventions.

7.12.2 4–6 week review

A formal follow-up assessment is usually required at 4–6 weeks to determine whether or not the treatment goals have been achieved and to identify any adverse effects and patient compliance with the post-injection regime (if serial injection is planned, the need for injection of further muscles may be considered at this point).

7.12.3 3–4 month review

The treating clinician must review the patient at 3–4 months post-injection, when the effect of the toxin is likely to have worn off, to determine the need for further BoNT-A treatment.

7.13 Documentation

Documentation for all injections should include:

- recording of patient consent (or consultee consultation as appropriate)
- a clear statement of treatment aims and the risks discussed
- baseline outcome measures appropriate to those aims
- BoNT-A brand, dose, dilution and muscles injected
- follow-up treatment plan
- evaluation of outcome, including goal attainment and repeat measures
- plans for future management
- adverse effects
- user satisfaction questionnaire.

8 Formal evaluation of effectiveness

Formal assessment of outcome should be a routine part of all treatment, including interventions for spasticity. However, outcome measurement in this context poses a number of challenges:

1. **Diversity of presentation** – patients present with different patterns of spasticity, symptoms and severity of functional impairment. Some will be totally dependent for all their care needs, while others are largely independent. In addition, their needs are expected to change over time.
2. **Diversity of expectation** – patients and their families have different priorities, and therefore different expectations of treatment.

Evaluation of outcome will include an overall clinical review with feedback from patients and their carers as appropriate. However, formal outcome measurement should be considered at three levels (Ashford and Turner-Stokes 2013):

1. **Goal attainment:** have the intended goals for treatment been achieved?
2. **Body structure or function impairment:** has the intervention produced an improvement in spasticity presentation and/or range of movement (or at least maintenance of the current state, if that was the intended goal)?
3. **Activity function:** if predicted, has this had any impact on function, either in terms of ‘passive’ (ease of care) or ‘active’ functional activity performed by the patient?

Because individual goals for treatment vary widely, there is no single outcome measure that will capture the benefits of treatment in all cases. Instead, a range of measures will be required. While agreeing the goals for treatment with the individual and their family, the treating team should consider which measures would be appropriate to assess outcome, and ensure these are recorded at baseline and re-evaluated at defined intervals.

There is now an evidence-based framework for doing this based on goal setting using Goal Attainment Scaling (GAS) and this is the method recommended in this document, although other methods of goal setting exist. GAS provides a useful framework for collaborative goal review and goal management training. It also offers a patient-centred outcome measure to evaluate the gains from intervention in the areas that matter most to patients and their families. Most patients will have more than one goal for treatment, some of which will be more important than others, and some will be harder to achieve. GAS provides a structured approach to the evaluation of goal attainment, which takes account of this variation. As originally described in the 1960s (Kiresuk and Sherman 1968), GAS uses a 5-point scale to

capture both over- and under-achievement of expected goals. The original GAS method was time-consuming and less practical for use in routine clinical practice, but a simplified 'GAS-light' method (Turner-Stokes 2009a) is feasible and practical for routine use.

GAS is now established as a sensitive tool for measuring clinically-important change in the context of spasticity (Turner-Stokes, Baguley *et al* 2010). It has been used as the primary outcome measure in several large international multicentre trials of BoNT-A for upper limb spasticity (Ward, Wissel *et al* 2014; Turner-Stokes, Baguley *et al* 2010; Borg, Ward *et al* 2011; Turner-Stokes, Fheodoroff *et al* 2013). However, it is a measure of the achievement of intention, rather than an outcome measure per se and does not support direct comparison between different practices or populations. Standardised measures therefore need to be collected alongside GAS to provide a common 'yardstick'.

8.1 Focal Spasticity Index

As noted in Chapter 7, goal analysis from four large international studies has identified six common categories for treatment goals (Ashford, Fheodoroff *et al* 2016), which are listed in Table 4. More recently a structured framework has been developed for use in spasticity management – the Focal Spasticity Index.

The **Focal Spasticity Index (FSI)** includes both patient-reported and clinician-rated elements. Developed originally in the context of upper limb intervention (Turner-Stokes, Ashford *et al* 2016), the approach has now been adapted to encompass outcome evaluation in both upper and lower limb spasticity.

- The FSI comprises a structured approach to GAS together with severity indicators and confounders to recovery, and a limited set of standardised measures determined by the selected goal areas of treatment for any given patient.
- The key components of the FSI are listed in Table 6, and further detail regarding the incorporated tools is included in Appendix 3. Further information on the FSI can also be found on the King's College London website at: www.kcl.ac.uk/nursing/departments/cicelysaunders/research/outcome/rehabilitation/Rehab-outcome-measures.aspx

8.1.1 Severity indicators and confounders to recovery

These data are collected by clinicians. The section includes:

- **Basic demographic characteristics** to define the population (eg age, gender, aetiology).
- **Distribution and severity of the spasticity.** Spasticity is a focal condition which may affect the whole upper limb – or just the proximal or distal part of it. Its severity and distribution will affect the types of goals for treatment. Despite its acknowledged limitations (Mehrholtz, Wagner *et al* 2005), the Modified Ashworth Scale (MAS) (Pandyan, Johnson *et al* 1999) is included as the most widely used measure of spasticity in clinical practice.
- **Factors that may confound outcome** include neurological impairments within the affected limb(s) (eg motor control, sensory loss, neglect) and general impairments (eg deficits in cognition, behaviour, communication, and mood) which may limit the individual's ability to engage successfully in rehabilitation and achievement of their set goals. These are captured using the Neurological Impairment Set adapted for spasticity (Turner-Stokes, Ashford *et al* 2016).

Table 6: Components of the Focal Spasticity Index

FSI	Measurement tools
A. Severity and confounders to recovery (history and examination)	<ul style="list-style-type: none"> • Duration of spasticity (months) • Distribution and severity of spasticity (<i>Modified Ashworth Scale</i>)* • Soft tissue contractures (<i>Loss of range</i>)* • Severity of underlying impairment (<i>Neurological Impairment Set</i>)*
B. Goals for treatment	<ul style="list-style-type: none"> • Individual goal attainment scaling using GAS-light • Goals negotiated between patient and team, categorised within one or more of the six main goal areas: <ul style="list-style-type: none"> ◦ Domain 1 <ol style="list-style-type: none"> 1. Pain 2. Involuntary movements 3. Impairment (prevention of contractures) ◦ Domain 2 <ol style="list-style-type: none"> 4. Passive function 5. Active function 6. Mobility • Recommended measures used to define goal parameters, selected according to the chosen goal area(s) eg: <ul style="list-style-type: none"> ◦ Pain: <i>Rating out of 10 (Verbal rating, NGRS or SPIN)</i> ◦ Ease of care: <i>Rating out of 10 (Verbal rating, NGRS)</i> ◦ Involuntary movement – Carry angle, spasm frequency or <i>Upper limb Associated Reaction Rating Scale</i> ◦ Mobility: <i>10m walking speed</i>
C. Standardised measures – recommended for all patients where relevant/possible	<p>Function – passive and active</p> <ul style="list-style-type: none"> • Upper limb: <i>Arm Activity measure (ArmA)</i> • Lower limb: <i>Leg Activity measure (LegA)</i> <p>Global benefits</p> <ul style="list-style-type: none"> • Patient reported: <i>Global benefit scale (–2 to +2)</i> • Clinician reported: <i>Global benefit scale (–2 to +2)</i> • Quality of life: <i>The Spasticity-related Quality of Life tool (SQoL-6D)</i>

MAS = Modified Ashworth Scale; NIS = Neurological Impairment Scale; NGRS = Numbered Graphic Rating Scale; SPIN = Scale of Pain Intensity (See Appendix 3)

* See www.kcl.ac.uk/nursing/departments/cicelysaunders/research/outcome/rehabilitation/Rehab-outcome-measures.aspx for more details

8.1.2 Individual Goal Attainment Scaling

The FSI incorporates a structured approach to Goal Attainment Scaling using the GAS-light. Goals are categorised within one of the six main goal areas (see Table 4). ‘SMART’ (ie specific, measurable, achievable, realistic and timed) goal statements are drawn up with reference to recommended measures (or ‘goal parameters’) wherever possible. This supports the collection of standardised measures alongside GAS, but the burden of data collected is reduced as only the measures relevant to the chosen goal categories are recorded for each patient.

For example, if pain reduction is a goal for treatment, the SMART goal statement may refer to a pain rating out of 10 – eg ‘*To reduce spasticity-related pain from 8/10 to 4/10 within 6 weeks*’.

Clinicians should be aware however, that patients with cognitive/communication deficits may have difficulty reporting their symptoms. A number of tools have been developed to facilitate pain reporting, such as the numbered graphic rating scale or the Scale of Pain Intensity (SPIN) (Jackson, Horn *et al* 2006) (See Appendix 3 for more details).

8.1.3 Standardised measures

The Arm Activity measure (ArmA) and Leg Activity measure (LegA) are patient-reported tools that are recommended as standardised measures to capture changes in passive and active function in the upper and lower limb respectively.

The clinician and patient rating of global benefit of the intervention are recommended to reflect overall change following intervention. Increasingly, quality of life measures are required by commissioners to capture health utility and cost-effectiveness. General health utility and quality of life measures are shown to be insensitive to change following focal interventions for spasticity. A specific health utility tool to capture spasticity-related quality of life (the SQoL6D) is currently undergoing evaluation, but there is insufficient evidence as yet to recommend its general use.

9 Prescribing, supply and administration by non-medical injectors (NMIs)

In most countries, doctors are responsible for prescription and administration of BoNT-A injections. However, therapists and nurses play a critical role in all aspects of spasticity management using BoNT-A – from patient selection, through treatment planning and goal setting, to follow-up and outcome evaluation. A logical extension to this role in the UK has been the prescribing, supply and administration of the BoNT-A itself.

Prescription, supply and administration of medicines in the UK have primarily been governed by the Medicines Act 1968, but subsequent amendments have made it possible to expand the role of non-medical injectors (NMIs) to prescribe. Research in other areas of healthcare has demonstrated the benefit on non-medical staff assuming advanced practice roles (Daker-White, Carr *et al* 1999). There is now evidence that non-medical prescribers provide benefits to patients and value for money (NHS National Treatment Agency 2007).

Within the UK legislation, supply and administration of medicines are considered separate issues from prescription. The purpose of this section is to define the activities involved in the administration and prescription of BoNT-A for NMIs, and the legal frameworks that govern them. More information is given in Appendix 7.

9.1 Supply and administration of BoNT-A

Any appropriately trained practitioner can administer an intramuscular injection of BoNT-A, but this is a skilled activity and NMIs must demonstrate that they meet the expected standards of care (see Chapter 10). Competencies may be acquired through formal training programmes or through in-house training, and some professional bodies have published expected standards for education and training in this area (Chartered Society of Physiotherapy 2011).

The two main forms of instruction under which non-prescribing injectors most commonly administer botulinum toxin are as follows:

- **A Patient Specific Direction (PSD)** is a written or electronic instruction signed by an independent prescriber for a medicine to be supplied and/or administered to a named patient after the prescriber has assessed the patient on an individual basis. The non-prescribing injector can only administer the medicine in accordance with the instructions that are written by the prescriber.

- A **Patient Group Direction (PGD)** is a written document authored by a doctor and pharmacist that describes the names and dosages of specific medicines that may be supplied and administered to specified groups of patients by named and authorised registered health professionals. It is written in advance of any patient presenting for treatment. Using a PGD is not a form of prescribing.

Particular challenges lie in the potentially toxic nature of BoNT-A. While side effects are very rare, they could (at least in theory) be life-threatening, so adequate arrangements for emergency medical back-up and support must always be in place regardless of who prescribes or administers it.

NMIs who administer BoNT-A **without** prescribing still hold a personal accountability for safe practice in administration and must have knowledge of the common indications, side effects and dosages of the medicine. They also need to understand which instruction and legal mechanism for supply they are working within.

9.1.1 Differences between a PSD and PGD

Currently, skilled non-registered staff can administer medicines identified in a standard prescription or PSD but only registered health professionals can administer medicines under a PGD.

Clinical decision-making by the non-prescribing injector

- For a PSD to be valid, the named patient must also have been seen and assessed by the independent prescriber. It does not allow for any clinical decision-making at the point of administration, eg variation of dose or site, but they can apply to licensed, unlicensed and off-label use of medicines.
- A PGD must meet specific criteria regarding the medications that can be given and the identity of the injector, but it does allow some clinical decision-making by the non-prescribing injector (eg variation to dose and site) providing it is acknowledged in the PGD, and is managed according to clear criteria or parameters.

Off-label and unlicensed usage

- PSDs can apply to licensed, unlicensed and off-label use of medicines.
- Off-label use of a licensed medicine can be included in a PGD only when clearly justified by best clinical practice. The PGD needs to clearly state that the medicine is being used outside the terms of the marketing authorisation on the PGD and the non-medical injector should consider informing the patient or their carer that the use is off-label.

NICE (National Institute of Health and Care Excellence 2013a) recommends that the majority of clinical care involving supplying and/or administering medicines occurs on an individual, patient-specific basis, with PGDs reserved for limited situations in which this offers an advantage for patient care, without compromising patient safety, and where there are clear governance arrangements and accountability.

PSDs are reasonably well-suited to multidisciplinary clinics, in which both the prescriber and non-prescribing injector are present, but are less well-suited to remote or community-based working, where both are unlikely to be present. In that context, PGDs are often appropriate because the tight restriction of site and dose under a PSD may not meet the needs of the individual where variation is clinically indicated.

9.2 Prescribing of BoNT-A

9.2.1 Independent prescribing

Independent prescribers are specified health professionals defined in law as being able to prescribe medicines independently. As well as doctors, some non-medical professions in the UK are able to train to acquire prescribing rights. At the time of writing, these include nurses, physiotherapists and podiatrists (see Appendix 7 for a full list).

To be able to prescribe the professional must be listed on the relevant regulatory register, and annotated on that register as an independent prescriber, having completed an approved training programme.

Independent prescribers are only able to prescribe medicines within their field of expertise. At the time of writing, nurse independent prescribers may prescribe licensed, unlicensed and off-label medicines. Physiotherapist and podiatrist independent prescribers can prescribe licensed and off-label medicines but not unlicensed medicines.

9.2.2 Supplementary prescribing

Supplementary prescribing is a voluntary prescribing partnership between an independent prescriber and a supplementary prescriber, to implement an agreed patient-specific clinical management plan (CMP). A CMP can include licensed, off-label and unlicensed medicines.

Supplementary prescribers are also specified health professionals who have undertaken the approved training. Supplementary prescribing is limited to the same professions as independent prescribing (see Appendix 7).

9.3 Current practice in the UK regarding BoNT-A for spasticity management

Rehabilitation medicine (RM) is a very small specialty in the UK with just 0.26 WTE consultants per 100,000 population, compared with 2–3/100,000 in most other European countries (Royal College of Physicians 2011). There is, therefore, a comparative shortage of medically qualified injectors who are trained in a holistic multidisciplinary approach to spasticity management. Hence many spasticity services have taken advantage of the change in UK legislation described above to develop the role of NMIs to improve both the access to services and their cost-efficiency.

Non-medical injection of BoNT-A by NMIs is now well-established in the UK – some NMIs having been in post for over 10 years. In a recent survey of 75 adult spasticity services using BoNT in the UK, 50% used NMIs, with non-medical staff delivering up to 100% of the treatments administered in some services.

A recent comparison of post-treatment goal attainment demonstrated that comparable safety and outcomes from physiotherapy and medical injectors (Turner-Stokes, Ashford *et al* 2016), and access to assessment and treatment have undoubtedly been improved by the development of NMI roles.

There are formally recognised training programmes for both the administration of BoNT-A and for prescribing rights in non-medical staff. At the time of writing, at least 180 NMIs have attended formal

programmes of study in administering BoNT-A at master's degree level, with many more trained using locally developed competency frameworks. There are increasing numbers of nurses and physiotherapists with prescribing rights and other professional groups, including occupational therapists, injecting under PGDs.

Table 7 summarises the role of the NMI under the various current methods to support prescribing, supply and administration of BoNT-A. Appendix 7 provides more detailed information concerning the legal frameworks for administration and prescribing.

Table 7: Summary of the role of the NMI under the various current methods to support prescribing, supply and administration of BoNT-A

Method	Role of the non-medical injector (NMI)
Administration, but not prescription	
Patient Specific Directions (PSD) (A written instruction from an independent prescriber for a medicine to be supplied/administered to a named patient by an appropriately qualified health professional)	The NMI may administer the medication <i>to a specific patient</i> under instructions from an independent prescriber. PSDs do not allow for any clinical decision-making at the point of administration, eg variation of dose or site, and may not meet the needs of the individual if dose variation is clinically indicated.
Patient Group Directions (PGD) (A formal document drawn up by an NHS trust, providing written instruction for the supply and/or administration of <ul style="list-style-type: none"> • a named medicine • by a named registered health professional • in a defined clinical situation • to groups of patients who may not have been identified before presenting for treatment) 	The NMI may administer medication for certain <i>patient groups</i> under circumstances specified in the PGD. Clinical decision-making (eg variation to dose and site) is allowed, providing it is acknowledged in the PGD, and is managed according to clear criteria or parameters.
Prescription as well as administration – requires prescribing qualification	
Supplementary prescribing (A voluntary prescribing partnership between the independent and supplementary prescriber, to implement an agreed patient-specific clinical management plan, with the patient's agreement)	In addition to administration, the NMI has a role in the prescription of medicines through the use of a patient-specific 'clinical management plan' – which is devised in partnership with a doctor and the patient. The supplementary prescriber may prescribe any medicine that is referred to in the plan until the next review by the independent prescriber.
Independent prescribing (Full responsibility for the prescription, supply and administration of licensed medicines)	The independent prescriber (IP) takes on full responsibility for the prescription, administration and monitoring of the treatment. At the current time in the UK, nurses and physiotherapists can become independent prescribers.

10 Organisation of services

10.1 Requirements

While some commissioning arrangements require treatment of spasticity with BoNT-A to be separately identified and funded, patients with troublesome spasticity should be managed within a broader service that can consider and arrange (if not provide themselves) all other modalities of treatment.

It is important for the MDT to have the necessary competencies to set up services to manage spasticity; this applies irrespective of the scope of the service. The optimal service configurations will vary according to staff skills, facilities, patient population, etc. A service will usually revolve around specialist rehabilitation units, neurology or stroke services or within departments of medicine for the elderly, but should be supported by a business case for all aspects of spasticity management.

The requirements include:

- clinicians trained in neurological rehabilitation and spasticity management in general, with specific additional training in BoNT-A treatment
- an integrated physiotherapy (PT), rehabilitation nursing and occupational therapy (OT) service, with a role in:
 - selecting appropriate patients for treatment
 - arranging or delivering targeted therapy after injection
 - ensuring appropriate provision of splinting and orthoses. There should also be good links with therapy departments in referring units elsewhere
 - access to specialist wheelchair seating, postural support services and neuromuscular electrical stimulation.

Appropriate and regular surgical advice should also be established (eg orthopaedic, neurosurgical, plastics) and accessed as appropriate.

Many patients who require focal interventions for spasticity are able to attend dedicated outpatient clinics. Such clinics provide a convenient and cost-effective model for service provision for those who can travel easily, and patients may benefit from assessment and treatment with access to all the relevant professionals under one roof.

For those less able to travel, BoNT-A injection therapy can also be provided to patients in their homes or wards away from the spasticity clinic. While this avoids the cost of ambulance transport, the additional staff time involved will need to be included in costs of the service.

Where possible, services should avoid the use of more than one of the available BoNT-A preparations in order to prevent confusion over doses. Stability of the drug outside a pharmacy fridge may influence choice of drug when undertaking domiciliary visits.

All services should have:

- clear, concise documentation (see Appendix 4)
- a system for obtaining informed consent
- standardised evaluation and assessment, including outcome measurement
- provision of appropriate patient and carer information leaflets
- appropriate arrangements for follow-up
- a clearly defined mechanism for paying for the spasticity management service. Ad-hoc arrangements can be financially risky for host institutions.

Without these service elements, successful patient management will be limited.

10.2 Service evaluation

The use of BoNT-A should be regularly audited, and documentation and follow-up should be arranged to facilitate this.

Audit assessments should evaluate compliance with the guidance, including:

- quality of documentation and recording
- evidence of consent obtained in all cases
- therapy intervention and follow-up
- outcomes from treatment, in particular achievement of treatment goals
- adverse events.

10.3 Training

BoNT-A and phenol should only be injected by clinicians with the appropriate skills and training. All clinicians involved in injection therapy should be trained in the assessment and management of spasticity in general, together with specific treatment techniques related specifically to BoNT-A and peripheral phenol blocks. Maintaining competency should be included within workplace ongoing performance review, utilising further training and support as appropriate.

Training may be delivered through a range of formats, including:

- short courses with lectures and practical demonstrations
- higher education institution MSc modules in spasticity management
- attachments to centres delivering BoNT-A and phenol treatments or working under the supervision of practitioners expert in spasticity management and the use of BoNT-A and phenol

- competencies should be set and assessed by the training programme to evaluate the attainment of expertise.

Key knowledge and skills should cover the areas shown in Box 1.

10.3.1 Minimum training requirements

- Attendance on a BoNT-A training course (to include a formal certificate) approved by the relevant higher education institution or professional body.
- Observation of the assessment of and injection technique in at least five patients with arm and five patients with leg spasticity-related problems.
- Ability to use the relevant equipment available in the service, eg EMG, nerve stimulation or ultrasound.

Box 1: Key competencies for BoNT-A injectors

Knowledge required	Skills required
<ul style="list-style-type: none"> • What is spasticity? • What is the impact of spasticity on patients, carers and the rehabilitation process? • The range of spasticity treatments • When is local injection therapy appropriate? • What are BoNT-A and phenol and their roles? • Adverse effects • Evidence base for the use of BoNT-A and phenol • Relevant functional anatomy • How to distinguish spasticity from contracture or soft-tissue shortening • Service organisation: • Role of physiotherapy, orthotics/splinting, information provision • Development of a business case to obtain funding • Outcome measurement • Understanding of pharmacology 	<ul style="list-style-type: none"> • Patient selection and application of clinical reasoning • How to assess the patient • Communication and negotiation skills • Identifying target muscles • Injection technique with guidance (EMG, stimulation or ultrasound) • Post-injection follow-up • Use and interpretation of outcome measures, including Goal Attainment Scaling

11 References

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Appendix 1

Evaluation of evidence for these guidelines

Proposed methodology for evaluation of evidence base and consensus.

Background

Concerns have been raised in several quarters about the disproportionate nature of the formal guideline development processes used by large organisations such as the National Institute for Health and Care Excellence (NICE) when guidelines are developed by specialist societies and other professional bodies. These smaller organisations typically lack the time, resources and machinery for the full systematic approach adopted by formal guidelines. In addition, the formal process is rigid and designed primarily for specific targeted interventions and procedures. It is poorly suited to guideline development for complex interventions or health systems.

In this set of guidelines we have used a methodology for a) the assimilation of published evidence and b) achievement of consensus which is tested, but we believe this may have further application in other areas.

The GRADE process

GRADE is a structured process for guideline development based on predefined questions, evaluation of the evidence in relation to the question and then reaching consensus on a recommendation (Novotna, Mares *et al* 2011; Braid, Kirker *et al* 2013). It starts from a basis of no assumed knowledge. The steps are summarised in Box 2.

Box 2: Summary of steps in the GRADE process

- 1 The Guideline Development Group (GDG) first identifies the key priority areas for the guidelines to address and sets one or more 'PICO' (Population, Intervention, Comparison and Outcome) questions for each priority area.
- 2 Systematic literature searches are conducted on each PICO question.
 - a. Each study is graded according to the strength of the evidence (based primarily on research design).
 - b. An overall evaluation of the quality of evidence for that PICO question is then made, ranging from 'High' to 'Very low', based on the confidence in the estimate of effect.
- 3 The GDG then considers its recommendation in respect of that PICO question according to a list of 11 questions relating to benefits and harms, resource use, equity, acceptability and feasibility.
- 4 The strength of recommendations is graded as 'Strong' or 'Conditional' based on consensus in relation to the 11 questions.

Methodology

Our methodology used a modified version of the GRADE process, with the following key principles in three main steps.

A. 'Top-down' approach

The task was to update an existing set of guidelines and recommendations, many of which were based on expert opinion rather than clinical research, according to the original evidence evaluation. It was therefore not appropriate to develop PICO questions from scratch in a 'bottom-up' approach. Instead we took a 'top-down' approach, considering the existing recommendations and updating literature reviews where it was expected that the recommendation was likely to have research-based evidence.

B. Evidence evaluation

For the assimilation of evidence for the benefits, instead of the GRADE evidence evaluation (which places a main emphasis on RCTs), we used the typology of evidence that was developed for the UK National Service Framework for Long Term Conditions (Department of Health 2005).

The advantages of this approach in this particular context are:

- a It is simple and timely to apply – thus proportionate for the purpose of our end product.
- b It recognises the appropriateness of a range of research designs, giving value to all study designs, so long as they are appropriate and methodologically robust to answer the research question.
- c It supports use of the best research evidence available, but also explicitly values expert opinion (either of professionals or patients/carers).

C. Strength of recommendations

For the strength of recommendations, the GDG reached consensus based on just three questions:

- 1 **Benefits:** What is the overall strength of evidence for the benefits of this recommendation?
- 2 **Harms:** Are the undesirable effects small?
- 3 **Costs:** Is the incremental cost small relative to the net benefits?

Benefits	1. What is the overall level of evidence for the benefits of this approach?**	<ul style="list-style-type: none"> • User/professional opinion only: (E1/E2)* • Low (Research Grade C)* • Moderate (Research Grade B)* • High (Research Grade A)*
Harms	2. Are the desirable effects large relative to undesirable effects?**	<ul style="list-style-type: none"> • No • Probably no • Uncertain • Probably yes • Yes • Varies
Costs	3. Is the incremental cost small relative to the net benefits?**	<ul style="list-style-type: none"> • No • Probably no • Uncertain • Probably yes • Yes • Varies

* Rated according to the National Service Framework (NSF) Typology ** Extracted from GRADE process

Interpretation:

Very strong: High level research evidence (Grade A) with minimal harms and costs

Strong: Lower level evidence but minimal harms and costs

Moderate: Lower level evidence and potentially significant harms and/or costs

Weak: Lower level evidence and potentially significant harms and costs

The NSF typology of evidence

Published in 2005, the UK Department of Health's National Service Framework for Long Term Conditions was a set of evidence-based standards for delivery of NHS services for people with long-term neurological conditions. The standards were strongly user-focused and it was recognised that evidence derived from RCTs was likely to be lacking in this area.

Instead, the NSF Research and Evidence Group developed and tested a novel typology that would a) take account of a wide range of research evidence, including both quantitative and qualitative research designs and b) place equal weight on expert evidence when gathered through consultation processes other than formal research.

The typology is shown to be valid (Turner-Stokes, Harding *et al* 2006) and suitable for the evaluation of evidence for complex interventions (Baker, Young *et al* 2010).

The process

Each piece of evidence is reviewed by the Guideline Development Group and given an E rating and an R rating, if possible.

E: reflects user/carer/professional opinion

R: reflects research-based evidence.

Expert evidence:

Expressed through consultation or consensus processes rather than formal research designs.

E1	User and/or carer opinion
E2	Professional or other stakeholder opinion

Research evidence

Each piece of evidence gathered through formal research processes, is categorised on three levels: **Design**, **Quality** and **Applicability**, by two or more evidence reviewers.

Design: Seven design groups

Primary research-based evidence	
P1	Primary research using quantitative approaches
P2	Primary research using qualitative approaches
P3	Primary research using mixed methods (qualitative and quantitative)
Secondary research-based evidence	
S1	Meta-analysis of existing data analysis
S2	Secondary analysis of existing data
Review-based evidence	
R1	Systematic reviews of existing research
R2	Descriptive or summary reviews of existing research

Quality assessment: Based on five simple questions

Each quality item is scored as follows: 2 = Yes, 1 = In part, 0 = No

	Score
Are the research question/aims and design clearly stated?	
Is the research design appropriate for the aims and objectives of the research?	
Are the methods clearly described?	
Is the data adequate to support the authors' interpretations/ conclusions?	
Are the results generalisable?	
Total	/10

(More detailed instructions for applying the quality assessment are available on request)

Applicability to the recommendation

Direct	Evidence from the same population/condition
Indirect	Extrapolated evidence from a different population/condition

Thus, a high quality cohort study might be assigned **P1 Direct**, and moderate quality narrative review in a related field might be assigned **R2 Medium Indirect**.

Assimilation of research evidence

A single grade of recommendation will be derived from the above evaluations:

Research Grade A:

- More than one study of high quality score ($\geq 7/10$) and
- At least one of these has direct applicability.

Research Grade B:

- One high quality study or
 - More than one medium quality study (4–6/10) and
 - At least one of these has direct applicability.
- or
- More than one study of high quality score ($\geq 7/10$) of indirect applicability

Research Grade C:

- One medium quality study (4–6/10) *or*
- Lower quality (2–3/10) studies *or*
- Indirect studies only.

In summary:

- Each evidence-based statement would have the following ratings according to the strength of supporting evidence:
 - Expert: E1 and/or 2 (if applicable)
 - Research: RA, B or C.

For example:

‘Individuals with spasticity should have access to botulinum toxin with appropriate concomitant therapies according to their individual needs (E1+2, RA)’

‘Individuals with spasticity should have clearly agreed goals for treatment prior to injection of BoNT-A (E2, RB)’

Appendix 2

Injection sites for BoNT-A

Muscle	Origin	Insertion	Action	Dose* BOTOX® Dysport® Xeomin®	Injection point
Trunk muscles					
Psoas major	Transverse processes and vertebral bodies of T12–L5	Lesser femoral trochanter	Flexes hip	100–200U 600–800U 100–200U	Approach posteriorly advancing spinal needle between transverse processes at L2, L3 and L4. 50–60U at each site
Iliacus	Floor of iliac fossa	Joins psoas tendon to form iliopsoas tendon to insert into lesser trochanter	Flexes hip	75–150U 200–400U 75–150U	Anterior approach under lateral third of inguinal ligament – lateral to femoral nerve and avoiding lateral cutaneous nerve of thigh
Quadratus lumborum	Iliolumbar ligament and iliac crest	12th rib and L1–5 transverse processes	Flexes vertebral column laterally	100U 400U 100U	Posterior approach lateral to vertebral column
Hip extensors and abductors					
Gluteus maximus	Posterior aspect ilium, sacrum, coccyx and sacrotuberous ligament	Greater trochanter	Extends thigh Laterally rotates hip	Rarely injected	
Gluteus medius	Large area of sacrum below iliac crest	Postero-superior angle of greater trochanter	Abducts leg	100U 400U 100U	

Muscle	Origin	Insertion	Action	Dose* BOTOX® Dysport® Xeomin®	Injection point
Gluteus minimus	Broad area of ilium between anterior and inferior gluteal lines	Lower lateral part of greater trochanter	Abducts leg	Rarely injected	
Thigh – knee extensors					
Rectus femoris	Anterior inferior iliac crest (straight head) and ilium (reflected head)	Tibial tubercle via quadriceps and patellar tendons	Hip flexion and knee extension	100–150U 400–500U 100–150U	Four points along the middle of quadriceps muscle mass
Vastus lateralis, intermedius and medialis	Anterior aspect of femur	Tibial tubercle via quadriceps and patellar tendons	Knee extension	100–150U 400–500U 100–150U	Two points in lateral aspect of thigh; one deep centrally in lower half of thigh and one to two medially
Thigh adductors and knee flexors					
Pectineus	Superior pubic ramus	Posterior aspect of femur below lesser trochanter	Adducts thigh and assists hip flexion	50–100U 200–400U 50–100U	Difficult to inject because of overlying neurovascular bundle below inguinal ligament medial to femoral vein
Adductor magnus	Ischial tuberosity	Posterior two thirds of femur down to adductor tubercle on medial femoral condyle	Adducts and laterally. Main action while sitting	100–200U into whole adductor group 400–750U 100–200U	Large muscle in upper medial thigh. Inject into upper third of thigh
Adductor longus	Body of pubis below pubic crest and symphysis	Post aspect of middle of femur into linea aspera	Adducts thigh. Main action on standing		Antero medial aspect of thigh one hand's breadth below inguinal ligament medial to femoral vein

Muscle	Origin	Insertion	Action	Dose* BOTOX® Dysport® Xeomin®	Injection point
Adductor brevis	Below pubic crest in superior pubic ramus	Upper femur posteriorly between lesser trochanter and linea aspera	Adducts and laterally rotates thigh	Rarely injected	Behind adductor longus and pectineus and in front of adductor magnus
Gracilis	Inferior pubic ramus	Pes anserinus on posterior aspect of medial tibial condyle	Adducts thigh and flexes knee Medially rotates flexed leg	80–120U 300–400U 80–120U	Postero medial edge of thigh several points of injection down medial thigh
Semi membranous	Ischial tuberosity	Pes anserinus on posterior aspect of medial tibial condyle	Flexes knee. Medially rotates flexed leg and extends hip	100–150U 400–500U 100–150U	Medial muscles in posterior thigh – multiple injection sites
Semi tendinosus	Common origin with long head of biceps femoris	Pes anserinus on posterior aspect of medial tibial condyle	Same as semi membranous	100–150U 400–600U 100–150U	Medial muscles in posterior thigh – multiple injection sites
Biceps femoris	Long head: ischial tuberosity Short head: linea aspera back femur	Head of fibula	Flexes knee, rotates leg externally and extends hip	100–150U 400–600U 100–150U	Lateral muscle in posterior thigh – multiple injection sites
Popliteus	Popliteal groove on lateral epicondyle anteriorly	Pierces joint capsule to post. aspect of upper medial tibia	Flexes knee and internally rotates lower leg at beginning of flexion	25–30U 100–120U 25–30U	Deep over back of medial tibial condyle. Down to bone medial aspect of popliteal fossa and then withdraw

Muscle	Origin	Insertion	Action	Dose* BOTOX® Dysport® Xeomin®	Injection point
Lower leg – antero lateral compartment					
Tibialis anterior	Upper half of lateral surface of tibia and interosseous membrane	Medial cuneiform bone	Dorsiflexes and inverts foot	75–120U 300–400U 75–120U	Front of shin, lateral to tibia
Extensor digitorum longus	Upper three-quarters of anterior surface of fibula	Bases on 2nd and 5th middle and terminal phalanges	Dorsiflexes foot and toes 2–5	50–75u 200–300U 50–80U	Lateral to tibialis anterior in front of and border of fibula
Extensor hallucis longus	Anterior surface of middle two-thirds of fibula and interosseous membrane	Base of distal phalanx of great toe	Extends great toe	50–60U 200–250U 50–60U	Between tibialis anterior and extensor digitorum longus in middle of shin
Peroneus tertius (not always present)	Distal fourth of anterior surface of fibula	Dorsal surface of 5th metatarsal (MT) base	Dorsi flexes and everts foot	30–40U 120–150U 30–40U	Attached to ext digitorum longus lateral surface
Peroneus longus	Upper two-thirds lateral surface of fibula	Under base of 5th MT and groove in cuboid to medial cuneiform and base of 1st MT	Everts and plantar flexes foot	50–80U 200–320U 50–80U	Lateral aspect of shin anterior to fibula
Peroneus brevis	Lower two-thirds of fibula shaft	Base of 5th MT	Everts foot	30–40U 120–160U 30–40U	Lower half of lateral shin anterior to peroneus longus

Muscle	Origin	Insertion	Action	Dose* BOTOX® Dysport® Xeomin®	Injection point
Lower leg – posterior compartment					
Gastrocnemius – medial head	Back of medial femoral condyle	via Achilles tendon (AT) to calcaneum	Plantar flexes foot and flexes knee	50–100U 200–400U 50–100U	Superficial muscle of medial aspect of calf
Gastrocnemius – lateral head	Back of lateral femoral condyle	via AT to calcaneum	Plantar flexes foot and flexes knee	50–100U 200–400U 50–100U	Superficial muscle of lateral aspect of calf
Soleus	Posterior surface of shaft of fibula and medial border of tibia	via AT to calcaneum	Plantar flexes foot	75–100U 300–400U 75–200U	Back of calf, midway down between muscle bellies of gastrocnemius
Flexor hallucis longus	Posterior surface of fibula below soleus	Through groove in posterior talus to terminal phalanx great toe	Flexes great toe (IP + MTP joints) maintains longitudinal arch	40–60U 160–240U 40–60U	Under soleus mid-calf immediately posterior to peroneus longus and fibula
Flexor digitorum longus	Posterior surface of tibia	Terminal phalanges of 2nd and 5th toes	Flexes toes 2–5 (IP + MTP joints) and maintains longitudinal arch	40–60U 160–200U 40–60U	Behind medial border of tibia in its upper mid area. Inject near origin just behind tibia
Tibialis posterior	Interosseous membrane and adjoining posterior surfaces of tibia and fibula	Tuberosity of navicular bone and medial cuneiform bone	Plantar flexes and inverts foot	50–80U 200–320U 50–80U	Mid-calf, deep behind tibia and in depression between tibia and fibula

Muscle	Origin	Insertion	Action	Dose* BOTOX® Dysport® Xeomin®	Injection point
Abductor hallucis	Medial aspect calcaneum and flexor retinaculum	Medial aspect base of great toe proximal phalanx	Abducts and plantar flexes great toe	10–20U 40–80U 10–20U	Medial aspect 1st metatarsal
Flexor hallucis brevis	Cuboid bone and tibialis tendon	Two bellies inserted into each side of the base of the 1st proximal phalanx	Flexes 1st MTP joint	10–20U 40–80U 10–20U	Plantar aspect of foot under 1st metatarsal
Flexor digitorum brevis	Medial aspect calcaneum and septal fascia	Middle phalanges of toes 2–5	Flexes 1st IP joint and lateral four MTP joints	10–20U 40–80U 10–20U	Plantar aspect of foot at base of metatarsals
Pectoral girdle					
Trapezius	Occiput down median line to last thoracic vertebra	Lateral third of clavicle, acromion and scapular spine	Scapular elevation and rotation	50–75U 200–300U 50–75U	Large muscle between neck and shoulder
Rhomboid	Spinous processes C7–T5	Medial border scapula	Extension of scapulae	50–60U 200–250U 50–60U	Superficial, between scapula and spine
Supraspinatus	Supraspinatus fossa scapula	Greater tubercle of humerus	Abd. of arm from 0–15° above 90°	40–50U 160–200U 40–50U	Supraspinous fossa on scapula
Infraspinatus	Post aspect scapula below spine	Greater tubercle of humerus	External rotation of arm	50–60U 200–240U 50–60U	Infraspinous surface of scapula

Muscle	Origin	Insertion	Action	Dose* BOTOX® Dysport® Xeomin®	Injection point
Subscapularis	Anterior aspect of scapula	Lesser tubercle of humerus	Internal rotation of arm	50–80U 200–320U 15–100U	Inject under lateral border of scapula
Deltoid	Scapular spine, Acromion and clavicle	Deltoid tuberosity of humerus	Arm adduct from 15–90°	50–75U 200–300U 20–150U	Inject anterior, middle and posterior fibres
Teres major	Dorsum of scapula at inferior angle	Crest of lesser tubercle of humerus	Adducts, medially rotates and extends arm	30–50U 120–200U 20–100U	Lateral aspect lower scapula
Teres minor	Lateral aspect of scapula	Back of greater tubercle of humerus	Adducts and laterally rotates	30–50U 120–200U 30–50U	Lateral aspect scapula above
Latissimus dorsi	Tips of lower six thoracic spines, thoracolumbar fascia and iliac crest	Floor of intertubercular groove of humerus	Adducts, retracts and medially rotates upper limb	60–80U 240–320U 25–150U	Find in posterior fold of axilla while asking patient to pull down elevated arm
Serratus anterior	Upper eight ribs in three parts	Medial border of scapula	Protracts upper limb	60–70U 250–275U 60–70U	Lateral aspect of upper eight ribs
Pectoralis major	Clavicle and 3rd–8th anterior ribs	Greater tubercle of humerus	Adducts and medially rotates	75–100U 300–400U 20–200U	Anterior axillary fold

Muscle	Origin	Insertion	Action	Dose* BOTOX® Dysport® Xeomin®	Injection point
Pectoralis minor	3rd, 4th and 5th ribs and costochondral cartilages	Coracoid process	Draw scapula down and forwards, depresses shoulder	40U 160U 40U	Deep to upper part of pectoralis major
Arm					
Biceps brachii	Short: coracoid process Long: supra glenoid tubercle scapula	Bicipital aponeurosis	Supination and elbow flexion	75–100U 100–300U 75–100U	Anterior aspect of upper arm. Inject both heads
Triceps brachii	Scapula and humerus	Olecranon	Elbow extension	75–100U 300–400U 75–100U	Three heads on post aspect of arm
Coracobrachialis	Coracoid process	Middle medial border humerus	Flexes and adducts upper arm	30–50U 120–200U 30–50U	Medial to upper humerus between it and neurovascular bundle
Brachialis	Front of distal half humerus	Coronoid process of ulna	Flexes elbow	50–75U 200–400U 50–75U	Lower anterior humerus medial and lateral of biceps tendon
Extensor aspect of forearm					
Brachioradialis	Left supracondylar ridge of humerus	Lateral surface distal radius	Elbow flexion	50–60U 200–240U 50–60U	Radial side upper forearm

Muscle	Origin	Insertion	Action	Dose* BOTOX® Dysport® Xeomin®	Injection point
Supinator	Radial notch of ulna	Shaft of proximal radius	Supinates forearm	30–40U 120–160U 30–40U	Extensor aspect of arm below radial neck – deep
Extensor carpi radialis longus	Distal third of lateral supracondylar ridge of humerus	Base of second metacarpal (MC)	Extends and adducts hand at wrist	30–40U 120–160U 30–40U	Posterior to brachio-radialis on back of forearm
Extensor carpi radialis brevis	Common extensor origin (lateral humeral epicondyle)	Base of 3rd MC	Extends and adducts hand at wrist	20–30U 75–120U 20–30U	Posterior and medial to ECR longus
Extensor carpi ulnaris	Common extensor origin	Base of 5th MC	Extends wrist and elbow and adducts hand	30–40U 120–160U 30–40U	Most medially placed extensor muscle. Halfway down ulna shaft
Extensor digitorum communis	Common extensor origin	Bases of middle and distal phalanges	Extends wrist and fingers	30–40U 120–160U 30–40U	Middle of back of forearm distal to radial tuberosity
Extensor digiti minimi	Common extensor origin	Bases of middle and distal 5th phalanges	Extends 5th finger	30–40U 120–160U 30–40U	Medial to ext digitorum
Extensor pollicis longus	Posterior surface middle third ulna	Base of distal phalanx thumb	Extends all joints of thumb	20–30U 75–120U 20–30U	Midway down back of forearm

Muscle	Origin	Insertion	Action	Dose* BOTOX® Dysport® Xeomin®	Injection point
Extensor pollicis brevis	Posterior surface of radius and interosseous membrane	Base of proximal phalanx of thumb	Extends CMC and MCP joints of thumb	20–25U 75–100U 20–25U	Distal third of forearm. Palpate by moving CMC and MCP joints
Adductor pollicis longus	Back of interosseous membrane and both radius and ulna	Base of 1st MC	Adducts thumb and hand	20–40U 80–120U 20–40U	Proximal to ext. pollicis brevis on back of forearm. Palpate action
Extensor indicis	Back of distal ulna and interosseous membrane	Extensor expansion of dorsum of 1st phalanx	Extends forefinger	20–30U 75–120U 20–30U	Found medial of most lateral tendon of ext digit communis
Flexor aspect of forearm					
Superficial flexor muscles	Humeral head medial humeral epicondyle. Ulna head from medial border of ulna coronoid process	Middle of lateral surface of radius	Pronates forearm and flexes elbow	30–40U 120–160U 30–40U	Medial border of anterior cubital fossa – medial to brachial artery
Pronator teres					
Flexor carpi radialis	Medial humeral epicondyle	Base of 2nd MC	Flexes wrist and elbow	30–40U 120–160U 30–40U	Upper forearm just below bicipital aponeurosis and medial to pronator teres

Muscle	Origin	Insertion	Action	Dose* BOTOX® Dysport® Xeomin®	Injection point
Flexor carpi ulnaris	Humeral head from medial humeral epicondyle. Ulna head from olecranon and upper two-thirds of its posterior border	Pisiform bone in wrist	Flexes and adducts hand at wrist	30–40U 120–160U 30–40U	Upper forearm medial aspect of flexor surface below bicipital aponeurosis. Medial to FCR. Observe action of wrist flexion
Flexor digitorum superficialis	Humero-ulnar head from medial epicondyle and coronoid process. Radial head from upper half of anterior border of radius	Middle phalanges of medial four digits	PIP joint flexor and MCP joint flexor	25–30U 100–120U 25–30U	Middle of forearm half way down to either side of palmaris tendon
Flexor digitorum profundus	Proximal two-thirds of ulna	Terminal phalanges of fingers	Flexes all finger joints	30–40U 120–160U 30–40U	Upper third of forearm. Deep muscle above lateral border of ulna
Flexor pollicis longus	Upper two-thirds of front of radius	Terminal phalanx of thumb	Flexes all joints of thumb	20–30U 75–120U 20–30U	Mid forearm over anterior aspect of radius
Pronator quadratus	Front of ulna (distal)	Front of distal radius	Pronates forearm	20–30U 75–120U 20–30U	Approach muscle from extensor aspect of forearm just proximal to wrist and advance through interosseous membrane

* ■ OnabotulinumtoxinA (BOTOX®) ■ AbobotulinumtoxinA (Dysport®) ■ IncobotulinumtoxinA (Xeomin®)

A number of 'apps' are available from the BoNT-A manufacturers which may be helpful to clinicians in identifying and localising muscles for injection.

Appendix 3

Tools to assess outcome

Structured approach to Goal Attainment Scaling

The Goal Attainment Scaling evaluation of upper limb spasticity (GAS-eous tool) was developed as a structured approach to Goal Attainment Scaling for upper limb spasticity. Where possible, clinicians are encouraged to define the SMART goal statements based on the suggested goal parameters to support more objective evaluation of goal attainment (Turner-Stokes, Ashford *et al* 2016).

The approach is adapted within these guidelines to encompass both upper and lower limb spasticity. Principal GAS domains within focal spasticity intervention, sub-categories and goal parameters are set out below.

Further information on how to use Goal Attainment Scaling is given in Appendix 4.

The full tools are available from: www.kcl.ac.uk/nursing/departments/cicelysaunders/research/outcome/rehabilitation/Rehab-outcome-measures.aspx

Domain 1: Impairment/symptoms		
Goal area	Sub-categories	Goal parameter (suggestions provided)
Pain/discomfort (b280, b780, b134)* Including stiffness	<ul style="list-style-type: none"> • Pain (b280) • Stiffness (b780) • Sleep disturbance (b134) 	Level of pain / stiffness / sleep disturbance eg rated /10 or on graphic rating scale* Score 0–10 in whole numbers (see Appendix 1)
Involuntary movements (b760, b765) eg spasms or flexed posturing of arm when walking)	<ul style="list-style-type: none"> • Associated reactions • Spasms • Posturing/dystonia 	Carry angle of elbow/height of hand up torso Spasm frequency (no. per day or night) Resting angle – degrees or % joint range
Range of movement/ prevention of contractures (b710, b735)	<ul style="list-style-type: none"> • Contracture prevention • Passive ROM • Active ROM • Splint tolerance 	Joint angles or anatomical distances eg – goniometry – % normal joint range (25, 50, 75 %) – fingertips to palm Splint tolerance – time per day
Cosmesis Perception of body image Facilitation of therapy	<ul style="list-style-type: none"> • Aesthetic appearance • Body image • Facilitating therapy 	Satisfaction with appearance / body image, eg rated /10 or on graphic rating scale Interference with therapy (team rating/10)

Domain 2: Activities / Function		
Goal area	Sub-categories	Goal parameter (suggestions provided)
Passive function (d520) Caring for the affected limb whether care is done by someone else or by the person him/herself.	<ul style="list-style-type: none"> • Hygiene – hand • Hygiene – axilla / elbow • Nail cutting • Dressing the limb • Positioning the limb • Splint application/removal 	Ease of care – eg rated /10 or on NGRS Time taken to achieve functional task
Active function (d430, d440, d445) Using the affected limb in some active task involving motor movement / dexterity	<ul style="list-style-type: none"> • Reaching (d445) • Grasp/release/grip (d445) • Holding/bimanual function (d445) • Manipulating objects (d445) • Dexterity/fine motor (d440) • Lifting/carrying (d430) 	Able to manage motor task, eg – holding and using the object – lifting cup to mouth etc Improved control / dexterity eg – rating/10, or NGRS etc. Improved speed
Ideally, goals should also have a clear functional purpose	<ul style="list-style-type: none"> • Eating /drinking (d550, d560) • Personal ADL (d510, d520, d540) • Extended ADL (d630, d640) • Typing/writing (d345, d360) • Hobbies/recreation (d920) • Work (d850) 	Achievement of functional task
Mobility (d415, d450) Improved mobility – transfers/standing/ walking due to better balance etc	<ul style="list-style-type: none"> • Ease of transfers (d420) • Balance (d415) • Gait quality (b770) • Speed/efficiency • Type of walking aid used 	Gait parameters – speed, distance Ability to climb stairs Falling/tripping frequency Safety/confidence /fatigue (NGRS) Video rating of gait quality

* Codes in brackets are ICF codes from the WHO International Classification of Functioning Disability and Health, Geneva 2001

Structured approach to Goal Attainment Scaling © Ashford and Turner-Stokes / Northwick Park Hospital and King's College London

The Numeric Graphic Rating Scale (NGRS)

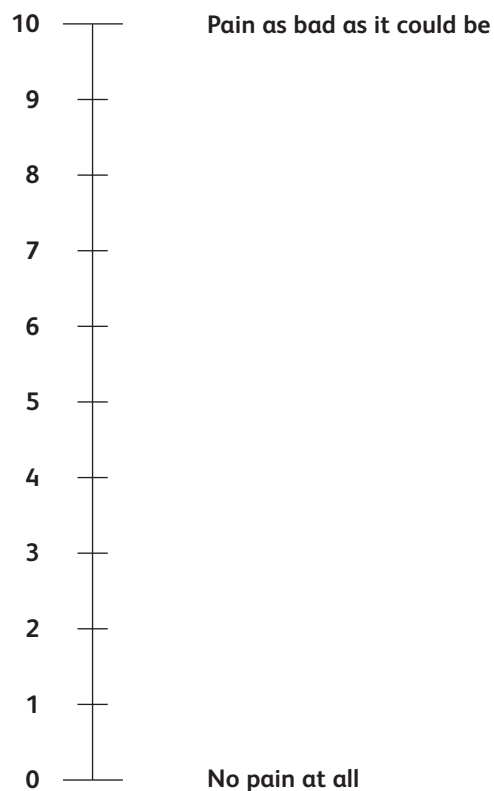
The NGRS can be used for patients to 'score' a number of different symptoms, but is commonly used for pain, which is given as the example below.

1. The scale below is a measure of pain

The top LEVEL (marked 10) indicates pain as bad as it could be

The bottom LEVEL (marked 0) indicates no pain at all

Which number best describes the pain that you feel?



2. To the administrator:

In your opinion, does the patient understand this scale?

- Yes
- No
- Not sure

Comments:

3. Which scale would they prefer to use to assess their pain next time?

- The SPIN
- The NGRS
- Either

The SPIN Screen

The SPIN is a visual scale that can be used instead of a numbered graphic rating scale and may be helpful in individuals who have communication impairment associated with language.

1. Do you have pain anywhere?



Yes



No

If yes, where?

NB if > 1 site,







complete separate sheet for both

2. The scale below is a measure of pain

The top red circle indicates pain as bad as it could be

The bottom clear circle indicates no pain at all

Which circle best describes the pain that you feel?

	Pain as bad as it could be
	
	
	
	
	No pain

3. To the administrator:

In your opinion, does the patient understand this scale?

Comments:

The SPIN Screen © Turner-Stokes and Jackson / Northwick Park Hospital

Associated Reaction Rating Scale (ARRS)

A Excursion and duration of associated reaction	
0	No involuntary movement/excursion of the limb
1	Excursion of the limb occurs on effort and disappears when effort ceases
2	Excursion of the limb occurs on effort May be variable through the task and remains present for some time after the task has been completed Residual posturing may be evident
3	Static 'stereotypical posturing' Limb reaction remains essentially present and unchanging throughout task
B Number of joints in the affected upper limb involved in associated reaction	
0	No involuntary movement of joints during task
1	Limb reaction confined to 1–2 joints
2	Limb reaction involves 3–4 joints
3	All joints of the limb involved and/or trunk
C Release of associated reaction	
0	No limb reaction. Release not required
1	Initial position is regained through the subject's conscious control or with the assistance of gravity alone
2	Subject needs to use unaffected hand in order to return affected limb towards starting position
3	Subject needs to use unaffected hand in order to return affected limb towards starting position, but limb immediately returns to stereotypical posture when handling ceases Or limb is unable to be released
D Effect of upper limb associated reaction on functional task (sit-to-stand, stand to sit).	
0	No limb reaction. Task unaffected
1	Limb reaction present but does not interfere with task
2	Obvious interference with task, but able to complete task
3	Significantly affects ability to complete task or task not completed

MODAL SCORE = 0 = None, 1 = Mild, 2 = Moderate, 3 = Severe

Most frequently occurring.

If scores are equally distributed between 2 levels, score the higher (more severe).

TOTAL SCORE =

(sum of all sections above)

Note whether the subject uses arm support during sit-to-stand: Yes/No (circle)

ARRS – scoring guidelines

- 1 Score each section A–D.
- 2 Chose one rating only from 0 to 3.
- 3 If you cannot decide between two levels, score the higher (more severe).
- 4 If the performance of the patient varies between tasks or during a single task score the worst performance.
- 5 If severity varies between joints of the upper limb, score the worst, most affected joint.
- 6 If using their unaffected limb to return the affected limb to its starting position provokes further associated reaction, score the worst situation observed during the test.

Clarifications

- 1 Arm swing of the affected limb during tasks such as sit-to-stand is not considered to be an involuntary movement or a limb reaction.
- 2 Number of joints.
Joints in this instance are said to be hand, wrist, elbow and shoulder. Each is taken to represent one joint.
- 3 Section D: Score 3 ‘Task not completed’.
This refers to a subject who can attempt a task independently, but does not complete it. For example, in sit-to-stand they initiate the task but fail to achieve full standing.

Associated Reaction Rating Scale © MacFarlane and Turner-Stokes / Northwick Park Hospital

Arm Activity measure (ArmA)

Guidance for completion of the ArmA:

Section A asks about ‘caring’ for your affected arm either yourself with your unaffected arm or by a carer or a combination of both of these. This section does not ask about using your affected arm to complete any of the tasks.

Section B asks what you can do with your affected arm or using both arms.

For each of the activities listed, please indicate (circle):

- 1 The amount of *difficulty* that you or your carer experience in doing the task, based on your activity over the *last 7 days*. Please estimate if you do the task but have not done so in the last 7 days (eg for cutting finger nails).
- 2 If the task is never done, but this has nothing to do with your arm or is never done with your affected arm, score 0 = no difficulty.

If you are unable to complete the questionnaire independently, you may:

- receive assistance from a carer or professional to act as scribe
- receive assistance from a carer or professional to facilitate understanding and completion question by question
- a carer may complete the questionnaire on your behalf based on difficulty in performance of the tasks.

In each column, please <u>CIRCLE</u> the amount of <u>difficulty</u> that you or your carer have experienced in doing the activity, over the <u>last 7 days</u> .					
Activities (affected arm)	Difficulty 0 = no difficulty 1 = mild 2 = moderate 3 = severe difficulty 4 = unable to do activity				
Section A: Caring for your affected arm (not using it in tasks or activities)					
1. Cleaning the palm of the hand	0	1	2	3	4
2. Cutting finger nails	0	1	2	3	4
3. Cleaning the armpit	0	1	2	3	4
4. Cleaning the elbow crease	0	1	2	3	4
5. Positioning arm on a cushion or support in sitting	0	1	2	3	4
(If never done, circle 0)					
6. Putting arm through a garment sleeve	0	1	2	3	4
7. Putting on a glove (If never done, circle 0)	0	1	2	3	4
8. Putting on a splint (If never done, circle 0)	0	1	2	3	4
Section B: Independently completing tasks or activities using your affected arm					
1. Difficulty with balance when walking due to your arm	0	1	2	3	4
2. Hold an object still while using unaffected hand	0	1	2	3	4
3. Open (affected hand) a previously opened jar	0	1	2	3	4
4. Pick up a glass, bottle or can	0	1	2	3	4
5. Drink from a cup or mug	0	1	2	3	4
6. Brush your teeth	0	1	2	3	4
7. Tuck in your shirt	0	1	2	3	4
8. Write on paper	0	1	2	3	4
9. Eat with a knife and fork	0	1	2	3	4
10. Dial a number on home phone	0	1	2	3	4
11. Do up buttons on clothing	0	1	2	3	4
12. Comb or brush your hair	0	1	2	3	4
13. Use a key to unlock the door	0	1	2	3	4
Total score	Section A		<input type="text"/> <input type="text"/>		
	Section B		<input type="text"/> <input type="text"/>		

Arm Activity measure © Ashford / Northwick Park Hospital and King's College London

Leg Activity measure (LegA)

Guidance for completion of the LegA:

Section A asks about ‘caring’ for your affected leg either yourself or by a carer or a combination of both of these.

Section B asks what activities you can do with your affected leg.

For each of the activities listed, please indicate (circle):

- 3 The amount of *difficulty* that you (or your carer) experience in doing the task, based on your activity over the *last 7 days*. Please estimate if you do the task but have not done so in the last 7 days.
- 4 If the task is never done, but this has nothing to do with your leg or is never done with your affected leg, score 0 = no difficulty.

Section C asks what general symptoms and difficulties you are having related to your leg which impact on your life.

For these questions you will need to score the extent to which each item impacts on you in your life based on the *last 7 days*.

If you are unable to complete the questionnaire independently, you may:

- receive assistance from a carer or professional to act as scribe
- receive assistance from a carer or professional to help you understand and complete questions
- for the passive function sub-scale, a carer may complete the questionnaire on your behalf based on difficulty in carrying out the tasks.

In each column, please CIRCLE the amount of difficulty that you or your carer have experienced in doing the activity, over the <u>last 7 days</u> .					
If the activity is never done, but this has nothing to do with your leg or is never done with your affected leg, Score 0 = No difficulty					
Section A: Caring for the affected leg (not using it in tasks or activities)					
	No difficulty	Mild difficulty	Moderate difficulty	Severe difficulty	Unable to do activity
1. Cleaning and washing the area between your legs	0	1	2	3	4
2. Putting on a splint (If never done, circle 0)	0	1	2	3	4
3. Positioning legs in a wheelchair (If never done, circle 0)	0	1	2	3	4
4. Putting your leg(s) through a trouser leg(s) (If never done, circle 0)	0	1	2	3	4
5. Transfer using a hoist, including positioning sling (If never done, circle 0)	0	1	2	3	4
6. Putting on underwear or continence pads	0	1	2	3	4
7. Positioning your leg(s) in bed using a positioning aid or pillow (If never done, circle 0)	0	1	2	3	4
8. Cleaning behind your knee (knees)	0	1	2	3	4
9. Putting on your footwear	0	1	2	3	4
Section B: Independently completing activities using your affected leg					
	No difficulty	Mild difficulty	Moderate difficulty	Severe difficulty	Unable to do activity
1. Turning in bed	0	1	2	3	4
2. Moving from lying to sitting	0	1	2	3	4
3. Being able to sit (including balance)	0	1	2	3	4
4. Transferring from bed to chair or wheelchair	0	1	2	3	4
5. Transferring from wheelchair to car	0	1	2	3	4
6. Moving from sitting to standing (including balance)	0	1	2	3	4
7. Standing (including balance)	0	1	2	3	4
8. Walking indoors (including balance)	0	1	2	3	4
9. Turning around (including balance)	0	1	2	3	4
10. Walking up stairs	0	1	2	3	4
11. Walking around obstacles or objects (including balance)	0	1	2	3	4
12. Walking over carpet	0	1	2	3	4
13. Walking outdoors	0	1	2	3	4
14. Walking over rough or uneven ground outdoors	0	1	2	3	4
15. Walking for half a mile or more	0	1	2	3	4

Section C: Symptoms (impairments) and impact on your life (participation)					
In each column, please CIRCLE how severe the symptom was over the last 7 days.					
	Not at all	A little	Moderately	Severely	Extreme
1. To what extent have you experienced pain or discomfort in your affected leg(s) or foot?	0	1	2	3	4
2. To what extent have you experienced involuntary movements or leg spasms in your affected leg(s) (ie movements or abnormal limb postures that you can't control)?	0	1	2	3	4
3. To what extent have you experienced involuntary movements or leg spasms impacting on your comfort or sleep?	0	1	2	3	4
4. To what extent have you experienced restricted range of movement (due to shortening of muscles or stiffness in joints) in your affected leg(s)?	0	1	2	3	4
5. To what extent is it difficult for you (or your carer) to care for your affected leg(s) (eg positioning your leg, putting on underwear or pads, or washing between your legs)?	0	1	2	3	4
6. To what extent has your affected leg(s) limited your daily activities (eg sitting, transferring, walking or doing stairs)?	0	1	2	3	4
7. To what extent have involuntary movements or tightness of your leg(s) or foot interfered with your mobility or balance?	0	1	2	3	4
8. To what extent has your affected leg(s) limited your normal activities with family, friends, neighbours or groups (eg social activities)?	0	1	2	3	4
9. To what extent has your affected leg limited your work or other regular activities (eg hobbies)?	0	1	2	3	4
Total score		Section A <input type="text"/> Section B <input type="text"/> Section C <input type="text"/>			
<div> Totalling section A, B and C separately produces a total score for each sub-scale of the measure. The sub-scales should not be combined. </div>					

The Spasticity-related Quality of Life tool (SQoL-6D)

Background

Spasticity is a condition in which certain muscles are continuously contracted. The resulting stiffness and tightness of muscles may affect your ability to move one or more of your limbs. Sometimes spasticity is so severe that it gets in the way of daily activities, sleep patterns, and caregiving.

Common unwanted effects of spasticity are:

- pain
- spasms or involuntary movements
- contracture and deformity
- decreased functional abilities
- difficulties with care, hygiene, dressing etc
- reduced mobility.

The SQoL-6D is a brief questionnaire in six domains, designed to assess quality of life in relation to spasticity.

1. Spasticity-related pain/discomfort:

Spasticity may cause pain arising from stiffness or a cramp-like sensation in the muscles, the joints being pulled into uncomfortable positions, or the fingernails digging into the palm. When severe, pain may interfere with activities or cause sleep disturbance at night.

- ☐ I have no pain or discomfort
- ☐ I have mild pain or stiffness only
- ☐ I have moderate pain, which does not interfere with my activities or sleep
- ☐ I have severe pain, which sometimes interferes with activities or disturbs my sleep
- ☐ I have extremely severe pain, which frequently limits my activities and/or disturbs my sleep

2. Involuntary movements

Spasticity may result in spasms or involuntary movements. For example when walking or moving, the spastic arm may pull into a tight fist or bend at the elbow. When severe, these involuntary movements or spasms can effectively limit normal activities.

- ☐ I have no problem with involuntary movements or spasms
- ☐ I have mild involuntary movements or spasms, but they do not interfere with any activities
- ☐ I have moderate involuntary movements or spasms which interfere with high-level activities
- ☐ I have severe involuntary movements or spasms which significantly limit my normal activities
- ☐ I have extremely severe involuntary movements or spasms which severely limit my activities

3. Restriction of movement

Spasticity may restrict the range of movement in joints causing abnormal posture in the affected limb(s). When severe, it can lead to contractures (permanent shortening of the muscles and tendons) and deformity of the bones and joints.

- ☐ I have no restriction of movement in any of my joints
- ☐ I have mild restriction of movement, but I am able to stretch my joints out fully with assistance
- ☐ I have moderate restriction of movement, or restriction affecting just a few joints
- ☐ I have severe restriction of movement, or restriction affecting many of my joints
- ☐ I have extremely severe restriction of movement, so that I can barely move my affected limb at all

4. Caring for the affected limb

Spasticity may result in difficulty caring for the affected limb. For example, keeping the palm or armpit clean, cutting the finger-nails or dressing the limb (eg getting the arm through a sleeve or the hand in a glove). When severe, it may prevent the limb from being properly cleaned and/or dressed.

- ☐ I have no difficulty caring for my affected limb
- ☐ I have mild difficulty caring for my limb – for example it takes some extra time or effort to care for my limb
- ☐ I have moderate difficulty caring for my limb – for example it takes me a long time or I need help from someone else to care for the limb
- ☐ I have severe difficulty, for example despite assistance my limb is sometimes smelly or left undressed
- ☐ I have extremely severe difficulty caring for my limb, and am unable to keep my limb clean and dressed

5. Using the affected limb in functional tasks

Spasticity may affect the ability to use the limb. For example, it may affect fine movement and dexterity to manipulate objects. When severe, it may limit ability to reach out for, grasp, hold and release objects.

- ☐ I am able to use my affected limb entirely normally
- ☐ I have slightly problems using my limb, but only with high level dexterity/coordination
- ☐ I have moderate problems using my limb, which affect my ability to reach; or to grasp and release objects
- ☐ I have severe problems using my limb, but am still able to use my limb as a 'prop' to steady an object
- ☐ I am unable to use my affected limb for any purpose

6. Mobility

Spasticity (even in the upper limb) may limit mobility, affecting ability to walk at normal speed or for long distances; or interfering with balance producing a tendency to fall. When severe, it may prevent the person from moving around independently.

- ☐ I have no problems with mobility
- ☐ I have mild problems with mobility, but they do not restrict my ability to get around
- ☐ I have moderate problems with mobility, which limit my ability to walk independently outdoors
- ☐ I have severe problems with mobility, which limit my ability to walk independently indoors
- ☐ I have extremely severe problems with mobility, requiring assistance from another person even to move around indoors

The Spasticity-related Quality of Life tool © Turner-Stokes and Ashford / Northwick Park Hospital and King's College London

Global assessment of benefit

Patient rating	Global assessment of benefit following the BoNT-A treatment cycle	Clinician rating
+2	Much better	+2
+1	A bit better	+1
0	The same	0
-1	Worse	-1
-2	Much worse	-2

Appendix 4

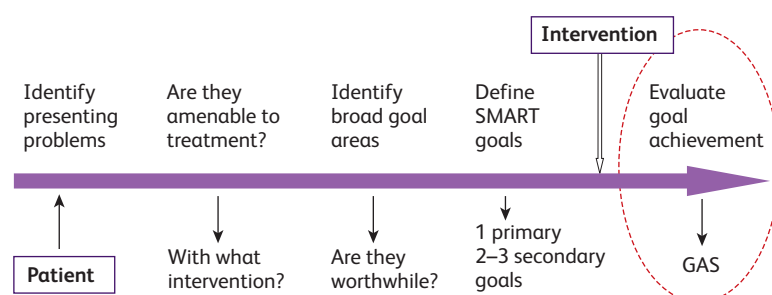
Goal Attainment Scaling – how to do it

What is GAS and how is it rated?

GAS is a method of scoring the extent to which patient's individual goals are achieved in the course of intervention.

- The most important step in GAS is the setting of clearly defined priority goals for treatment that are agreed between the individual and their treating team *before starting treatment*.
- Goals should be SMART (specific, measureable, achievable, realistic, and timed) so that the extent of achievement can be accurately rated.
- Goals may be weighted to take account of the relative importance of the goal to the individual, and/or the anticipated difficulty of achieving it.
- Normally 2–4 goals are identified, which are incorporated into the single composite GAS T- score, which provides an overall rating of the achievement of goals for that patient across all the goal areas.
- At the point of evaluation, GAS is rated on a 5-point scale, (–2 to +2) with the degree of attainment captured for each goal area:
- If the patient *achieves* the expected level, they score 0.
- If they achieve *more* than the expected outcome this is scored:
 - +1 (a little more) or
 - +2 (a lot more)
- If they achieve less than the expected outcome this is scored:
 - 1 (a little less) or
 - 2 (a lot less)

The key steps to goal setting in clinical practice are illustrated below:



Problems with GAS for use in routine clinical practice

A number of problems have arisen with the application of GAS as originally described by Kiresuk and Sherman when used in routine clinical practice:

GAS provides a flexible and responsive method of evaluating outcomes in complex interventions, but clinicians have reported a number of problems that have limited its uptake as an outcome measure for routine clinical practice:

- 1 According to the original GAS method, descriptions of achievement should be pre-defined for each of the five outcome score levels (-2, -1, 0, +1 and +2) using a 'follow-up guide. This is very time-consuming, when ultimately only one level will be used.
- 2 Clinicians are confused by the various different numerical scoring methods reported in the literature.
- 3 They generally dislike applying negative scores, which may be discouraging to patients, and are put off by the complex formula.

In addition, the 5-point GAS score does not allow 'partial achievement' of a goal to be recorded if the baseline score was -1. But on the other hand, if all baseline scores are recorded at -2, this does not allow for worsening.

The '**GAS-light**' model has been devised to help clinicians to build GAS into their clinical thinking so that GAS is not a separate outcome measurement exercise but an integral part of the decision-making and review process. Key differences between GAS-light and the original method are:

- 1 The only predefined scoring levels are for the goal (ie a clear description of the intended level of achievement) and the baseline score (ie where they are at the start of treatment) – all other levels are rated retrospectively.
- 2 The patient and treating team are both involved in goal setting and evaluation.
- 3 Clinicians often think in terms of change from baseline. Instead, goal rating is done using a 6-point verbal score in the clinic setting (which is later translated into numerical scores on a 5-point scale to derive the T-score)*

The **GAS-light verbal scoring system** is shown below:

At baseline	With respect to this goal do they have	Some function? <input type="checkbox"/>
		No function? (as bad as they could be) <input type="checkbox"/>
At outcome: Was the goal achieved?	Yes	A lot more <input type="checkbox"/> A little more <input type="checkbox"/> As expected <input type="checkbox"/>
	No	Partially achieved <input type="checkbox"/> No change <input type="checkbox"/> Got worse <input type="checkbox"/>

* For more information see the website: <http://www.kcl.ac.uk/lsm/research/divisions/cicelysaunders/resources/tools/gas.aspx>

Appendix 5

Focal Spasticity Index example proforma

FSI Focal Spasticity Index Management Form 1		Date of injection
First Name	<input type="text"/>	<input type="text"/>
Surname	<input type="text"/>	<input type="text"/>
Gender	<input type="text"/>	<input type="text"/>
DOB	<input type="text"/>	<input type="text"/>
Age	<input type="text"/>	<input type="text"/>
Episode No. <input type="text"/>		RHRUCode <input type="text"/>
NHS No. <input type="text"/>		Hospital No. <input type="text"/>
Form Status <u>B1</u> <u>B2</u> <u>B3</u> <u>B4</u> <u>B5</u>		
Date of Onset	<input type="text"/>	BTX Active <input type="radio"/> Yes <input type="radio"/> No
Previous Treatment	<input type="text"/>	Reason for Referral <input type="text"/>
Applies to: <input type="radio"/> Left <input type="radio"/> Right <input type="radio"/> Both <input type="radio"/> Upper <input type="radio"/> Lower <input type="radio"/> Other... (specify) <input type="text"/>		
Diagnosis <input type="checkbox"/> Acquired Brain Injury (stroke, trauma, etc) <input type="checkbox"/> Progressive Neurological Condition <input type="checkbox"/> Spinal Cord Injury <input type="checkbox"/> Congenital - eg CP		
Aetiology <input type="checkbox"/> Trauma <input type="checkbox"/> Inflammatory / infective <input type="checkbox"/> Vascular (Infarct or haemorrhage) <input type="checkbox"/> Tumour <input type="checkbox"/> Hypoxic <input type="checkbox"/> Degenerative		
Duration <input type="text"/> Months since onset spasticity or injury		
Dominant Side <input type="radio"/> Right <input type="radio"/> Left		
Who cares for the limb (e.g. washing, dressing, hygiene) <input type="radio"/> The patient themselves <input type="radio"/> A carer <input type="radio"/> Both together		
Review Date of Review <input type="text"/>		
Concurrent <input type="checkbox"/> Splinting <input type="checkbox"/> Orthotics <input type="checkbox"/> Exercise Programme <input type="checkbox"/> Positioning <input type="checkbox"/> Seating Modification <input type="checkbox"/> Medication		Medication Notes <input type="text"/>
		Overall Response <input type="radio"/> None <input type="radio"/> Some <input type="radio"/> Marked

FSI Focal Spasticity Index Management Form 2			
First Name <input style="width: 90%;" type="text"/> Surname <input style="width: 90%;" type="text"/>	Episode No. <input style="width: 90%;" type="text"/> RHRUCode <input style="width: 90%;" type="text"/>	Date of Injection <input style="width: 90%;" type="text"/>	<input style="width: 95%;" type="text"/>
Goals for FSI			
Primary Goal			
1 <input type="radio"/> Pain / discomfort <input type="radio"/> Involuntary movement <input type="radio"/> Range of movement <input type="radio"/> Cosmesis	<input type="radio"/> Passive Function <input type="radio"/> Active Function <input type="radio"/> Mobility <input type="radio"/> Facilitating therapy	Baseline <input type="radio"/> Some <input type="radio"/> Bad as could be	Diff. <input style="width: 50%;" type="text"/> Imp. <input style="width: 50%;" type="text"/>
Secondary Goal			
2 <input type="radio"/> Pain / discomfort <input type="radio"/> Involuntary movement <input type="radio"/> Range of movement <input type="radio"/> Cosmesis	<input type="radio"/> Passive Function <input type="radio"/> Active Function <input type="radio"/> Mobility <input type="radio"/> Facilitating therapy	Baseline <input type="radio"/> Some <input type="radio"/> Bad as could be	Diff. <input style="width: 50%;" type="text"/> Imp. <input style="width: 50%;" type="text"/>
3 <input type="radio"/> Pain / discomfort <input type="radio"/> Involuntary movement <input type="radio"/> Range of movement <input type="radio"/> Cosmesis	<input type="radio"/> Passive Function <input type="radio"/> Active Function <input type="radio"/> Mobility <input type="radio"/> Facilitating therapy	Baseline <input type="radio"/> Some <input type="radio"/> Bad as could be	Diff. <input style="width: 50%;" type="text"/> Imp. <input style="width: 50%;" type="text"/>
4 <input type="radio"/> Pain / discomfort <input type="radio"/> Involuntary movement <input type="radio"/> Range of movement <input type="radio"/> Cosmesis	<input type="radio"/> Passive Function <input type="radio"/> Active Function <input type="radio"/> Mobility <input type="radio"/> Facilitating therapy	Baseline <input type="radio"/> Some <input type="radio"/> Bad as could be	Diff. <input style="width: 50%;" type="text"/> Imp. <input style="width: 50%;" type="text"/>
GAS Calculation			
Baseline <input style="width: 50%;" type="text"/> Achieved <input style="width: 50%;" type="text"/> Change <input style="width: 50%;" type="text"/>			

Focal Spasticity Index Management Form 3			
Patient First Name <input style="width: 90%;" type="text"/> Surname <input style="width: 90%;" type="text"/>	Episode No. <input style="width: 90%;" type="text"/> RHRUCode <input style="width: 90%;" type="text"/>	<input style="width: 95%;" type="text"/>	
BTX Injection			
Date of Injection <input style="width: 90%;" type="text"/>	Applies to: <input type="radio"/> Left <input type="radio"/> Right <input type="radio"/> Both	<input type="radio"/> Upper <input type="radio"/> Lower <input type="radio"/> Other...	
Injector <input style="width: 90%;" type="text"/>	Consent <input type="checkbox"/> Patient <input type="checkbox"/> Next of Kin <input type="checkbox"/> Injector		
Muscle Identification <input style="width: 90%;" type="text"/>	<input type="checkbox"/> Palpation <input type="checkbox"/> EMG <input type="checkbox"/> NM Stimulation <input type="checkbox"/> Other...		
(or specify) <input style="width: 90%;" type="text"/>			
Agent <input style="width: 90%;" type="text"/>	Dilution: 500 units in: <input type="radio"/> 2 ml <input type="radio"/> 2.5 ml <input type="radio"/> 5 ml	<input style="width: 95%;" type="text"/>	
L or R	Muscles Injected Name	No. of Sites Injected	Dose
1	<input style="width: 90%;" type="text"/>	<input style="width: 50%;" type="text"/>	<input style="width: 50%;" type="text"/>
2	<input style="width: 90%;" type="text"/>	<input style="width: 50%;" type="text"/>	<input style="width: 50%;" type="text"/>
3	<input style="width: 90%;" type="text"/>	<input style="width: 50%;" type="text"/>	<input style="width: 50%;" type="text"/>
4	<input style="width: 90%;" type="text"/>	<input style="width: 50%;" type="text"/>	<input style="width: 50%;" type="text"/>
5	<input style="width: 90%;" type="text"/>	<input style="width: 50%;" type="text"/>	<input style="width: 50%;" type="text"/>
6	<input style="width: 90%;" type="text"/>	<input style="width: 50%;" type="text"/>	<input style="width: 50%;" type="text"/>
7	<input style="width: 90%;" type="text"/>	<input style="width: 50%;" type="text"/>	<input style="width: 50%;" type="text"/>
8	<input style="width: 90%;" type="text"/>	<input style="width: 50%;" type="text"/>	<input style="width: 50%;" type="text"/>
Signature			
<input type="button" value="Submit Baseline"/>			

Appendix 6

Sample Patient Information Sheet

Introduction

This leaflet gives you information about botulinum toxin injections and how they can help you. Staff will discuss everything in this leaflet with you, but if you have any questions, please speak to a member of the clinic team.

What are botulinum toxin injections?

Botulinum toxin is a substance produced by a type of bacterium and it has been developed into a treatment for spasticity. The toxin is diluted in order to inject it into a muscle, where it blocks the communication between nerves and the muscle. This leads to temporary weakness and relaxation of that muscle. The injection of spastic muscles with botulinum toxin is only done when the muscle overactivity is actually causing a significant problem or risk to the individual.

What is focal spasticity?

After damage to the brain or spinal cord, muscles can become overactive and stiff (this is known as spasticity). When this happens to a single muscle or a small group of muscles, rather than throughout the body, it is called focal (localised) spasticity. Sometimes this stiffness in a muscle can help a person to do something, such as standing when leg muscles are very weak. However, it can sometimes lead to problems, such as difficulties with daily tasks or pain. Prolonged spasticity can lead to a loss of a range of movement in a muscle.

What are the aims of botulinum toxin injections?

Botulinum toxin injections are used for a number of different reasons:

- to optimise the effect of treatments aimed at maintaining or increasing a range of movement
- to improve/enable tasks (such as being able to open your hand for washing)
- to improve or enable active functional activity (such as relaxing the calf muscles to enable the foot to be flat on the ground when standing)
- to decrease pain
- to improve posture.

What are the alternatives to botulinum toxin injections?

Botulinum toxin injections are used to help staff carry out physical treatments, such as putting a splint on. These interventions can be undertaken without the injection, but may not be as effective. Alternatively or additionally, tablet medications for spasticity can be tried on certain patients.

How long do the effects last?

The effects of botulinum toxin injections come on gradually and usually peak at approximately 2 weeks. They usually last for approximately 3 to 4 months, gradually wearing off.

Are there side effects from botulinum toxin injections?

Serious complications following botulinum toxin injections are rare, however the following have been known to occur:

- pain where the injection is given
- bruising where the injection is given
- flu-like symptoms
- excessive muscle weakness and temporary swallowing problems
- rarely, there is potential for anaphylaxis, which is a severe allergic reaction to the medication and requires urgent medical attention.

If you believe you have had a serious reaction to an injection please seek urgent medical attention at the nearest Accident and Emergency Department. For less serious possible side effects please consult your GP.

If you are pregnant or think you may become pregnant, please inform the clinic team.

If you have concerns about the injection or associated treatments, or you would like to discuss the issues raised in this leaflet, please speak to the clinic team.

Contact details for advice during working hours:

XXXXXXXXXXXXXXXXXX

Tel: XXX XXXX XXXX

General trust information

- Patient Advice and Liaison Service (PALS)
- PALS is a confidential service for people who would like information, help or advice about the services provided by any of our hospitals.
- Please call XXXX XXXX XXXX between 10am and 4pm or e-mail XXXX. Please note that this service does not provide clinical advice so please contact the relevant department directly to discuss any concerns or queries about your upcoming test, examination or operation.
- For a translation of this leaflet or for an English version in large print, audio or Braille please ask a member of staff or call XXXX XXXX XXXX.

Sample Patient Information Sheet © Ashford / Northwick Park Hospital

Appendix 7

Methods for prescribing, supply and administration by non-medical injectors

Prescription, supply and administration of medicines in the UK was primarily governed by the Medicines Act 1968 and subsequently amended under European Law. The regulations have been consolidated by the Medicines and Healthcare products Regulatory Agency (MHRA) in the Human Medicines Regulations 2012, and its subsequent amendments.

Within the UK legislation, supply and administration of medicines is considered a separate issue from prescription.

Key definitions

Administration is defined as the giving of a medicine by either introduction into the body (for example, orally or by injection) or external application.

Prescribing is defined as the process of issuing a written or electronic prescription for a medicine for a single individual by an appropriate practitioner.

A **licensed medicine** is a medicine with a valid marketing authorisation (product licence) in the UK. Licences apply to a particular product and particular indications. These are summarised in the ‘Summary of product characteristics’ (SPC). Currently, the licensing arrangements for the different BoNT-A products are quite narrow and limit injection within the terms of the licence to certain muscles in the arm and/or leg. See Section 6.3 for the licensing arrangements in place at the time of guideline publication for the different products. To check current product licensing please visit www.medicines.org.uk.

Off-label usage: Use of a medicine outside its licensed indications (as contained within the SPC) is described as ‘off-label’. Off-label use only applies to medicines that are already licensed ie hold a valid marketing authorisation. For example, the use of one of the BoNT-A products to treat focal spasticity in a person with multiple sclerosis or traumatic brain injury would be classified as off-label. Equally, the use of botulinum toxin to treat muscle groups not covered by the licence is also off-label.

An **unlicensed medicine** is one that does not possess a valid UK marketing authorisation (product licence), or is manufactured on the specific instruction of an independent prescriber to meet an individual patient need.

Supply and administration of botulinum toxin

Currently there are three instructions that enable a non-prescriber to administer medicines:

- 1 A standard prescription
- 2 A Patient Specific Direction
- 3 A Patient Group Direction

The standard prescription

A standard prescription is a written or electronic instruction signed by a doctor, dentist, or non-medical prescriber. It is effectively a type of Patient Specific Direction.

The Patient Specific Direction (PSD)

A PSD is a written or electronic instruction signed by a doctor, dentist, or non-medical prescriber for a medicine to be supplied and/or administered to a named patient after the prescriber has assessed the patient on an individual basis.

- Writing a PSD is a form of prescribing.
- A non-medical injector must only administer the medicine in accordance with the instructions that are written by the prescriber.
- PSDs do not allow for any clinical decision-making at the point of administration, eg variation of dose or site, and may not meet the needs of the individual if dose variation is clinically indicated.
- PSDs can apply to licensed, unlicensed and off-label use of medicines.

There is no set template for PSDs but the following apply:

- the patient must be individually identified on the PSD
- the written instruction must be signed and dated by the independent prescriber
- for a PSD to be valid, the named patient must also have been seen by the doctor/dentist or other independent prescriber.

The administration of medicines prescribed using a PSD may be delegated by an independent prescriber to other appropriately qualified health professionals.

- Medical prescribers and nurse independent prescribers may delegate the administration of both licensed, 'off-label' and unlicensed medicines, but physiotherapist independent prescribers may only delegate the administration of licensed and off-label medicines.

The Patient Group Direction (PGD)

A PGD is a written document authored by a doctor and pharmacist that describes the names and dosages of specific medicines that may be supplied and administered to specified groups of patients by named and authorised registered health professionals. It is written in advance of any patient presenting for treatment. Using a PGD is not a form of prescribing.

Off-label use of a licensed medicine can be included in a PGD only when clearly justified by best clinical practice. The PGD needs to clearly state that the medicine is being used outside the terms of the marketing authorisation on the PGD and the non-medical injector should consider informing the patient or their carer that the use is off-label.

Clinical decision-making (eg variation to dose and site) is allowed, providing it is acknowledged in the PGD, and is managed according to clear criteria or parameters. However, administration under a PGD cannot be delegated to a professional not named on the PGD.

- PGDs are formal documents written by individual NHS trusts for supply and administration.
- The formulation of the document should include the signed agreement of an NHS trust's medicines management committee and/or medical directors.
- In order to be valid, a PGD must meet specific legal criteria. This includes the requirements that the therapist/nurse is registered with the HPC/NMC, and that the supply and administration of the drugs listed in the PGD is not delegated to anyone else.
- PGDs tend to be used in hospital and primary care settings but are also valid in other non-NHS clinical settings.

Prescribing of BoNT-A

Prescribing is the process of authorising in writing or electronically the supply and administration of a medicine for a named individual patient.

Independent prescribing

Independent prescribers are specified health professionals defined in law as being able to prescribe medicines independently. The current professions with independent prescribing rights are:

- doctors
- dentists
- nurses
- pharmacists
- optometrists
- physiotherapists
- podiatrists

If the professional is not a doctor or dentist, in order to be an independent prescriber, a member of one of the listed professions must also be:

- 1 Listed on the relevant regulatory register
- 2 Annotated on that register as an independent prescriber, having completed an approved training programme.

Independent prescribers are only able to prescribe within their field of expertise. In addition, there are some restrictions in prescribing rights:

Nurse independent prescribers

Nurse independent prescribers are able to prescribe licensed, unlicensed and 'off-label' medicines.

Physiotherapist independent prescribers

Physiotherapist independent prescribers are able to prescribe licensed and 'off-label' medicines. They are not entitled to prescribe unlicensed medicines.

Supplementary prescribing

Supplementary prescribing is a voluntary prescribing partnership between an independent prescriber and a supplementary prescriber, to implement an agreed patient-specific clinical management plan (CMP). A clinical management plan is a written plan relating to the treatment of an individual patient agreed by the patient, the doctor party to the plan and the supplementary prescriber who is to prescribe.

Supplementary prescribers will also need to be listed on the relevant regulatory register, and annotated on that register as a supplementary prescriber, having completed an approved training programme. CMPs can include licensed, off-label and unlicensed medicines and can allow mixing of licensed medicines.

Further information

For further information on supply, administration and prescribing please see the following references:

- Health Professions Council (2013) *Standards for prescribing*. www.hpc-uk.org/aboutregistration/standards/standardsforprescribing/ (Health Professions Council 2013).
- NICE (2013) *Patient Group Directions*. www.nice.org.uk/guidance/mpg2 (National Institute of Health and Care Excellence 2013a).
- Nursing and Midwifery Council (2006) *Standards of proficiency for nurse and midwife prescribers*. www.nmc.org.uk/globalassets/sitedocuments/standards/nmc-standards-proficiency-nurse-and-midwife-prescribers.pdf (Nursing and Midwifery Council 2006).

Summary chart of the medicines frameworks for non-medical clinicians

Profession	PSD	PGD	Supplementary prescribing (SP) within a CMP	Independent prescribing			
				Licensed	Off-label	Unlicensed	Mixing
Nurse	Licensed medicines Off-label use of licensed medicines Unlicensed medicines Mixing permitted	Licensed medicines Off-label use of licensed medicines Schedule 4–5 controlled drugs Schedule 2 morphine/diamorphine for sick and injured NO MIXING	Licensed medicines Off-label use of licensed medicines Mixing of licensed medicines including all controlled drugs Schedule 2–5 controlled drugs Unlicensed medicines	Full formulary	Full formulary	Yes	Permitted Including mixing Schedule 2–5 controlled drugs
				Full formulary (some restrictions on controlled drugs)	Full formulary	No	Permitted No mixing controlled drugs
Physiotherapist				Full formulary (some restrictions on controlled drugs)	Full formulary	No	Permitted No mixing controlled drugs
Podiatrist				Full formulary (some restrictions on controlled drugs)	Full formulary	No	Permitted No mixing controlled drugs
Occupational therapist			No	No	No	No	No

Adapted from Chartered Society of Physiotherapy (2016) *Summary chart of medicines frameworks for all UK medical and health professions*. CSP: London.

Appendix 8

Physical interventions and physical therapies

Provision of anti-spasticity medications including botulinum toxin may be used to enable and support physical treatment methods to enhance and supplement the overall management programme. The COT/ACPIN splinting practice guidelines (College of Occupational Therapists and Association of Chartered Physiotherapists in Neurology 2015) state that ‘**Whilst focusing neurological rehabilitation on facilitating neural recovery and preventing spasticity is important, it is equally essential that steps are taken to prevent and, if needed, treat the detrimental changes associated with maladaptive musculoskeletal plasticity.**’

Passive stretching

Although splinting is a common component of treatment and management in neurological practice (Edwards and Charlton 2002; Coppard and Lohman 2007), the effectiveness of splinting as a stretch intervention for adaptive muscle shortening remains the subject of ongoing debate (Katalinic, Harvey *et al* 2010; Lannin and Ada 2011) and (Kilbride, Hoffman *et al* 2013).

A Cochrane review of the provision of stretching for the maintenance of joint mobility and prevention of contracture (Katalinic, Harvey *et al* 2010) identified benefits in traumatic brain injury, particularly in the lower limb, but these were not maintained once intervention had ceased.

- The authors concluded that there was no discernible benefit to providing stretch for less than 7 months.
- There were no studies which looked at stretch over a longer period so the benefits in long-term management were unclear.
- However, difficulties were acknowledged within the included studies due to the consistency and methods of application, as well as intervention duration, which was generally short (days to weeks) in most studies.

Prolonged stretch may be provided through splinting, casting or strapping as described in Chapter 4.

Upper limb splinting

The splinting practice guidelines published in 2015 (College of Occupational Therapists and Association of Chartered Physiotherapists in Neurology 2015) suggest that upper limb splinting should not be

provided to all patients following a neurological event. However, splinting may have value in certain situations, eg:

- patients with stroke or acquired brain injury (ABI) may benefit from splint use for correction of secondary complications, such as realignment, support and stretch
- splinting of the wrist in a neutral wrist position may prevent pain.

Splinting may have value in spasticity management for the prevention of contractures and for the reduction in spasticity – particularly in combination with BoNT-A injection (Kilbride, Hoffman *et al* 2013; College of Occupational Therapists and Association of Chartered Physiotherapists in Neurology 2015).

Lower limb splinting

The splinting practice guidelines (College of Occupational Therapists and Association of Chartered Physiotherapists in Neurology 2015) recommend that prevention or improvement of ankle range can be achieved through the use of ankle splinting (orthoses) for people with stroke and ABI. However, the risks of pressure areas should be considered carefully when providing off-the-shelf orthoses for the ankle.

The NICE stroke rehabilitation guidelines (National Institute of Health and Care Excellence 2013b) indicate that lower limb orthoses should be considered for difficulties with foot clearance during walking, or problems in the control of the stance-phase of gait.

Casting

There is evidence for efficacy of casting in traumatic brain injury (Moseley, Hassett *et al* 2008) and as an intervention to relieve pain in patients with severe joint malalignment (Burge 2008).

Current evidence suggests that casting the elbow, knee or ankle joint at end range can improve range of movement, prior to the development of established contracture, while the musculotendinous structures are still amenable to change.

The splinting practice guidelines recommend that casts should be considered in the acute phase, and that short applications of casts (for 1–4 days) may have fewer complications than casts applied for longer periods (College of Occupational Therapists and Association of Chartered Physiotherapists in Neurology 2015).

Strapping/taping

There is modest trial-based evidence to suggest that strapping/taping the ankle is superior to just stretching following BoNT-A injection (Baricich, Carda *et al* 2008) and one small study suggests that the use of strapping may allow lower doses of BoNT-A (Reiter, Danni *et al* 1998).

A case control study from two centres in Italy provides weak evidence for taping as an adjunct to BoNT-A in reducing spasticity in the wrist and fingers (Carda and Molteni 2005).

Active exercise therapies

If an individual has some volitional selective motor control then more active movement re-education may be indicated. Most interventions to support the recovery of active function involve a form of task practice exercise therapy.

Task-related training

Upper limb

Pollock *et al* demonstrated improved upper limb function when task training was delivered at a high dose involving at least 20 hours of practice (Pollock, Farmer *et al* 2014). NICE recommends that stroke patients be offered the opportunity to undertake repetitive task training (National Institute of Health and Care Excellence 2013b).

Lower limb

A Cochrane systematic review of task training for lower limb function found evidence for modest benefit in comparison with other groups (French, Thomas *et al* 2010).

Constraint-induced movement therapy and modified constraint-induced movement therapy

Constraint-induced movement therapy (CIMT) involves restriction of the non-affected limb for certain periods to counteract 'learned non-use' of the affected limb, effectively forcing its use in active tasks.

Eligibility criteria for CIMT include (Wolf, Thompson *et al* 2010; National Institute of Health and Care Excellence 2013b):

- some retained active movement in the wrist and fingers
- good compliance and limited pain or spasticity
- at least 20° of wrist extension and 10° of finger extension
- ability to stand and no significant cognitive impairment.

There are also criteria for the amount of time that a limb is restricted and the exercises/activities to be carried out (Bohannon and Smith 1987; Turner-Stokes 2009b).

Modifications to the original outlined programme were made to enhance compliance by reducing the amount of time the limb was restricted. Several studies, including the EXCITE Stroke Trial (Wolf, Milton *et al* 2011) and a meta-analysis (Baricich, Carda *et al* 2008) provide evidence for the effectiveness of CIMT/modified CIMT (mCIMT) following stroke. However, there is continued uncertainty regarding optimal timing, duration and intensity of any CIMT/mCIMT programme (Reiter, Danni *et al* 1998, Baricich, Carda *et al* 2008; Sun, Hsu *et al* 2010; Wolf, Thompson *et al* 2010), and a recent revision of the Cochrane review by Corbetta and colleagues (Reiter, Danni *et al* 1998; Corbetta, Sirtori *et al* 2015) noted that early estimations of the benefits may have been over-optimistic.

As yet there has been little exploration of CIMT specifically in relation to spasticity, but one small study comparing BoNT-A injection combined with mCIMT with BoNT-A and neurodevelopmental treatment demonstrated greater functional gains with mCIMT but acknowledged that larger studies are needed (Sun, Hsu *et al* 2010).

Strength training

A systematic review of early strength training following stroke (Ada, Dorsch *et al* 2006) concluded that it was effective and did not increase spasticity.

Pollock *et al* (Pollock, Farmer *et al* 2014) demonstrated that strength training can improve active function and Jolk *et al* (Jolk, Alcantara *et al* 2012) concluded that 60 minutes per week of progressive strength training, or core and stability training did result in improved muscle strength with no adverse effects.

NICE recommends that clinicians should consider strength training using both body weight activities and resistance exercises following stroke (National Institute of Health and Care Excellence 2013b).

Mental imagery/mental rehearsal/mirror therapy

In these techniques the individual imagines their affected limb (usually upper limb) carrying out a series of movements, which may be supplemented by watching a reflection in a mirror or attempting to move the affected limb. This is hoped to initiate cortical reorganisation and enhance brain activity and ‘fool’ the brain into thinking the affected limb is moving.

The evidence for effectiveness is mixed. Small studies of mirror therapy (General Medical Council 2013; Gracies 2016) and mental imagery (Esquenazi, Mayer *et al* 2009) provide limited evidence for improvement in active function. However, there is currently little indication of appropriate dosing regimens and carry over, and other studies have failed to show any benefit (Pandyan, Johnson *et al* 1999).

Again, the evidence in spasticity management is scant. One publication of three case reports combined BoNT-A injection with mental imagery and found improvements in active function (Santamato, Panza *et al* 2010). Further research and evaluation is required before these techniques could be recommended for use in clinical practice.

Electrical stimulation

Electrical stimulation of muscles may be applied for reducing pain, exercise therapy or for initiation of movement in the upper and lower limb (for example functional electrical stimulation for foot drop). One systematic review concluded that electrical stimulation may be beneficial as part of a strength training programme (Glinsky, Harvey *et al* 2007).

Upper limb

- Pandyan *et al* showed that although electrical stimulation to treat spasticity in the wrist flexors did improve range of movement, the effect was not sustained post treatment (Simpson, Patel *et al* 2017).
- There is currently little evidence to support the use of electrical stimulation to improve active function of the hand and routine use is not recommended in this area (Pollock, Farmer *et al* 2014).

Lower limb

NICE (National Institute of Health and Care Excellence 2013b) indicates that, for foot drop of central origin, there is sufficient evidence to demonstrate improved gait quality and efficiency, reduction in falls and quality of life improvements, such as return to work.

Summary

In summary, there is modest evidence that physical interventions can improve both active and passive function, but as yet there is only weak evidence for the added benefit of concomitant therapies in conjunction with BoNT-A injection. Further research is required to explore optimal types, intensity and duration of treatment as well as their cost benefits and utility in terms of improved quality of life.

Appendix 9

Conflicts of interest

The following conflicts of interest were declared by the GDG members

Dr Stephen Ashford
(Chair and editor)

- I practise in clinical rehabilitation and use BoNT-A regularly in the management of spasticity
- I have a specific interest in outcome measurement for rehabilitation and have been responsible for the development of some of the outcome measures included in these guidelines
- I have undertaken research sponsored by investigator-led grants from Ipsen Ltd
- I have received sponsorship from Allergan, Ipsen and Merz to attend conferences and meetings in the UK and overseas
- I have no personal financial interest in BoNT-A or any related product

Prof Lynne Turner-Stokes
(Co-editor)

- I practise in clinical rehabilitation and use BoNT-A regularly in the management of spasticity for my patients
- I have a specific interest in outcome measurement for rehabilitation and have been responsible for the development of some of the measures included in these guidelines
- I have undertaken research sponsored by investigator-led grants from Ipsen Ltd
- I have undertaken consultancy work for Allergan, Ipsen and Merz and have received sponsorship from these companies at various times to attend conferences and meetings in the UK and overseas
- I have no personal financial interest in BoNT-A or any related product

Dr Rhoda Allison

- I practise in clinical rehabilitation and use BoNT-A regularly in the management of spasticity
- I have undertaken consultancy work for Allergan
- I have received sponsorship from Allergan and Merz to attend conferences and meetings in the UK and from Allergan to attend meetings overseas
- I have no personal financial interest in BoNT-A or any related product

Ms Lynsay Duke	<ul style="list-style-type: none"> • I practise in clinical rehabilitation and management of spasticity • I have received sponsorship from Ipsen Ltd and Merz to teach on and attend conferences and meetings in the UK and overseas. • I have undertaken research sponsored by an investigator-led grant from Ipsen Ltd. • I have no personal financial interest in BoNT-A or any related product
Dr Ganesh Bavikatte	<ul style="list-style-type: none"> • I practise in rehabilitation medicine and use BoNT-A regularly in the management of spasticity and hyper-salivation. • I have undertaken research sponsored by grants from Allergan and Ipsen • I have undertaken consultancy work for Allergan, Ipsen and Merz and have received sponsorship from these companies to attend conferences and meetings in the UK and overseas • I have no personal financial interest in BoNT-A or any related product
Dr Stephen Kirker	<ul style="list-style-type: none"> • I practise in clinical rehabilitation and use BoNT-A regularly in the management of spasticity for my patients • I have undertaken research sponsored by grants from Allergan, Ipsen and Merz • I have undertaken consultancy work for Allergan, Ipsen and Merz and have received sponsorship from these companies at various times to teach at and attend conferences and meetings in the UK and overseas • I have no personal financial interest in BoNT-A or any related product
Dr Peter Moore	<ul style="list-style-type: none"> • I practise in clinical neurology and use BoNT-A regularly in the management of spasticity for my patients • I have undertaken research sponsored by grants from Allergan, Ipsen and Merz • I have undertaken consultancy work for Allergan, Ipsen and Merz and have received sponsorship from these companies at various times to teach at and attend conferences and meetings in the UK and overseas • I have no personal financial interest in BoNT-A or any related product
Prof Anthony Ward	<ul style="list-style-type: none"> • I practise in rehabilitation medicine and use BoNT-A regularly in the management of spasticity for my patients • I have undertaken research sponsored by investigator-led grants from Allergan • I have undertaken consultancy work over several years for Allergan, Ipsen and Merz and have received sponsorship from these companies at various times to teach at and attend conferences and meetings in the UK and overseas • I have no personal financial interest in BoNT-A or any related product
Prof Diana Bilton	<ul style="list-style-type: none"> • I have been a patient undergoing rehabilitation requiring spasticity management • I have no personal financial interest in BoNT-A or any related product

Appendix 10

Summary of evidence

SUMMARY OF EVIDENCE for recommendation 1.1

- | | | |
|-----|---|-------|
| 1.1 | Botulinum toxin type A (BoNT-A) is a safe and effective treatment for upper and lower limb spasticity, resulting in both passive and active functional gains: | RA E2 |
| | <ul style="list-style-type: none"> Commissioning of spasticity management programmes should include provision for use of BoNT-A injection, when administered in line with the recommendations below. | |

DIRECT EVIDENCE within the field of spasticity

- | | | |
|---|--|-------------------|
| 1 | Ashford S, Fheodoroff K, Jacinto J, Turner-Stokes L. Common goal areas in the treatment of upper limb spasticity: A multicentre analysis. <i>Clin Rehabil</i> 2016 Jun;30(6):617–22 | R2 High
Direct |
| | Retrospective article reviewing five previously published research articles. Goal attainment and goal setting were the terms of search in this paper and it used them in the context of the ICF domains of impairment and activities. The paper addresses recommendation 1. | |
| 2 | Turner-Stokes L, Baguley IJ, De Graaff S, Katrak P, Davies L, McCrory P, Hughes A. Goal Attainment Scaling in the evaluation of treatment of upper limb spasticity with botulinum toxin: a secondary analysis from a double-blind placebo-controlled randomized clinical trial. <i>J Rehabil Med</i> 2010 Jan;42(1):81–9 | P1 High
Direct |
| | Goal Attainment Scaling provides a responsive measure for evaluating focal intervention for upper limb spasticity, identifying outcomes of importance to the individual/carers, which are not otherwise identifiable using standardised measures. This paper is a suitable reference for recommendation 1. | |
| 3 | Turner-Stokes L, Fheodoroff K, Jacinto J <i>et al.</i> Upper limb international spasticity study: rationale and protocol for a large, international, multicentre prospective cohort study investigating management and goal attainment following treatment with botulinum toxin A in real-life clinical practice. <i>BMJ Open</i> 2013;3: e002230. | P1 High
Direct |

This paper used assessment methodology with achievable patient-centred goals that could lead to meaningful benefits. The content of this article addresses recommendation 1.

- | | | |
|---|--|-------------------|
| 4 | Turner-Stokes L, Ashford S, Jacinto J <i>et al.</i> Impact of integrated upper limb spasticity management including botulinum toxin A on patient-centred goal attainment: rationale and protocol for an international prospective, longitudinal cohort study (ULIS-III). <i>BMJ Open</i> 2016;6:e011157. | P1 High
Direct |
|---|--|-------------------|

The study reflects actual clinical practice in managing post-stroke patients' upper limb spasticity management and the authors highlight the need for realistic goals and a level of competence and communication between the various members of the multidisciplinary team. Communication with patients/caregivers is vital to agree on treatment realistic goals. The content meets the criteria of recommendation 1.

- | | | |
|---|---|-------------------|
| 5 | Ward AB, Wissel J, Borg J <i>et al.</i> Functional goal achievement in post-stroke spasticity patients: The BOTOX® Economic Spasticity Trial (BEST). <i>J Rehabil Med</i> 2014 Apr 8;46:504–13. | P1 High
Direct |
|---|---|-------------------|

Prospective RCT of Onabotulinumtoxin A versus placebo (both + standard care) using GAS as a primary outcome. The patient and investigator together defined principal and secondary active functional and passive treatment goals and used the GAS to demonstrate functional benefits. Demonstrated significantly increased passive goal achievement. The authors demonstrated statistically significant benefits in active functional goals in the upper limb.

Derived from research evidence:

Research Grade A: >1 direct high quality studies
E2 from this consensus

RA E2

Compiled by Anthony B Ward

References

- 1 Ashford S, Fheodoroff K, Jacinto J, Turner-Stokes L. Common goal areas in the treatment of upper limb spasticity: A multicentre analysis. *Clin Rehabil* 2016 Jun;30(6):617–22. **R2 High Direct**
- 2 Turner-Stokes L, Baguley IJ, De Graaff S, Katrak P, Davies L, McCrory P, Hughes A. Goal Attainment Scaling in the evaluation of treatment of upper limb spasticity with botulinum toxin: a secondary analysis from a double-blind placebo-controlled randomized clinical trial. *J Rehabil Med* 2010 Jan;42(1):81–9. **P1 High Direct**
- 3 Turner-Stokes L, Fheodoroff K, Jacinto J *et al.* Upper limb international spasticity study: rationale and protocol for a large, international, multicentre prospective cohort study investigating management and goal attainment following treatment with botulinum toxin A in real-life clinical practice. *BMJ Open* 2013;3: e002230. **P1 High Direct**
- 4 Turner-Stokes L, Ashford S, Jacinto J *et al.* Impact of integrated upper limb spasticity management including botulinum toxin A on patient-centred goal attainment: rationale and protocol for an international prospective, longitudinal cohort study (ULIS-III). *BMJ Open* 2016;6:e011157. **P1 High Direct**
- 5 Ward AB, Wissel J, Borg J *et al.* Functional goal achievement in post-stroke spasticity patients: The BOTOX® Economic Spasticity Trial (BEST). *J Rehabil Med* 2014 Apr 8;46:504–13. **P1 High Direct**

SUMMARY OF EVIDENCE for recommendation 2.4

2.4	BoNT-A injection must be part of a rehabilitation programme involving physical management and/or rehabilitation to achieve an optimal clinical effect.	RA
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DIRECT EVIDENCE within the field of spasticity

- | | | |
|---|--|-------------------|
| 1 | Moseley AM, Hassett LM, Leung J, Clare JS, Herbert RD, Harvey LA. Serial casting versus positioning for the treatment of elbow contractures in adults with traumatic brain injury: a randomized controlled trial. <i>Clin Rehabil</i> 2008;22:406–417. | S1 High
Direct |
|---|--|-------------------|

In this RCT effects of stretch intervention (serial casting) were clearly demonstrated, though not maintained once intervention ceased.

Practice implications are however apparent with common practice following serial casting being the provision of a longer term orthotic combined with task-practice in some instances when appropriate.

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|---|--|-------------------|
| 2 | Moseley AM. The effect of casting combined with stretching on passive ankle dorsiflexion in adults with traumatic head injuries. <i>Phys Ther</i> 1997;77:240-247; discussion 248–259. | S1 High
Direct |
|---|--|-------------------|

Initial evidence of benefit for serial casting as a passive stretch intervention.

- | | | |
|---|---|-------------------|
| 3 | Katalinic OM, Harvey LA, Herbert RD. Effectiveness of stretch for the treatment and prevention of contractures in people with neurological conditions: a systematic review. <i>Physical Therapy</i> 2011;91(1):11–24.
(extraction of patients with a neurological condition from the Cochrane review published 2010) | S1 High
Direct |
|---|---|-------------------|

Conclusion: Regular stretch does not produce clinically important changes in joint mobility, pain, spasticity, or activity limitation in people with neurological conditions. Stretch interventions applied indiscriminately are ineffective.

Changes were however noted in traumatic brain injury following serial casting, but these were not sustained.

The review again emphasises the need to evaluate more carefully when stretch intervention is applied and how this should be followed up and maintained following improvements in range of movement.

Derived from research evidence:

Research Grade A: >1 direct high quality studies show improvement following intervention but was not maintained once intervention ceased.	RA E2
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And Expert E2 from this consensus

Patient selection probably also important.

Compiled by Stephen Ashford

References

- 1 Moseley AM, Hassett LM, Leung J, Clare JS, Herbert RD, Harvey LA. Serial casting versus positioning for the treatment of elbow contractures in adults with traumatic brain injury: a randomized controlled trial. *Clin Rehabil* 2008;22:406–17. **S1 High Direct**
- 2 Moseley AM. The effect of casting combined with stretching on passive ankle dorsiflexion in adults with traumatic head injuries. *Phys Ther* 1997;77:240–7; discussion 248–59. **S1 High Direct**
- 3 Katalinic OM, Harvey LA, Herbert RD. Effectiveness of stretch for the treatment and prevention of contractures in people with neurological conditions: a systematic review. *Physical Therapy* 2011;91(1):11–24. **S1 High Direct**

SUMMARY OF EVIDENCE for recommendation 3.5

3.5 EMG, nerve stimulation and/or ultrasound should be used to localise the BoNT-A injection according to the site and purpose of the injection.

DIRECT EVIDENCE within the field of spasticity

- | | | |
|---|--|--------|
| 1 | Picelli A, Roncari L, Baldessarelli S <i>et al.</i> Accuracy of botulinum toxin type A injection into the forearm muscles of chronic stroke patients with spastic flexed wrist and clenched fist: Manual needle placement evaluated using ultrasonography. <i>J Rehabil Med</i> 2014;46:1042–45. | Direct |
|---|--|--------|

Small study examining manual needle placement into FCR, FCU, FDS, FDP – then checking accuracy with ultrasound in 41 participants with spasticity. Accurate manual needle placement occurred on 51% of occasions (less accurate for wrist than finger flexors).

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|---|--|--------|
| 2 | Picelli A, Bonetti P, Fontana C <i>et al.</i> Accuracy of botulinum toxin type A injection into the gastrocnemius muscle of adults with spastic equinus: Manual needle placement and electrical stimulation guidance compared using ultrasonography. <i>J Rehabil Med</i> 2012;44:450–2. | Direct |
|---|--|--------|

Small study examining injection of gastrocnemius comparing manual needle placement with needle placement under electrical stimulation – 42 participants with spasticity had needle inserted under manual placement and 39 under electrical stimulation. Accuracy of needle placement was assessed using ultrasound. With manual needle placement 80% of injections were correctly sited, while 92% of injections under electrical stimulation were sited correctly.

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|---|--|--------|
| 3 | Guirao L, Costea M, Llorensi G <i>et al.</i> Accuracy of the ultrasonography-guided injection of botulinum toxin into the tibialis posterior by using the anterior approach. <i>PM and R</i> , 2011;3/10:S346. | Direct |
|---|--|--------|

Small study examining ultrasound guided needle placement into tibialis posterior, then checking accuracy with electrical stimulation in 19 participants with spasticity. Accurate ultrasound guided needle placement occurred on 84% of occasions.

- 4 Santamato A, Micello M.F, Panza F *et al.* Can botulinum toxin type A injection technique influence the clinical outcome of patients with post-stroke upper limb spasticity? A randomized controlled trial comparing manual needle placement and ultrasound-guided injection techniques. *J Neurol Sci* 2014;347/1–2(39–43) Direct

Very small randomised controlled trial (RCT) comparing outcomes (modified Ashworth and finger resting posture) in 15 participants with ultrasound guided injection of forearm flexors (FCR, FCU, FDP, FDS) and 15 participants injected under manual needle placement. Both groups showed improved outcomes but there were significantly better outcomes in those injected under ultrasound guidance.

- 5 Pokhabov D, Abramov V, Nesterova Y. The efficacy of botulinum toxin injections in deep muscles of upper limb with and without using needle electrical stimulation. *J Neurol Sci* 2013;333,1, e103 Direct

Very small study comparing outcomes (modified Ashworth) in 23 participants with manual needle placement injection of forearm flexors (FDP and PT) and 18 participants injected under electrical stimulation. Both groups showed improved outcomes but there were significantly better outcomes in those injected under electrical stimulation.

Derived from research evidence: Research Grade: B

More than one medium quality study (4-6/10)

Manual needle placement appears more accurate in larger muscles such as gastrocnemius than smaller and deeper muscles. Accurate needle placement can be improved by localisation techniques and there is weak evidence that this improves outcomes.

Compiled by Rhoda Allison

References

- 1 Picelli A, Roncari L, Baldessarelli S *et al* Accuracy of botulinum toxin type A injection into the forearm muscles of chronic stroke patients with spastic flexed wrist and clenched fist: Manual needle placement evaluated using ultrasonography. *J Rehabil Med* 2014;46:1042–5.
- 2 Picelli A, Bonetti P, Fontana C *et al* Accuracy of botulinum toxin type A injection into the gastrocnemius muscle of adults with spastic equinus: Manual needle placement and electrical stimulation guidance compared using ultrasonography. *J Rehabil Med* 2012;44:450–2.
- 3 Guirao L, Costea M, Llorensi G *et al* Accuracy of the ultrasonography-guided injection of botulinum toxin into the tibialis posterior by using the anterior approach. *PM and R*, 2011; 3/10 S346.
- 4 Santamato A, Micello M.F, Panza F *et al* Can botulinum toxin type A injection technique influence the clinical outcome of patients with post-stroke upper limb spasticity? A randomized controlled trial comparing manual needle placement and ultrasound-guided injection techniques. *J Neurol Sci* 2014; 347/1–2(39–43).
- 5 Pokhabov D, Abramov V, Nesterova Y. The efficacy of botulinum toxin injections in deep muscles of upper limb with and without using needle electrical stimulation. *J Neurol Sci* 2013;333,1, e103.

SUMMARY OF EVIDENCE for recommendation 4.1

- 4.1 Passive stretch intervention (often splints, casts or positioning of sufficient duration should be implemented in individuals at risk of contracture or further contracture development when it is still possible to influence the muscle-tendon length and associated structures.

DIRECT EVIDENCE within the field of spasticity

- | | | |
|---|--|-------------------|
| 1 | Moseley AM, Hassett LM, Leung J, Clare JS, Herbert RD, Harvey LA. Serial casting versus positioning for the treatment of elbow contractures in adults with traumatic brain injury: a randomized controlled trial. <i>Clin Rehabil</i> 2008;22:406–417. | S1 High
Direct |
|---|--|-------------------|

In this RCT effects of stretch intervention (serial casting) were clearly demonstrated, though not maintained once intervention ceased.

Practice implications are however apparent with common practice following serial casting being the provision of a longer term orthotic combined with task-practice in some instances when appropriate.

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|---|--|-------------------|
| 2 | Moseley AM. The effect of casting combined with stretching on passive ankle dorsiflexion in adults with traumatic head injuries. <i>Phys Ther</i> 1997;77:240–247; discussion 248–259. | S1 High
Direct |
|---|--|-------------------|

Initial evidence of benefit for serial casting as a passive stretch intervention.

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|---|--|-------------------|
| 3 | Katalinic OM, Harvey LA, Herbert RD. Effectiveness of stretch for the treatment and prevention of contractures in people with neurological conditions: a systematic review. <i>Phys Ther</i> 2011;91(1):11–24.
(extraction of patients with a neurological condition from the Cochrane review published in 2010). | S1 High
Direct |
|---|--|-------------------|

Conclusion: Regular stretch does not produce clinically important changes in joint mobility, pain, spasticity, or activity limitation in people with neurological conditions. Stretch interventions applied indiscriminately are ineffective.

Changes were however noted in traumatic brain injury following serial casting, but these were not sustained.

The review again emphasises the need to evaluate more carefully when stretch intervention is applied and how this should be followed up and maintained following improvements in range of movement.

Derived from research evidence: Research Grade A:

>1 direct high quality studies show improvement following intervention but was not maintained once intervention ceased.

Patient selection probably important.

Compiled by Stephen Ashford

References

- 1 Moseley AM, Hassett LM, Leung J, Clare JS, Herbert RD, Harvey LA. Serial casting versus positioning for the treatment of elbow contractures in adults with traumatic brain injury: a randomized controlled trial. *Clin Rehabil* 2008;22:406–417.
- 2 Moseley AM. The effect of casting combined with stretching on passive ankle dorsiflexion in adults with traumatic head injuries. *Phys Ther* 1997;77:240–247; discussion 248–259.
- 3 Katalinic OM, Harvey LA, Herbert RD. Effectiveness of stretch for the treatment and prevention of contractures in people with neurological conditions: a systematic review. *Phys Ther* 2011;91(1):11–24.

SUMMARY OF EVIDENCE for recommendation 4.2

4.2 Task-practice training (repetitive practice) should be considered when improvement in activity performance and motor control are the target or goal of treatment.

DIRECT EVIDENCE within the field of spasticity

- | | | |
|---|--|-------------------|
| 1 | Pollock A, Farmer SE, Brady MC <i>et al.</i> Interventions for improving upper limb function after stroke. <i>Cochrane Database Syst Rev</i> 2014;11:CD010820. | S1 High
Direct |
| | Evidence through meta-analysis for clinical effect of task practice interventions, including constraint-induced movement therapy. Not possible with current evidence to compare different task practice interventions in the upper limb to indicate which is/are most effective. | |
| 2 | Pollock A, Baer G, Campbell P <i>et al.</i> Physical rehabilitation approaches for the recovery of function and mobility following stroke. <i>Cochrane Database Syst Rev</i> 2014;4:CD001920. | S1 High
Direct |
| | Meta-analysis evidence for practice-based interventions for physical rehabilitation in the lower limb. Optimal interventions cannot yet be identified, but reasonably robust evidence to indicate that practice produces functional improvement. | |
| 3 | Wolf SL, Winstein CJ, Miller JP <i>et al.</i> Retention of upper limb function in stroke survivors who have received constraint-induced movement therapy: the EXCITE randomised trial. <i>Lancet Neurol</i> 2008;7:33–40. | P1 High
Direct |

Constraint-induced movement therapy is one task practice intervention (plus constraint) that has had trial evaluation in the form of EXCITE with adequate power. This study demonstrated the long term (2 years) sustained effects of this intervention. Importantly it should be noted that patient selection is likely to be critically important for the application and effectiveness of this intervention.

Derived from research evidence: Research Grade A:

>1 direct high quality studies although the systematic reviews showed weak effect
Patient selection important.

Compiled by Stephen Ashford

References

- 1 Pollock A, Farmer SE, Brady MC *et al*. Interventions for improving upper limb function after stroke. *Cochrane Database Syst Rev* 2014;11:CD010820.
- 2 Pollock A, Baer G, Campbell P *et al*. Physical rehabilitation approaches for the recovery of function and mobility following stroke. *Cochrane Database Syst Rev* 2014;4:CD001920.
- 3 Wolf SL, Winstein CJ, Miller JP *et al*. Retention of upper limb function in stroke survivors who have received constraint-induced movement therapy: the EXCITE randomised trial. *Lancet Neurol* 2008;7:33–40.

SUMMARY OF EVIDENCE for recommendation 5.1

- 5.1 When provided as part of a multidisciplinary programme, prescribing and injecting of BoNT-A by non-medical practitioners is safe, effective, and potentially highly cost-efficient. Rb E2
- Providers should consider the development of these roles to support optimal clinical services for patients
 - Summaries of product characteristics for BoNT-A preparations should be updated to reflect current practice and legislations with respect to non-medical injectors in the UK.

DIRECT EVIDENCE within the field of spasticity

- 1 Turner-Stokes *et al* 2013 (ULIS-II) – large international cohort study n = 456 P1 High Direct

GAS T-scores were strongly correlated with global benefit and other standard measures (correlations of 0.38 and 0.63, respectively; $p < 0.001$). BoNT-A demonstrated a clinically significant effect on goal attainment for the real-life management of upper-limb spasticity following stroke. The study confirms the feasibility of a common international dataset to collect systematic prospective data, and of using GAS to capture person-centred outcomes relating to passive and active functions and to pain.
- 2 Ward *et al* 2014 (BEST study) an RCT P1 High Direct

Prospective RCT of onabotulinum toxin A vs placebo (both + standard care) used GAS as a primary outcome. Demonstrated significantly increased passive goal achievement and was associated with higher levels of active function.

- 3 Spasticity in adults: management using botulinum toxin. National guidelines. Royal College of Physicians: London, 2009 R2 E1 E2

Recommends the use of GAS alongside standardised outcome measures.

- 4 International consensus statement botulinum toxin assessment, intervention and after-care for upper limb hypertonicity in adults: Sheehan *et al*, 2010. R2 E2

Derived from research evidence:

Research Grade B (one or more high-quality studies, at least, directly related to the recommendation)
And Expert E2 RB E2

Compiled by Lynne Turner-Stokes and Stephen Ashford

References

- 1 Ashford S, Turner-Stokes L. Goal attainment for spasticity management using botulinum toxin. *Physiotherapy Research International* 2006;11(1):24–34.
- 2 McCrory P, Turner-Stokes L, Baguley IJ *et al*. Botulinum toxin A for treatment of upper limb spasticity following stroke: a multi-centre randomised placebo-controlled study of the effects on quality of life and other person-centred outcomes. *J Rehabil Med* 2009;41:536–44. P1 High Direct
- 3 Turner-Stokes L, Fheodoroff K, Jacinto J *et al*. Results from the Upper Limb International Spasticity Study-II (ULIS-II): a large, international, prospective cohort study investigating practice and goal attainment following treatment with botulinum toxin A in real-life clinical management. *BMJ Open* 2013;3:e002771. P1 High Direct
- 4 Ward AB, Wissel J, Borg J *et al*. Functional goal achievement in post-stroke spasticity patients: The BOTOX® Economic Spasticity Trial (BEST). *J Rehabil Med* 2014 Apr 8;46:504–13. P1 High Direct
- 5 Royal College of Physicians. *Spasticity in adults: management using botulinum toxin*. ISBN: 9781860163500 2009. R2 E1 E2
- 6 Sheehan G, Lannin NA, Turner-Stokes L *et al*. Botulinum toxin assessment, intervention and after-care for upper limb hypertonicity in adults: international consensus statement. *European Journal of Neurology* 2010 Aug;17 Suppl 2:74–93. R2 E2

SUMMARY of EVIDENCE for recommendation 6.2

- 6.2 Injections should be followed by a formal assessment of outcome that includes: RA E1 E2
 - severity of presentation at baseline
 - achievement of intended goals for treatment using Goal Attainment Scaling
 - standardised measures selected according to the goals for treatment.

DIRECT EVIDENCE in the field of spasticity

- 1 **McCrory *et al* 2009 – a multicentre RCT of BoNT-A for upper limb spasticity patients in Australia (n=96).** P1 High Direct

Used GAS as a secondary outcome alongside other standardised measures of quality of life, disability and carer burden. The groups did not differ significantly with respect to quality of life, pain, mood, disability or carer burden. However, patients treated with botulinum toxin type A had significantly greater reduction in spasticity (MAS) ($p < 0.001$), which translated into higher GAS scores ($p < 0.01$) and greater global benefit ($p < 0.01$).
- 2 **Turner-Stokes *et al* 2013 (ULIS-II) – large international cohort study n = 456** P1 High Direct

GAS T-scores were strongly correlated with global benefit and other standard measures (correlations of 0.38 and 0.63, respectively; $p < 0.001$). BoNT-A demonstrated a clinically significant effect on goal attainment for the real-life management of upper-limb spasticity following stroke. The study confirms the feasibility of a common international dataset to collect systematic prospective data, and of using GAS to capture person-centred outcomes relating to passive and active functions and to pain.
- 3 **Ward *et al* 2014 (BEST study) – an RCT** P1 High Direct

Prospective RCT of onabotulinum toxin A vs placebo (both + standard care) used GAS as a primary outcome. Demonstrated significantly increased passive goal achievement and was associated with higher levels of active function.
- 4 **Spasticity in adults: management using botulinum toxin. National guidelines. Royal College of Physicians: London, 2009. Recommendations 2.1 and 2.2:** E1 E2

 - 2.1 Patients should be selected for BT on the basis of...
 - clearly identified goals for treatment and anticipated functional gains.
 - 2.2 Patients and their families/carers should:
 - be given appropriate information
 - have an understanding of the realistic goals and expected treatment outcomes
 - agree treatment goals before BT is given.
- 5 **International consensus statement botulinum toxin assessment, intervention and after-care for upper limb hypertonicity in adults: Sheehan *et al* 2010.** E2

Recommendations within the guidelines state:

Recommendation 2
In summary, the following is recommended:
 - 1 Goals for treatment typically include managing symptoms, preventing or slowing down the progression of impairments, and improving passive or active function
 - 2 Treatment goals should be collaboratively determined with the patient and their carers.

Having identified the main goal areas, clearly defined treatment goals should be collaboratively determined with the patient and their carers.

Agreed goals should be SMART (ie specific, measurable, achievable, realistic and timed). The expected outcome, thus carefully defined, should be agreed by all parties to be worth- while, and the time-point for evaluation should be set in advance.

INDIRECT EVIDENCE

- | | | |
|---|--|--------------------------|
| 6 | Bovend'Eerd TJH, Botell RE, Wade DT. Writing SMART rehabilitation goals, 2009. | E2
(Indirect) |
| | <p>This article by Thamar Bovend'Eerd and colleagues sets out practical advice for SMART Goal setting, and is much quoted, but is E2 evidence as it is not accompanied by any evidence for benefit.</p> | |
| 7 | Playford ED, Areas of consensus/ controversy about goal setting in rehabilitation, 2009. | P3
Medium
Indirect |
| | <p>The Delphi studies provided consensus that goal setting is a core component of the rehabilitation process.</p> <ul style="list-style-type: none"> • Goals should be specific, ambitious, relevant and time-limited, with incremental steps that lead to progressive achievement. • Negotiating the goal core with patients is part of a patient-centred approach to rehabilitation. | |
| 8 | Locke and Latham: a 35-year odyssey, 2002.
Comprehensive review based on 35 years of literature to suggest that patient engagement in goal setting is effective in improving goal-related outcomes | E2/R2
(Indirect) |
| | <p>There were four main theoretical premises:</p> <ol style="list-style-type: none"> 1 Goals serve a directive function; they direct attention and effort toward goal-relevant activities and away from goal irrelevant activities. 2 Goals have an energising function. High goals lead to greater effort than low goals. 3 Goals affect persistence. 4 Goals affect action indirectly by leading to the arousal, discovery, and/or use of task-relevant knowledge and strategies <p>This is a seminal narrative review article but with selected literature.</p> | |
| 9 | Levack WM, Is goal planning in rehabilitation effective, A systematic review. 2006. | S1 High
Indirect |
| | <ul style="list-style-type: none"> • Systematic review of the RCT based literature only: • There is strong evidence that goal setting improved patient performance on simple cognitive or motor tasks in some specific contexts. • Some limited evidence goal planning leads to improved patient adherence • But no consistent evidence for any generalisable effects of goal planning on improved patient outcomes following rehabilitation programmes. <p>So a high-quality study but small effect.</p> | |

Derived from research evidence: RA E1 E2

Compiled by Lynne Turner-Stokes and Stephen Ashford

References

- 1 Royal College of Physicians (2009) *Spasticity in adults: management using botulinum toxin*. National guidelines. London: RCP.
- 2 Sheehan G, Lannin NA, Turner-Stokes L *et al* Botulinum toxin assessment, intervention and after-care for upper limb hypertonicity in adults: international consensus statement. *European Journal of Neurology* 2010 Aug;17 Suppl 2:74–93.
- 3 Locke EA, Latham GP. Building a practically useful theory of goal setting and task motivation: A 35-Year Odyssey. *American Psychologist* 2002; 57 (9:705–7).
- 4 Bovend'Eerdt TJH, Botell RE, Wade DT. Writing SMART rehabilitation goals and achieving Goal Attainment Scaling: a practical guide. *Clin Rehabil* April 2009 23: 352–61.
- 5 Playford ED, Siegert RJ, Levack WMM Freeman J. Areas of consensus and controversy about goal setting in rehabilitation: a conference report. *Clin Rehab* 2009; 23: 334–44.
- 6 Locke EA Latham GP. Building a Practically Useful Theory of Goal Setting and Task Motivation: A 35-Year Odyssey. *American Psychologist* 2002 Vol. 57, No. 9, 705–17.
- 7 Levack WM, Taylor K, Siegert RJ, Dean SG, McPherson KM, Weatherall M. Is goal planning in rehabilitation effective? A systematic review. *Clin Rehabil* 2006; 20: 739–55.

SUMMARY of EVIDENCE for 7.2

7.2 Clinicians should have access to facilities to aid assessment, selection and treatment planning, eg electromyography, nerve/muscle stimulation, ultrasound etc. RC E2

It is difficult to find research literature to support this general statement but there is supportive evidence of expert opinion from professions from other guidelines and non-research documents:

INDIRECT EVIDENCE

- 2 International consensus statement botulinum toxin assessment, intervention and after-care for upper limb hypertonicity in adults: Sheehan *et al* 2010.** R2 E2

Recommendations within the guidelines state:

Recommendation 2

In summary, the following is recommended:

- 3 Goals for treatment typically include managing symptoms, preventing or slowing down the progression of impairments, and improving passive or active function
- 4 Treatment goals should be collaboratively determined with the patient and their carers

Having identified the main goal areas, clearly defined treatment goals should be collaboratively determined with the patient and their carers.

Agreed goals should be SMART (ie specific, measurable, achievable, realistic and timed). The expected outcome, thus carefully defined, should be agreed by all parties to be worthwhile, and the time-point for evaluation should be set in advance.

- 3 **Spasticity in adults: management using botulinum toxin. National guidelines. Royal College of Physicians: London, 2009.** E1 E2

Recommendations 2.1 and 2.2:

- 2.1 Patients should be selected (for BT in this case) on the basis of:
- clearly identified goals for treatment and anticipated functional gains.
- 2.2 Patients and their families/carers should:
- be given appropriate information
 - have an understanding of the realistic goals and expected treatment outcomes
 - agree treatment goals before BT is given.

Derived from research evidence:

RC E1 E2 – Mainly expert evidence – research evidence from indirect studies only RC E2

Compiled by Stephen Ashford

References

- 8 Royal College of Physicians (2009) *Spasticity in adults: management using botulinum toxin*. London: RCP. R2 E1 E2
- 9 Sheean G, Lannin NA, Turner-Stokes L *et al* Botulinum toxin assessment, intervention and after-care for upper limb hypertonicity in adults: international consensus statement. *European Journal of Neurology* 2010 Aug;17 Suppl 2:74–93. R2 E2
- 10 Playford ED, Siegert RJ, Levack WMM Freeman J. Areas of consensus and controversy about goal setting in rehabilitation: a conference report. *Clin Rehab* 2009;23:334–44.

Spasticity in adults: management using botulinum toxin

These guidelines provide recommendations for the treatment of adults with spasticity with botulinum toxin as part of an overall patient management programme. They offer a background understanding of this complex field of intervention, as well as some practical tools for implementation. This updated edition replaces the original guidance published in 2009.

11 St Andrews Place
Regent's Park
London NW1 4LE
www.rcplondon.ac.uk



**Royal College
of Physicians**

