Rehabilitation management of post-stroke spasticity

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Abstract

Spasticity is a common manifestation of a neurological condition such as stroke and contributes to long-term disability. Spasticity is disordered sensorimotor control that results from damage to upper motor neurons and presents as involuntary activation of muscles that can be intermittent or sustained. The resulting limb deformity and abnormal positioning cause a diverse range of patient-centred problems such as pain; difficulty walking, transferring, feeding or dressing; and can make it difficult for a caregiver to clean the palm or apply a splint. Given the complexity of spasticity related issues, expert opinion is that spasticity management should entail a multidisciplinary rehabilitation program that may be complemented with botulinum toxin treatment. However, there is a paucity of evidence for the efficacy of rehabilitation programs for spasticity management. In this thesis, four studies address current gaps in evidence-based practice.

Study 1 is a systematic review of the effectiveness of multidisciplinary rehabilitation following botulinum toxin and other intramuscular treatments for post-stroke spasticity. Despite low-quality evidence that multidisciplinary care lessens impairment and improves active function in the upper limb, the types and intensities of rehabilitation programs that improve patient-centred outcomes remain unknown. No trials to date have explored the effect of multidisciplinary rehabilitation on passive function, caregiver burden, or the individual’s priority goals for treatment. This study identifies gaps in current research relating to methodological rigour, appropriate study designs and meaningful outcome evaluation.

Study 2 compares the effectiveness of a high-intensity ambulatory rehabilitation program and a usual care, low-intensity therapy program in improving patient-centred outcomes after botulinum toxin type A treatment. Goal achievement and satisfaction benefits persisted beyond the duration of spasticity reduction in both groups. While patient-centred outcomes were not influenced by the intensity of the ambulatory rehabilitation program, high-intensity therapy was associated with greater upper limb goal attainment. This suggests that intensive
therapy may modify the black box of rehabilitation. Further research is required to evaluate this effect and determine which elements of therapy programs optimise outcomes.

Study 3 demonstrates the use of a stroke rehabilitation taxonomy to describe the activities and interventions that therapists used during rehabilitation programs. The relationships between rehabilitation activities prescribed and treatment goals and limbs injected are also examined.

Study 4 explores the key implementation processes that may affect the outcome of the high-intensity rehabilitation programs compared with usual care. The influence of program adaptations such as provision of group rather than individual sessions, contextual or organisational differences between rehabilitation centres, therapists’ experiences with managing patients following BoNT-A injections and the effect of goal-directed therapy on outcomes needs further evaluation.

This work was undertaken to test the hypothesis that multidisciplinary rehabilitation programs following botulinum toxin type A injections for post-stroke spasticity improve patient-centred outcomes. The study findings guide the recommendations for future research and clinical practice that can be used to improve service delivery and the evidence base for rehabilitation interventions after treatment with botulinum toxin type A for post-stroke spasticity.
Declaration

This is to certify that:

i. the thesis comprises only my original work towards the PhD except where indicated in the Preface

ii. due acknowledgement has been made in the text to all other material used

iii. the thesis is fewer than 100,000 words in length, exclusive of tables, maps, bibliographies and appendices.

This study was partially funded by the Australasian Faculty of Rehabilitation Medicine, Ipsen Open Research Fellowship. The funder has had no influence on the interpretation of data and the final conclusions drawn.

........................................................

Marina Demetrios
Preface

I certify that this thesis is my original work. I am extremely grateful to my colleagues who provided valuable assistance in the following areas:

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- Caroline Brand – advice, research design and review of all chapters
- Ian Baguley – advice, interpretation of results and review of all chapters
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- Mary Galea – external support and advice.

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Multi-author papers

Copies of the three multi-author publications arising from this thesis are presented in Appendix 1. The contributions of the co-authors are listed below:

Demetrios M, Khan F, Turner-Stokes L, Brand C, McSweeney S.

- Fary Khan – advice, study design and review of manuscript
- Lynne Turner-Stokes – appraisal of included studies and review of manuscript
- Caroline Brand – appraisal of included studies and review of manuscript
- Shane McSweeney – assistance with screening studies in results of searches

- Alexandra Gorelik – assistance with statistical analyses
- Julie Louie – assistance with recruitment and review of manuscript
- Caroline Brand – advice and review of manuscript
- Ian Baguley – advice and review of manuscript
- Fary Khan – advice, study design and review of manuscript


- Caroline Brand – advice and review of manuscript
- Julie Louie – assistance with data entry and review of manuscript
- Fary Khan – advice and review of manuscript

**Conflict of interest**

Marina Demetrios and Ian Baguley have been on the Advisory Board for Ipsen and received sponsorship to attend meetings from makers of botulinum toxin (Allergan and Ipsen). Julie Louie and Lynne Turner-Stokes have received honoraria from Ipsen. No author has a personal financial interest in botulinum toxin or in any of the methods used in this research.

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Julie Louie

Shane McSweeney
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Related to this thesis


Other publications


Glossary

Spasticity

Spasticity is a motor disorder characterised by a velocity-dependent increase in tonic stretch reflexes that results from abnormal intra-spinal processing of primary afferent input and results in sustained and involuntary muscle activation. It is a positive component of the upper motor neuron syndrome.

Stroke

Stroke is defined by the World Health Organization as rapidly developed clinical signs of focal (or global) disturbances of cerebral function, lasting more than 24 hours or leading to death, with no other apparent cause than of vascular origin. A stroke may be ischaemic or haemorrhagic (including subarachnoid, intraventricular or intracerebral haemorrhage).

Botulinum toxin type A

Botulinum toxin type A is a neurotoxin from the bacteria Clostridium botulinum. When injected intramuscularly to treat spasticity, botulinum toxin type A prevents the vesicle-dependent release of acetylcholine from the pre-synaptic nerve terminal by cleaving the synaptosome-associated protein (SNAP-25), thereby blocking peripheral cholinergic transmission at the neuromuscular junction. This causes temporary muscle weakness and alters spindle cell function. It is a reversible treatment with the neuromuscular junction being restored after the end of the effect.

Rehabilitation

Rehabilitation is a problem-solving educational process aimed at reducing disability and increasing participation in people who have disease or injury. The aim is to optimise a person’s physical, psychological, social, vocational, avocational and educational potential in the presence of physiological or anatomic impairment and environmental limitations.
Multidisciplinary care

Multidisciplinary care includes any intervention that aims to maximise activity and participation that is delivered under medical supervision by two or more disciplines. The disciplines could include nursing, physiotherapy, occupational therapy, orthotics, social work and exercise physiology. Multidisciplinary care varies in its content, intensity and frequency, and is tailored to an individual’s needs.

International Classification of Functioning, Disability and Health

The International Classification of Functioning, Disability and Health has been developed by the World Health Organization to provide a framework to code a wide range of information about health and health-related domains. The classification uses a standardised common language that permits communication about health and health care across the world in various disciplines and sciences.

Passive function

The provision of care to an affected limb.

Active function

The execution of a functional task by the individual.
### Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>ARAT</td>
<td>Action Research Arm Test</td>
</tr>
<tr>
<td>BoNT</td>
<td>botulinum toxin</td>
</tr>
<tr>
<td>BoNT-A</td>
<td>botulinum toxin type A</td>
</tr>
<tr>
<td>CI</td>
<td>confidence interval</td>
</tr>
<tr>
<td>CIMT</td>
<td>constraint-induced movement therapy</td>
</tr>
<tr>
<td>GAS</td>
<td>goal attainment scaling</td>
</tr>
<tr>
<td>GRADE</td>
<td>Grades of Recommendation, Assessment, Development and Evaluation</td>
</tr>
<tr>
<td>HREC</td>
<td>Human Research and Ethics Committee</td>
</tr>
<tr>
<td>ICF</td>
<td>International Classification of Functioning, Disability and Health</td>
</tr>
<tr>
<td>IQR</td>
<td>interquartile range</td>
</tr>
<tr>
<td>MAL</td>
<td>Motor Activity Log</td>
</tr>
<tr>
<td>MAS</td>
<td>Modified Ashworth Scale</td>
</tr>
<tr>
<td>RCT</td>
<td>randomised controlled trial</td>
</tr>
<tr>
<td>RE-AIM</td>
<td>Reach, Effectiveness, Adoption, Implementation and Maintenance</td>
</tr>
<tr>
<td>SD</td>
<td>standard deviation</td>
</tr>
<tr>
<td>SMART</td>
<td>specific measureable achievable realistic and timed</td>
</tr>
<tr>
<td>UMN</td>
<td>upper motor neuron</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
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<tr>
<td>WHOQoL-BREF</td>
<td>World Health Organization Quality of Life</td>
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Chapter 1. Thesis introduction

This thesis investigates the effectiveness of rehabilitation management for improving patient-centred outcomes following botulinum toxin type A (BoNT-A) injections for post-stroke spasticity.

1.1. Impact of post-stroke spasticity: global and individual level

1.1.1. Global impact

Stroke is the second leading cause of mortality and disease burden among adults aged 60 years and over [1]. The global burden of stroke through the associated long-term disability is increasing as a result of the decline in the mortality rate for stroke and the ageing population. Annually, 15 million people worldwide suffer a stroke. Of these, five million die and another five million are left permanently disabled, placing a burden on families and communities [2].

While the incidence of spasticity is not known with certainty, it has been estimated to affect 38% of stroke survivors after 12 months [3]. Direct costs for stroke survivors with spasticity have been found to be approximately four times those for stroke survivors without spasticity [4]. The burden of post-stroke spasticity is high in terms of treatment costs, quality of life consequences, caregiver burden and the effects of comorbidities such as falls and fractures [5, 6]. Thus, stroke has a considerable impact on not only the person and their family members, but society as a whole due to the increased demand for health care.

1.1.2. Individual impact: World Health Organization (WHO)

International Classification of Functioning, Disability and Health (ICF)

Impairment: spasticity

Spasticity is a common manifestation of a neurological injury such as stroke and contributes to long-term disability. Spasticity is one of the positive components of
the upper motor neuron (UMN) syndrome and is traditionally defined as a ‘a motor disorder characterized by a velocity dependent increase in the tonic stretch reflexes (muscle tone) with exaggerated tendon jerks, resulting from hyper excitability of the stretch reflex, as one component of the upper motor neurone syndrome’ [7]. There is controversy over the optimal definition of spasticity because pathophysiological theories and understanding of clinical impact have evolved over time [8]. More recently, spasticity has been defined as ‘a disordered sensori-motor control, resulting from an UMN lesion, presenting as intermittent or sustained involuntary activation of muscles’ [9].

Clinical problems

Clinically, patients or caregivers may report tightness with passive or active movement of the limb [10], which may result in a diversity of individualised problems [11]. Post-stroke spasticity results in abnormal limb movement, positioning and posturing.

The WHO’s ICF [12] is a useful framework for describing the impact of disease on a person and the effects of treatment (Figure 1.1). Three levels of human functioning are classified by the ICF: the body or body part, the whole person, and the whole person in a social context. Disability involves dysfunction at one or more of these levels of human functioning, with issues relating to post-stroke spasticity being:

- impairments (problems with body structures or physiological function) such as restricted joint range of movement, pain [13] and involuntary movements (e.g., associated reactions and spasms) [14]
- activity limitations (difficulties executing a task or action) affecting
  - active function (the execution of a functional task by the individual) such as reduced mobility [15] and difficulty feeding or dressing that limit independence with self-care [11]
  - passive function (provision of care to an affected limb) such as difficulty maintaining palmar hygiene or applying a splint or orthotic, and increased caregiver burden [11, 16, 17]
• restrictions in participation (problems limiting societal participation), such as engagement in work, family roles and leisure activities, or affecting quality of life.

Contextual factors are environmental (extrinsic) and personal (intrinsic) factors that interact with the other constructs to influence how the individual and their caregiver experience disability.

Adapted from WHO 2001 [12].

Figure 1.1. Interactions between the components of the World Health Organization’s International Classification of Functioning, Disability and Health.
1.2. Recommendations for management of post-stroke spasticity

1.2.1. Clinical indications for treatment

The decision to treat an impairment of body structure or function, such as spasticity, should be based on the potential for the intervention to increase activity and participation, to improve quality of life for patients and their families, and to enhance specialist provision as well as save health care costs [18, 19]. Spasticity requires treatment when it interferes with activity or the ability to provide care to the stroke survivor [18, 19]. Failure to effectively treat spasticity may lead to complications including joint contractures, limb deformity, pain and loss of function.

The general consensus is that optimal spasticity management uses an individualised, goal-directed multidisciplinary rehabilitation approach to achieve long-term functional improvement after spasticity reduction treatment with BoNT-A [6, 18, 20, 21].

1.2.2. Role of BoNT-A: scientific evidence

BoNT-A is considered the gold standard pharmacological treatment for focal problematic (moderate or severe) spasticity that has not responded to physical therapies [18, 22]. The effectiveness of BoNT-A in reducing spasticity [23-25], by causing muscle weakness, following stroke has been well established for both the upper limb [17, 24-28] and the lower limb [24, 28-30]. BoNT-A is a costly intervention that has a temporary effect [31], although repeated treatments have shown benefits in the longer term [32]. While BoNT-A provides a window of opportunity to facilitate gains to be made during rehabilitation, it is considered an adjunct to a multidisciplinary rehabilitation program rather than vice versa [18].

Benefit has also been reported in terms of goal attainment, particularly in the domains of impairments (pain and associated reactions) and passive function (maintaining hygiene and reducing care needs) [26, 33], and reducing disability and caregiver burden [14, 27] in the upper limb. The impact of BoNT-A on active
function [6, 34], including lower limb outcomes [15, 28], participation and quality of life [25, 26, 28] is less clear.

**1.2.3. Role of rehabilitation: gaps in the literature**

Although rehabilitation therapies are considered to be more important in producing functional change than a single intervention such as BoNT-A injections [6, 11, 18], there is a lack of scientific evidence for this belief [35]. Published studies of physical interventions following BoNT-A injections have tended to focus on single treatment modalities or therapy approaches, rather than the complex array of interventions delivered in real-life rehabilitation settings [36]. Studies have demonstrated variable degrees of effectiveness and outcomes [35] for interventions including electrical stimulation [37, 38], stretch (casting, splinting or taping) [37, 39, 40], constraint-induced movement therapy (CIMT) [41], task-specific motor training [41] and exercise programs [35]. Despite this inconsistent evidence, spasticity management guidelines advocate a multidisciplinary rehabilitation approach based on expert opinion [6, 18, 19, 21, 22]. However, the guidelines lack details on optimal therapy programs (such as types, settings, intensity, timing and interventions) that contribute to patient-centred outcomes. Hence, rehabilitation is described as a *black box*, where little is known about what the active ingredients are in the rehabilitation process [36]. This highlights the need to identify treatments that are effective and efficient [22].

**1.2.4. Components of successful rehabilitation programs**

Rehabilitation is defined as a reiterative, active, educational and problem-solving process that is focused on a patient’s behaviour (disability) and aims to increase activity and participation while incorporating personal and environmental factors [42]. Key components of rehabilitation are shown in Table 1.1. Multidisciplinary care is a holistic approach involving a range of medical and other health personnel who adapt treatment plans to the specific medical and psychosocial needs of each patient. Rehabilitation encompasses multiple therapeutic interventions and educating patients and their caregivers in the management of spasticity.
Table 1.1. Key components of rehabilitation

**Structure**
A rehabilitation service comprises a multidisciplinary team of people who:
- work together towards common goals for each patient
- involve and educate the patient and family
- have relevant knowledge and skills
- can resolve important problems faced by their patients.

**Process**
Rehabilitation is a reiterative, active and educational problem-solving process that is focused on a patient’s behaviour (disability). Rehabilitation includes the following components:
- assessment – the identification of the nature and extent of the patient’s problems and the factors relevant to their resolution
- goal setting
- intervention, which may include either or both of (a) treatments which affect the process of change, and (b) support, which maintains the patient’s quality of life and safety
- evaluation – to assess the effects of any intervention.

**Outcome**
The rehabilitation process aims to:
- maximise function and achieve patient-centred goals
- minimise the pain and suffering experienced by the patient
- minimise the burden on the patient’s family and caregivers
- maximise the participation of the patient in their social setting.

Adapted from Wade 2000 [42].

Coordinated delivery of a multidisciplinary rehabilitation program following BoNT-A injections requires effective communication between health professionals, the patient and their caregiver, and a focus on achieving patient-centred goals [18, 19, 22, 43]. Important considerations include setting individualised, specific, measureable, attainable, realistic and timed goals (SMART) [44] and appropriate evaluation.

1.3. **Recommendations for outcome evaluation**

1.3.1. **Patient-centred outcomes: goal achievement following spasticity management**

Training clinicians in the assessment of meaningful outcomes for patients and their caregivers that assess impact at the levels of the ICF is vital in evaluating outcomes of spasticity management [6, 19, 21, 45]. Use of a responsive outcome
measure, such as goal attainment scaling (GAS) [46], is recommended because other standardised measures are not effective in identifying outcomes of importance to patients and their caregivers [33, 34, 47, 48]. GAS provides a responsive measure of functional gains when treatment goals are diverse [11, 33, 34, 49] because it combines goals related to impairment, activity and participation into a single measure. Importantly GAS provides a valuable outcome measurement in patients with complex disabilities. GAS is more sensitive than global measures such as quality of life measures [33], the Barthel Index [34] and Functional Assessment Measure [50], which tend to have floor and ceiling effects. However, GAS is a measure of achievement of expectation rather than a measure of outcome as such [48]. So it is recommended that GAS be used alongside standardised measures, rather than replacing them, to assist in interpreting results [48]. GAS has also been shown to be useful in measuring outcomes of rehabilitation for other neurological conditions, such as brain injury [50] and multiple sclerosis [47, 51], and spasticity management in children with cerebral palsy [49]. There are difficulties in applying GAS as part of a blinded assessment as the patient and the treating team should undertake the evaluation of goal achievement collaboratively in order to improve reliability [48]. However, application by a blinded assessor may be the best way of reducing bias in studies of physical interventions which are hard to conceal from patients and treating therapists [48].

1.3.2. GAS process

GAS is a method for the assimilation of achievement in a number of individually set goals that are focused on the individual’s priorities into an aggregated goal attainment score [46, 52]. A statement of expected outcome is set for each weighted goal, and achievement of each goal is measured on a five-point scale ranging from −2 to 2 (Appendix 2). Goals may incorporate an outcome assessment tool to further define the different levels of achievement (e.g., a visual analogue scale for rating pain or degree of difficulty in performing a task) and a time frame for the expected outcome.

The GAS is calculated using a mathematical formula [46] in which goals are weighted by multiplying their importance by their difficulty where:
• importance of the goal to the patient is graded as 1 = fairly important,
  2 = very important and 3 = extremely important
• difficulty of achieving the goal is rated according to the health professional’s perception of likelihood of success as 1 = probable, 2 = possible and 3 = doubtful.

The GAS T-score is normally distributed with a mean of 50 (if the goals are achieved precisely) and a standard deviation (SD) of 10 (if the goals are overachieved or underachieved) [46, 52]. As well as providing a quantitative assessment of goal attainment, GAS provides qualitative information about the patient’s priority goals for treatment and their respective importance [33].

From a clinical perspective, the goal-setting process supports an interdisciplinary team approach as well as communication with the patients and their family members or caregivers, and offers an additional opportunity to negotiate mutually agreed realistic expectations for outcome [33, 50]. Applying GAS in routine clinical practice may be facilitated by developing standardised item banks of common goals for spasticity management, which would overcome limitations in its use where clinicians lack sufficient knowledge, training and experience in goal setting [33].

1.4. Issues in implementation of rehabilitation programs following BoNT-A injections for post-stroke spasticity

1.4.1. Factors contributing to inconsistencies in service delivery

While management of spasticity requires a multidisciplinary team [19], there is no evidence for the best type of setting (acute, subacute or community) in which care should be delivered and therapy components that are effective. For acute stroke management there is clear evidence for providing rehabilitation programs in comprehensive stroke units or stroke rehabilitation units because the increased intensity programs are often provided in the context of more organised services [22]. Practical factors such as allocated resources, funding, clinician expertise and access to services may influence the availability and quality of rehabilitation management following BoNT-A injections.
In Australia, rehabilitation physicians and neurologists administer BoNT-A injections for post-stroke spasticity [43]. The settings and structures of the services for BoNT-A treatment and post-injection management are variable. BoNT-A injections are more often provided in public hospital spasticity management clinics (72%), with half (49.5%) given in multidisciplinary services and over one quarter (28.5%) in physician-only services [43]. Barriers to injection and adjunctive therapy are waiting times for BoNT-A injections, access to specialist adjunctive therapists and referral for treatment [53].

Rehabilitation practices vary in terms of whether the key components for success (Section 1.2.4) are implemented, whether therapy programs are delivered as planned [54] and the timing of follow-up. When patients do receive physical therapy following BoNT-A injections, variability is inevitable because the physical therapy interventions are based on the clinicians’ level of expertise, clinical judgement and trial-and-error [43, 55]. While Australian physiotherapy and occupational therapy practice for patients who receive upper limb BoNT-A injections show trends in assessment, goals and treatment practice, greater consistency could be achieved if evidence-based therapy practice guidelines existed [43]. However, the limited evidence provides inadequate descriptions of the therapy (intensity, dose, activities and interventions) beyond generic terms, prohibiting accurate replication of the interventions in clinical practice.

1.4.2. Recommendations for improving rehabilitation practices after BoNT-A treatment

Because practices vary widely, it is difficult to compare outcomes across centres to improve processes and quality of care. In the absence of evidence-based spasticity management guidelines, recommendations for improving post-injection care in Australia are to:

- improve communication between physicians and therapists regarding patients’ treatment plans and goals [43, 53]
- provide targeted professional development to enhance each therapist’s expertise in administering treatment modalities and implementing functional patient-centred outcome measures [43]
• develop local treatment protocols within services to overcome inconsistencies in therapy delivery and approaches [43].

1.5. Factors contributing to the limited evidence base for rehabilitation programs following BoNT-A injections for post-stroke spasticity

1.5.1. Difficulty characterising and standardising complex interventions

Rehabilitation is a complex and costly individualised intervention that is difficult to characterise and standardise, therefore limiting the ability to conduct high-quality randomised controlled trials (RCTs) [55]. Barriers to effective research include:

- difficulty replicating an intervention across centres
- impracticality of having a control group with no intervention because the intervention is in widespread use
- difficulty standardising the design and delivery of the intervention, particularly because practices vary between rehabilitation centres, programs are individualised and spasticity management goals are diverse
- sensitivity to aspects of the local context that are difficult to control, including organisational factors (e.g., funding, resources and service delivery protocols); personal factors (e.g., patients’ activity level outside of formal therapy, motivation, self-efficacy and compliance); and therapist factors that influence patient–therapist interaction, delivery of therapy and outcomes (e.g., level of expertise, attitudes, beliefs and behaviours)
- the organisational and logistical difficulty of applying experimental methods to service delivery [56].
1.5.2. Limitations in study designs and outcome evaluation

There is a critical need for large-scale rigorous clinical trials that investigate the efficacy of therapy types – independently or combined with BoNT-A injection – to establish evidence-based guidelines for spasticity management in rehabilitation [35]. Synthesis of evidence is limited by:

- inconsistent terminology and definitions of spasticity causing ambiguity in what is being treated and measured, and limiting the interpretation and application of evidence [57, 58]
- selection of inappropriate outcome measures that do not show change following therapy or do not correlate with meaningful outcomes for patients and their caregivers [59]
- heterogeneity of studies in terms of study population, intervention type and intensity, study design and outcome measures [35].

The inconsistency between clinical practices, recommendations in spasticity management guidelines and scientific evidence for rehabilitation interventions necessitated this thesis to bridge some of the gaps in knowledge and identify key areas for future research.

1.6. Hypothesis

Multidisciplinary rehabilitation programs following BoNT-A injections for post-stroke spasticity improve patient-centred outcomes.

1.7. Objectives

This thesis comprises four original studies (Chapters 4 to 7) that were conducted in a real-life clinical setting through the Royal Melbourne Hospital in Victoria, Australia, by applying the best available scientific evidence to address some of the issues discussed above.

The main aim of the thesis is to assess the effectiveness of multidisciplinary rehabilitation following BoNT-A injections for post-stroke spasticity in improving patient-centred outcomes. The specific objectives relating to this are to:
• determine whether coordinated multidisciplinary rehabilitation achieves better outcomes than the absence of such services in persons with post-stroke spasticity (Chapter 4, Study 1). The specific research questions are:
  o What types of rehabilitation programs are effective, and in which setting?
  o Does a greater intensity (time or expertise) of rehabilitation lead to better outcomes?
• explore the effectiveness of ambulatory rehabilitation programs following BoNT-A injections for post-stroke spasticity in Australian adults by comparing the benefits of high-intensity ambulatory rehabilitation programs with lower intensity usual care programs (Chapter 5, Study 2)
• demonstrate the use of a stroke rehabilitation taxonomy to describe ambulatory rehabilitation programs (physical and occupational therapy activities and interventions) following BoNT-A injections for post-stroke spasticity, and explore the relationship between the therapeutic activities prescribed and the functioning of the injected limb and treatment goals (Chapter 6, Study 3).
• evaluate implementation of a high-intensity ambulatory rehabilitation program following BoNT-A injections using a framework for process evaluation.

1.8. Overview of Methods

1.8.1. Incorporating Medical Research Council guidelines for researching complex interventions

Rehabilitation is a complex intervention that contains several interacting components in addition to having several dimensions of complexity [60]. Key questions in evaluating complex interventions include: (a) Are they effective in everyday practice? and (b) How does the intervention work? What are the active ingredients? and How are they exerting their effect [60]?
Recognition that complex interventions may work best if they are adapted to local contexts rather than being strictly standardised [60] is important in rehabilitation. The updated Medical Research Council (United Kingdom) guidance for the evaluation of complex interventions emphasises the importance of studies including a detailed description of the intervention to enable replication, evidence synthesis and wider implementation [60]. Use of a range of outcome measures to detect unexpected effects is also advised. Including a process evaluation is recommended to explain discrepancies between expected and observed outcomes, to understand how context influences outcomes and to provide insights to aid implementation [56]. These recommendations and key questions were taken into consideration when developing the studies for this thesis to ensure comprehensive evaluation of the complex intervention.

**Effectiveness in everyday practice**

The intervention study (Study 2, Chapter 5) investigates patient-centred outcomes following differing intensities of rehabilitation programs after BoNT-A injections for post-stroke spasticity. This reflects real-life clinical practice where therapy is individualised, complex interventions are delivered and a range of outcomes are possible. Generally, published studies of physical interventions following BoNT-A injections for post-stroke spasticity have focused on single treatment modalities or single-discipline therapy.

**A detailed description of the intervention**

The descriptive study (Study 3, Chapter 6) of the interventions and activities that comprise the rehabilitation programs provided to study participants is the first to describe rehabilitation programs for spasticity management in detail using a standardised stroke rehabilitation taxonomy [36, 55]. Relationships between rehabilitation activities and treatment goals or limbs injected are examined, thereby determining therapy relevance and key areas of importance. A similar approach can be used in future studies to enable investigation of the contribution of the individual components of rehabilitation programs to outcomes, individually and combined, to explore the black box of rehabilitation.
Process evaluation to identify issues related to implementation and
delivery of the intervention

The mixed methods (qualitative and quantitative) process evaluation study (Study 4, Chapter 7) addresses issues related to delivery of rehabilitation programs, in particular the high-intensity intervention (Study 2). Process factors and contextual variables that may have influenced the findings of Study 2 are explored.

1.8.2. Methods: quantitative and qualitative methods

The methodological approach used in this thesis encompasses quantitative methods to assess program effectiveness and mixed methods to evaluate rehabilitation program components and aspects of program implementation. Qualitative methodology is needed to capture the range of participant experiences in the real-life clinical setting.

Cochrane methodology [61] is used to conduct a systematic review of the current evidence for multidisciplinary rehabilitation following BoNT-A injections for post-stroke spasticity (Chapter 4, Study 1). Grades of Recommendation, Assessment, Development and Evaluation (GRADE) [61] provide a qualitative synthesis of the best evidence.

Quantitative methods are used to compare the effectiveness of high-intensity programs with usual care low-intensity rehabilitation programs following BoNT-A injections for post-stroke spasticity in the upper and lower limbs (Chapter 5, Study 2). This prospective study uses a range of standardised outcome measures related to the components of the ICF (impairments, activity and participation) to evaluate patient-centred outcomes. These included measures of goal achievement, spasticity, active function, passive function and caregiver burden.

The black box of rehabilitation is explored (Chapter 6, Study 3) using descriptive analyses and quantitative methods to analyse data on the types of and amount of time spent in rehabilitation activities and the types of interventions used to facilitate these activities. Data is collected using standardised therapy documentation forms [36, 55, 62] (Appendix 3).
Mixed methods analyses are used for process evaluation to assess program effectiveness, delivery and implementation (Chapter 7, Study 4). Qualitative exploration of participants’ and therapists’ experiences with implementation of the rehabilitation programs and attitudes and beliefs towards the high-intensity rehabilitation program is undertaken. A more detailed description of the methodology is provided in Chapter 3.

1.8.3. Setting

This trial was conducted at the Royal Park Campus of the Royal Melbourne Hospital in Victoria, Australia, at a tertiary hospital rehabilitation service. Participants were recruited from an ambulatory multidisciplinary spasticity management clinic from January 2011 to June 2012. Approval was obtained from the Melbourne Health Human Research and Ethics Committee (HREC number 2010.165).

1.8.4. Participants

Participants were 59 adults who, more than three months before recruitment, had a stroke that resulted in problematic spasticity involving the upper or lower limb, were considered suitable for treatment with BoNT-A injections and were able to participate in an ambulatory rehabilitation program. Patients were excluded if they: had received treatment with BoNT-A within six months; were receiving intrathecal baclofen or other anti-spasticity medications; had undergone neurolysis or surgery to the affected limb; had concomitant neurological conditions; were pregnant; or were unable to participate in therapy due to cognitive impairment, language impairment, psychiatric illness or medical illness.

1.8.5. Group allocation

This trial was designed to reflect real-life clinical practices. In this setting, participants are referred to a community-based rehabilitation program as determined by their geographical catchment area and closest available service. Those residing in the catchment area of the hospital at which the study was based received high-intensity therapy, while subjects outside of this geographical catchment area underwent usual care, which was lower intensity therapy at their...
local community or hospital rehabilitation service. Participants were not informed of their allocation within the trial.

1.8.6. Assessments

At baseline, up to three individualised goals for each treated limb (to a maximum of six goals if both limbs were treated) were negotiated between participants, caregivers and the clinic therapist. An independent blinded research assistant measured outcomes at six, 12 and 24 weeks following BoNT-A injections.

The treating therapists completed therapy documentation forms [55, 62, 63] (Appendix 3) for a total of 925 physical and occupational therapy sessions for 47 participants. Therapists received written, and in some cases verbal, instructions for completion of the forms and relevant references [55, 63]. Information collected included types of therapeutic activities and interventions prescribed, duration of time spent in various activities and the therapist’s discipline.

After completion of the intervention and study assessments, qualitative questionnaires (Appendix 4) were administered verbally over the phone or in person to assess participants’ and therapists’ experiences with the delivery of the rehabilitation programs.

1.9. Thesis overview

Figure 1.2 shows an outline of this thesis. A narrative review identifies spasticity management issues in the current literature (Chapter 2), firstly, to draw on existing evidence and theory regarding post-stroke spasticity to develop a theoretical understanding of the likely process of change and relevant outcomes expected from the intervention [60], and secondly, to identify gaps in the literature. A detailed description of methodology used in the thesis then follows (Chapter 3). A Cochrane review (Chapter 4, Study 1) determines what is already known about similar interventions and the methods that have been used to evaluate them.

The effectiveness of rehabilitation programs following BoNT-A injections for post-stroke spasticity is evaluated (Chapter 5, Study 2). Ambulatory rehabilitation programs of variable intensities (high-intensity versus usual care low-intensity) are compared to explore the effect of program intensity on goal achievement and outcomes related to the ICF categories (Figure 1.1).
Objective

Assess the effectiveness of multidisciplinary rehabilitation following BoNT-A injections for post-stroke spasticity in improving patient centred outcomes

Introduction (Chapter 1)

Narrative review of the literature to identify key issues in management of post-stroke spasticity (Chapter 2)

Methodology (Chapter 3)

Study 1 – Systematic review

Cochrane review of the effectiveness of multidisciplinary rehabilitation following BoNT-A injections for post-stroke spasticity (Chapter 4)

(3 RCTs including 91 participants)

Study 2 – Quantitative methods

Prospective controlled clinical trial examining the effectiveness of high-intensity versus usual care (low intensity) rehabilitation programs following BoNT-A for upper or lower limb spasticity (Chapter 5)

(N = 59)

Allocated to high-intensity therapy (N = 28)
Intervention completed (N = 28)

Allocated to usual care (N = 31)
Intervention completed (N = 30)
Intervention not completed (N = 1)

Analysed (N = 28)

Analysed (N = 31)

Study 3 – Descriptive and quantitative analyses

Use of a stroke rehabilitation taxonomy to describe the fundamentals of rehabilitation programs (including activities and interventions) following BoNT-A for spasticity in adults with stroke (Chapter 6)

(N = 47)
Further evaluation of the complex dimensions comprising the rehabilitation programs provided in Study 2 is conducted. Firstly, the programs are described in detail, using a standardised stroke rehabilitation taxonomy to identify the key therapeutic activities and interventions and relationships with limbs injected and treatment goals, thereby exploring the black box of rehabilitation (Chapter 6, Study 3). Secondly, process evaluation is used to assess the delivery and implementation of high-intensity rehabilitation programs and expand on recommendations for wider implementation of the intervention (Chapter 7, Study 4).

Finally, the research findings are discussed in relation to the gaps identified in the literature, recommendations for future research and clinical implications for managing post-stroke spasticity in rehabilitation (Chapter 8).

Chapter 2 provides a narrative review of key issues in spasticity management that are relevant to the studies in this thesis.
Chapter 2. Overview of post-stroke spasticity

This chapter examines the current literature on issues related to post-stroke spasticity including patient-centred problems, management (pharmacological and non-pharmacological) and outcome evaluation. The pathophysiology and presentations of spasticity are also described.

2.1. Introduction

Spasticity is a chronic impairment that contributes to stroke-related disability and requires long-term management. Spasticity is a motor disorder and is one of the positive features of the UMN syndrome, with a key feature being hyperexcitability of muscle stretch reflexes [7]. There is debate surrounding the definition and pathophysiological mechanisms of spasticity [9]. Spasticity typically develops over a few weeks following stroke due to abnormal patterns of supraspinal descending drive [64].

Spasticity management guidelines recommend comprehensive multidisciplinary rehabilitation aimed at achieving long-term functional goals. Temporary focal spasticity reduction with BoNT-A is considered an adjunctive treatment to rehabilitation interventions [18] that allows a window of opportunity to remediate other impairments such as weakness and reduced dexterity, and to improve function such as walking, transfers, and use of the upper limb for feeding and dressing. Patient-centred goals are diverse [11, 33] and may relate to the ICF categories discussed in Chapter 1. Outcome evaluation should encompass a measure of attainment of priority goals, particularly because other standardised outcome measures fail to capture the range of effects [33].

There is an obvious gap in the literature with a lack of evidence for multidisciplinary rehabilitation interventions for post-stroke spasticity and sparse information in the spasticity management guidelines as to what such treatment should entail.
2.2. Economic impact of spasticity

It is difficult to precisely quantify the economic and human burden of post-stroke spasticity. Stroke accounts for approximately 2–4% of health care costs globally, with approximately one-third of the treatment cost of stroke attributable to rehabilitative care [65]. Direct costs for stroke survivors with spasticity have been found to be approximately four times those for stroke survivors without spasticity [4].

2.3. Stroke

2.3.1. Definition

Stroke is defined by the WHO as ‘rapidly developed clinical signs of focal (or global) disturbances of cerebral function, lasting more than 24 hours or leading to death, with no other apparent cause than of vascular origin’ [66]. Strokes may be ischaemic or haemorrhagic (subarachnoid, intraventricular or intracerebral). Ischaemic strokes are more common, but haemorrhagic strokes have a higher mortality rate.

2.3.2. Stroke related impairments

Stroke related impairments may be associated with the following neurological domains [67]:

- motor – hemiparesis, spasticity, loss of dexterity, impaired coordination, cranial nerve deficits, hyperreflexia, incoordination and apraxia
- sensory – loss of primary sensations to more complex loss of perception. Includes somatosensory deficits and loss of proprioception. The more complex sensory losses include astereognosis, agraphia, visuospatial deficits (neglect) and extinction to double simultaneous stimuli
- vision – monocular visual loss, homonymous hemianopia or cortical blindness.
- language – dysphasia
• cognition – deficits in memory, attention, orientation, calculation abilities, construction and new learning
• affect – depression.

2.4. Spasticity

2.4.1. What is it?

Spasticity is a complex phenomenon that is poorly understood and difficult to measure [57]. Currently, there is no universal consensus on the definition of spasticity. Rather, defining spasticity is an evolving process as our understanding of the pathophysiological mechanisms and clinical interpretations of the condition continue to advance.

Spasticity is a neurological impairment. Traditionally, spasticity has been defined as ‘a motor disorder characterized by a velocity dependent increase in the tonic stretch reflexes (muscle tone) with exaggerated tendon jerks, resulting from hyper excitability of the stretch reflex, as one component of the upper motor neurone syndrome’ [7]. This definition has been described as narrow and limiting [59] and poorly validated [9]. The pathophysiological mechanisms underpinning this condition, while not fully understood, are far more complex than those described by Lance [7]. Contrary to Lance’s definition of spasticity, the tonic stretch reflex has been shown to have a low correlation with the phasic stretch reflex (tendon jerks) [8]. Furthermore, there is evidence that spasticity and stretch reflex hyperexcitability are not mutually exclusive [68]. Additionally, the altered mechanical properties of muscles may contribute to hypertonia in conjunction with spasticity [69, 70].

Spasticity can be considered a form of hypertonia that is velocity dependent; a higher velocity stretch produces greater electrical activity in the muscle [9, 71] and greater resistance to passive movement [72]. Hence, spasticity is present during movement rather than at rest. Spasticity is also length dependent. The tonic stretch response is greater when the muscle is shortened and becomes inhibited when the muscle is stretched beyond a certain length. This relationship is not true for all muscles (e.g., quadriceps versus hamstrings).
A subsequent expanded definition describes spasticity as ‘a motor disorder characterised by a velocity-dependent increase in tonic stretch reflexes that results from abnormal intraspinal processing of primary afferent input’ [73]. Spasticity, and other positive features of the UMN syndrome, have been postulated to be related to activity in afferent pathways (e.g., cutaneous), supraspinal control pathways and alpha motor neurones rather than stretch reflex hyperexcitability exclusively [9].

More recently, spasticity has been described as ‘disordered sensori-motor control, resulting from an upper motor neurone lesion, presenting as intermittent or sustained involuntary activation of muscles’ [9]. This definition implies that the term spasticity can be used generically to describe the entire array of signs and symptoms described as positive features of the UMN syndrome (Section 1.5.2) while excluding the negative features and pure biomechanical changes in the soft tissues and joints [9]. Because spasticity is a part of, rather than synonymous with, the UMN syndrome, the overall clinical problem is variable and does not conform to any of the standard definitions, particularly those related to the role of muscle tone [74]. Abnormal processing of proprioceptive input in the spinal cord results in abnormal motor responses. Consequently under this definition, spasticity is no longer considered a pure motor problem.

Terminology used to describe spasticity in the literature is inconsistent. This may result in confusion as to what is actually being measured, and the debate over an ideal definition of spasticity continues. The term hypertonia is often used, but other features of the UMN syndrome, such as rheological changes, may contribute to increased tone. To further understand the complexities of spasticity, one must first explore the underlying pathophysiological mechanisms of this condition and other features of the UMN syndrome.

2.4.2. Spasticity and the UMN syndrome

The interaction between spasticity and other features of the UMN syndrome is complex [75]. The UMN syndrome is characterised by positive features associated with muscle overactivity or inappropriate activity (such as spasticity, co-contraction, associated reactions, dystonia and clonus) and negative features (such as weakness and fatigability). Positive and negative signs often interact at
the same time. The term spasticity is commonly incorrectly applied to describe most of the positive phenomena. Although spasticity can co-exist with other positive symptoms, these are not mutually exclusive and must be considered different entities because the clinical features and underlying mechanisms are different.

Adaptive features of the UMN syndrome may develop due to untreated spasticity and underlying muscle weakness [76]. These include contractures and rheological changes of muscle such as fibrosis or atrophy with a relative increase in collagen compared with elastin [70, 77], tendons and joints. These changes contribute to increased stiffness, further exacerbating limb positioning, movement and function. Weakness and muscle overactivity contribute to muscles being in a shortened position. Elongating a spastic muscle may alter the viscoelastic and excitability properties, thereby reducing muscle tone [64], but the exact mechanisms remain uncertain. Stretching and positioning are used to maintain muscle length and prevent contractures though there is a lack of evidence for these interventions [78]. The relative contribution of weakness and spasticity to the development of contractures is debated. Some authors have reported weakness to be the major contributor to the development of upper limb contractures following stroke [70, 79]. Alternatively, spasticity has been shown to be the major independent contributor to contracture for the first four months after stroke and to weakness thereafter [76]. Another author postulates that, instead of spasticity causing contracture, contracture may potentiate spasticity in some patients [70].

The overall pattern of spasticity combined with other UMN symptoms and the resulting problems may be variable; hence, individualised, goal-directed treatment is essential. Therapeutically, most active interventions are directed towards reducing the positive phenomena and their consequences. Neurorehabilitation of the negative phenomena focuses on maximising the function of the weakened parts, while accepting that often little can be done to improve strength [72]. In addition to the broader effects of the UMN syndrome described above, other stroke-related impairments (Section 1.3.2) can have an impact on function in conjunction with spasticity. Therefore, management of spasticity is complex, requiring comprehensive multidisciplinary neurorehabilitation programs to address the needs of patients and their caregivers.
2.4.3. Pathophysiology

Although the pathophysiology of spasticity is not clearly understood, several theories have been proposed. UMN s include supraspinal inhibitory and excitatory fibres that descend to the spinal cord exerting a balanced control on the excitability of spinal reflexes [80]. Spasticity develops when an imbalance occurs in the excitatory and inhibitory input to alpha motor neurons, with a net disinhibition leading to hyperexcitability [81]. The mechanisms for this excitation are different for spasticity following cerebral and spinal lesions.

Because the excitatory and inhibitory tracts run in different locations in the spinal cord and play different roles, supraspinal control can be variably affected depending on which tracts are damaged. Thus, the site of the lesion (cortex, brainstem or spinal cord) plays an important role in the severity of spasticity and the pattern of UMN features [80].

According to Lance [7], increased proprioceptive spinal stretch reflexes are responsible for most of the positive features of the UMN syndrome [7], but the pathophysiological mechanisms of this are not well understood, leading to controversy in the literature. A certain velocity of movement is required to elicit a stretch reflex; hence, spasticity is not present without movement.

2.4.4. Other positive phenomena of the UMN syndrome

Associated reactions

Associated reactions are abnormal postural reactions occurring in the limbs affected by an UMN lesion even when there is only mild spasticity present [14]. Associated reactions result from an increase in involuntary and unnecessary activation of muscles that are remote from those engaged in a effortful task [80]. Associated reactions have been implicated in precluding the return of selective movement in the hemiplegic limb [82], increasing the likelihood of contracture formation and interfering with balance and function (e.g., increased elbow flexion during standing or ambulation).
**Co-contraction**

Simultaneous activation of agonist and antagonist muscles (co-contraction) is an important component of normal reciprocal innervation [80]. However, in the UMN syndrome, it can occur inappropriately and be dysfunctional.

**Spastic dystonia**

Unlike spasticity, spastic dystonia is not dependent on sensory input and continues in the absence of movement. Spastic dystonia is mediated by the efferent or continuous supraspinal drive to the alpha motor neurone, rather than the afferent reflex arc [80].

### 2.5. Spasticity: epidemiology and evolution

#### 2.5.1. Epidemiology

Epidemiological data relating to spasticity is limited due to the variable definitions and methods of measurement. Spasticity can be the result of a number of neurological conditions including stroke, brain injury, multiple sclerosis, spinal cord injury and cerebral palsy. Approximately one-third of stroke patients, 60% of patients with severe multiple sclerosis and 75% with physical disability after traumatic brain injury develop spasticity requiring treatment of which approximately one-third may require BoNT-A injections [19, 83].

#### 2.5.2. Prevalence of post-stroke spasticity

Reported prevalence rates of spasticity are variable due to the different study designs in terms of time following stroke and approaches used to measure and define spasticity (Table 2.1). Most studies report a prevalence rate from 17% [84] to 43% [85] in stroke survivors, with disabling or severe spasticity affecting 4% [84] to 20% [86]. The prevalence of spasticity in stroke survivors has been reported to be 70% in those requiring inpatient rehabilitation services [87] and 78% in those requiring outpatient rehabilitation services [88], with severe or symptomatic spasticity requiring treatment in 50% [87] and 39% [88], respectively, of stroke survivors.
<table>
<thead>
<tr>
<th>Study</th>
<th>Participants</th>
<th>Spasticity diagnosis/definition</th>
<th>Time post stroke</th>
<th>Prevalence of spasticity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urban 2010 [85]</td>
<td>N = 211</td>
<td>MAS ≥ 1</td>
<td>6 months</td>
<td>42.6%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>15.6% with severe spasticity (MAS ≥ 3)</td>
</tr>
<tr>
<td>Wissel 2010 [89]</td>
<td>N = 94</td>
<td>MAS ≥ 1</td>
<td>2 weeks</td>
<td>24.5%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>6 weeks</td>
<td>26.7%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>12–24 weeks</td>
<td>21.7%</td>
</tr>
<tr>
<td>Kong 2010 [88]</td>
<td>N = 140</td>
<td>Spasticity in general (AS ≥ 1)</td>
<td>Mean 41.7 (SD 35.1) months</td>
<td>78.6%²</td>
</tr>
<tr>
<td></td>
<td>Patients attending outpatient rehabilitation clinic</td>
<td>2. Severe spasticity (AS ≥ 3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>3. Symptomatic spasticity (spasticity affecting upper limb function)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lundstrom 2008 [84]</td>
<td>N = 140</td>
<td>MAS ≥ 1</td>
<td>1 year</td>
<td>17% (4% with disabling spasticity*)</td>
</tr>
<tr>
<td>Welmer 2006 [90]</td>
<td>N = 66</td>
<td>MAS ≥ 1</td>
<td>18 months</td>
<td>20%</td>
</tr>
<tr>
<td>Sommerfeld 2004</td>
<td>N = 95</td>
<td>MAS ≥ 1</td>
<td>&lt; 1 week</td>
<td>21%</td>
</tr>
<tr>
<td>[91]</td>
<td>First ever stroke (TIA, ischemic and haemorrhagic)</td>
<td>Self-reported muscle stiffness Tendon reflexes</td>
<td>3 months</td>
<td>19%</td>
</tr>
<tr>
<td>Leathley 2004 [86]</td>
<td>N = 106</td>
<td>TAS ≥ 1</td>
<td>12 months</td>
<td>36%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>20% severe spasticity</td>
</tr>
<tr>
<td>Study</td>
<td>Participants</td>
<td>Spasticity diagnosis/definition</td>
<td>Time post stroke</td>
<td>Prevalence of spasticity</td>
</tr>
<tr>
<td>------------------------</td>
<td>-----------------------</td>
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<td>--------------------------</td>
</tr>
<tr>
<td>Watkins 2002 [3]</td>
<td>N = 106</td>
<td>MAS (elbow) TAS ≥ 1</td>
<td>12 months</td>
<td>27% (MAS) 36% (TAS) 39% (combined) (39% in first ever strokes and 44% in recurrent strokes)</td>
</tr>
<tr>
<td>O’Dwyer 1996 [70]</td>
<td>N = 24</td>
<td>EMG activity</td>
<td>13 months</td>
<td>21%</td>
</tr>
</tbody>
</table>

MAS, Modified Ashworth Scale; AS, Ashworth Scale; TAS, Tone Assessment Scale; TIA, transient ischemic attack; EMG, electromyography; * studies assessing upper limb spasticity only (all others investigated upper and lower limb spasticity); * disabling spasticity requiring an intervention.
Studies using neurophysiological measures of spasticity of the upper limb at the elbow [70] and wrist [92] found 21% and 87%, respectively, had abnormal involuntary muscle activation. Neurophysiological measures have greater sensitivity for quantifying abnormal muscle activation associated with spasticity than clinical measures such as the MAS.

Spasticity after stroke is more common in the upper than lower limb [84, 89, 91, 93, 94], where it also tends to be more severe (MAS ≥ 3) [85]. Antigravity muscles (arm flexors and leg extensors) are more commonly affected up to three months after stroke [93].

2.5.3. Predictors and associations of spasticity

Knowledge of risk factors and predictors of severe spasticity may assist in targeting patients for early and more aggressive treatment. Spasticity seems to be more common among younger than older stroke survivors [93, 94]. Risk factors for developing severe spasticity (MAS ≥ 3) include more severe paresis at stroke onset [85, 89, 95] and moderate tone (MAS = 2; particularly affecting the arm or more than two joints) in acute stages [89]. Other risk factors for spasticity are greater disability [89, 96], dysphasia [88], hemihypesthesia (light touch) [85], left-sided weakness and having ever smoked [86]. Of patients attending rehabilitation services, those with spasticity have been found to have more significant motor impairments and functional limitations, suggesting that problematic spasticity is associated with more severe impairments [87, 88]. Sex and location of stroke or type of stroke have not been found to be associated with the development of spasticity [85, 89].

Stroke survivors with spasticity have been reported to have greater disability [3, 84, 89, 90, 96], poorer quality of life [85, 89], and higher incidences of pain, institutional care and nursing home placement [3, 89]. Patients with upper and lower limb spasticity, rather than single limb involvement, have been found to have lower Barthel Index at six months after stroke [85].

2.5.4. Time course of development of spasticity

It is recognised that a lag may exist between stroke and the onset of spasticity; however, studies have shown variable time courses for the development of
spasticity after stroke. Patients who are not initially spastic may develop spasticity within three to six months, and patients who are initially spastic may have normal muscle tone by this time [89, 91]. Spasticity after a first-ever stroke tends to occur within three months [90, 91]. The severity of spasticity increases after three months, despite neurally mediated muscle tone reaching its maximum between one and three months after stroke [8, 70, 97]. This suggests that intrinsic muscle changes may play a larger role than neural components with greater time after stroke [70, 93, 97]. Thus, there are limitations in using the MAS to measure spasticity because it does not differentiate spasticity from increased tone due to rheological changes (Section 2.7.2). Further research is needed to establish timeframes for when spasticity is expected to stabilise.

2.5.5. Motor recovery in stroke

Patients are often advised after six to twelve months that they have reached a plateau in their stroke recovery when they fail to respond positively to motor rehabilitation [98, 99]. This may be due to neuromuscular adaptation to therapeutic exercise rather than a diminished capacity for motor improvement [99]. Rather than terminating therapy, modifying motor rehabilitation programs to apply novel or different parameters (e.g., intensity) and modalities can result in substantial motor and functional improvement after chronic stroke [99, 100]. Neuroplasticity allowing cortical reorganisation plays a significant role in these changes [101]. Thus, stroke is a chronic disease that should be managed on a continual basis to maintain functional gains.

2.6. Spasticity: patient-centred problems

2.6.1. Patterns of post-stroke spasticity

Post-stroke spasticity may be focal (affecting a localised part of a limb), multifocal (affecting more than one part of a limb) or regional (affecting the upper or lower limbs), whereas generalised spasticity typically results from spinal origin UMN syndrome [102]. The overall pattern of spasticity combined with other UMN symptoms and resulting problems often varies among individual stroke survivors. Spasticity results in stiffness and abnormal posturing of the limb due to
a net imbalance of forces between agonist and antagonist muscles affecting static joint position and dynamic limb movement [72]. Stereotypical UMN syndrome postural patterns are (Figure 2.1):

- upper limb flexor posturing – adducted and internally rotated shoulder, flexed elbow, pronated forearm, flexed wrist and clenched fist
- lower limb extensor posturing – flexed hip, adducted thigh, extended knee and equinovarus foot (plantarflexion and inversion).


Figure 2.1. Typical postural patterns in the upper and lower limb resulting from spasticity.

2.6.2. Spasticity related clinical problems and treatment goals

Thorough clinical evaluation is vital in identifying patient-centred spasticity-related problems and the other factors that contribute to its impact, such as contractures, weakness and loss of dexterity, as described in Sections 2.3.2 and
2.4.2. While some consider spasticity to be a significant contributor to activity limitations, others have found weakness to be a more important factor, in particular limiting execution of upper limb active tasks [76, 103, 104]. Rehabilitation goals for management of the hemiparetic upper limb include restoring active function if there is return of motor control or, if not possible, improving passive function to facilitate care for the limb [105].

Classifying spasticity-associated problems according to the ICF (Section 1.1.2) is important in the context of spasticity management for demonstrating change, not only at the level of impairment but also at the functional level [6, 19, 21]. Clinicians often focus on the direct effects (i.e., impairments) of post-stroke spasticity, such as increased muscle tone, rather than the indirect effects (i.e., limitation of activities) that more importantly affect daily functioning and quality of life [98]. This was highlighted in a study investigating goal attainment in BoNT-A management for upper limb spasticity where 28% of the goals set were within domains relating to impairment or body functions, reflecting pain, passive movement, maintaining joint range, reducing unwanted involuntary reactions and simple active movements of the hand or arm [33]. Other goals were classified into domains of activities and participation:

- upper limb activities, such as lifting, carrying and holding objects still (18%)
- mobility, including maintaining balance or improving gait (7%)
- self-care tasks, such as hygiene, dressing or feeding (35%)
- domestic and community tasks, such as housework or recreational activities (13%) [33].

The following classification for key goals for upper limb spasticity management after stroke has also been determined [105]:

- passive function (e.g., hand hygiene, skin integrity, and application of splint or orthotic)
- active function (e.g., use of upper limb during functional activities such as reaching, grasp and release)
- associated reactions or impairments
- symptoms (e.g., pain)
- cosmesis.
Patients may have problems in more than one domain. Improvement of active function is the most frequent treatment goal in the first three months after the onset of upper limb spasticity, but is less common than improvement of passive function in the chronic stage of spasticity [11]. For passive function, dressing, prevention of contractures and hygiene are common goals [11, 43]. Pain relief during movement or at rest is a common secondary treatment goal in both stages [11].

The relationship between pain and spasticity is often multifactorial. Spasticity may result in pain due to musculoskeletal complications and soft tissue damage, such as joint contractures and pressure ulcers resulting from abnormal postures; neuropathic pain or muscle spasms may also cause pain [106-108]. Noxious stimuli such as pain can exacerbate spasticity; thus, the effective treatment of spasticity involves treating the underlying provocative condition [108]. Patients with spasticity (MAS ≥ 2) have significantly higher incidences of pain in the upper limb within the first 12 weeks after stroke [89]. Such a close association is not found in the lower limb.

There is limited literature regarding goals of lower limb spasticity management compared with upper limb spasticity management. Common post-stroke spasticity-related problems in the lower limb include difficulty walking, interference with dressing the limb for the patient or caregiver, and problems relating to clawed toes, such as pain or discomfort and difficulty donning shoes [109].

2.7. Assessment and outcome evaluation of spasticity related problems

Clinicians tend to assess the effectiveness of treatment for spasticity with impairment level scales, while functional outcome measures including goal achievement seem to be rarely used in clinical practice [11, 43]. The use of these measures is necessary to assess whether the reduction in muscle tone translates into functional benefit to patients and their caregivers [11]. There is no one test that is superior for measuring spasticity and functional outcomes following interventions. Rather, a battery of tests may be required.
2.7.1. Identifying spasticity requiring treatment

In patients with spasticity, multidisciplinary assessment that encompasses evaluation of spasticity and other impairments, and identification of treatment goals for active and passive function is important. Assessment should help inform goal-setting between patients, caregivers, therapists and physicians and evaluation of goal attainment.

Observing motor movement patterns during activities such as walking and transferring, drinking from a cup, picking up objects or donning a splint provides valuable information. Functional extremity movement may be limited by co-contractions of agonist and antagonist muscles, poor agonist muscle activation, overactive agonist muscles and synergistic patterns involving gross flexor and extensor movements limiting a patient’s ability to voluntarily contract individual muscles. It is essential to determine the impact of spasticity on function to establish if, and what type of, treatment is required.

A clinically useful patient-reported screening tool for health care providers to identify patients with spasticity in need of treatment has been developed [109]. The spasticity screening tool consists of 13 items relating to patients’ symptoms and impacts relating to stiffness and passive and active function of the upper and lower limbs. The spasticity screening tool allows for early identification and intervention, which may improve outcomes of focal spasticity management.

2.7.2. Measures of spasticity

Measuring spasticity can be challenging for a number of reasons. Reliable assessments are complicated by the fact that spasticity can vary throughout the day, change with different body positions and increase with noxious stimuli, such as urinary tract infection, pressure areas or constipation. Noxious stimuli need to be controlled, assessed and managed to accurately measure spasticity. Muscle tone variation depends on whether the muscle is active or at rest. Often there is little correlation between static tone at rest and dynamic tone with active movements.

The most frequent routinely used methods for the clinical assessment of spasticity are measurement of the joint’s active and passive range of motion and the Modified Ashworth Scale (MAS) followed by the Tardieu Scale [11, 43]. The
Ashworth Scale and the MAS have varying degrees of inter-rater reliability, partly due to differences in examiner techniques leading to scoring inaccuracies as well as uncontrolled patient and environmental factors, spasticity characteristics related to aetiology, and limitations in sensitivity and reliability [109-112]. The Tardieu Scale has a velocity component to its measurement of tone and has been shown to have higher validity, reliability and clinical utility [112] because it is better at distinguishing spasticity from soft tissue hypertonia. The Modified Tardieu Scale has been found to have only moderate inter-rater reliability in assessing spasticity of the plantar-flexor muscle in patients with post-stroke spasticity [113].

In the literature, the term spasticity is inconsistently defined, as discussed above (Section 2.4.1), and the outcome measures used often do not correspond to the definition or the description of the key clinical features; thus, the internal validity of research can be compromised [57].

### 2.7.3. Measures of function

Spasticity, almost universally, has at least some impact on a person’s ability to function. However, tests of general functional ability such as the Barthel Index and the Functional Independence Measure [96] have a larger number of unchanging items and do not have sufficient sensitivity to measure functional changes in people with spasticity [19, 34].

As discussed in detail in Chapter 1, evaluating goal achievement, using GAS for example, is recommended following focal spasticity management [33]. Goals for treatment of post-stroke spasticity are diverse, depending on the individual priorities of the patient and their family. This diversity presents a challenge for outcome measurement in this context leading to the recommended use of GAS as a primary outcome measure. GAS is more sensitive than other standardised outcome measures as it captures change in different domains, such as active and passive function, reflects clinical practice and allows quantification of the level of goal attainment [33, 34, 48, 50].

The Canadian Occupational Performance Measure [114] has been used to measure functional changes and patient satisfaction following spasticity treatment.
The Arm Activity Measure [115] has been developed specifically for measuring changes in active and passive upper limb function following focal spasticity treatments (Section 3.7.1). The Disability Assessment Scale also measures upper limb functional disability related to hygiene, dressing, pain and limb position in those with spasticity [27, 116]. Measures for active function in the upper limb that have been used following BoNT-A injections or CIMT include the Motor Activity Log (MAL) and Action Research Arm Test (ARAT) [117], but these do not necessarily correlate with real-life function and are more specific for those with residual active motor function of the upper limb.

In the lower limb, clinically based measures of active function, such as the 10 metre walk test or six minute walk [118], are useful and valid measures of performance in the clinical environment under test conditions [119]. However, following BoNT-A injection in adults with lower limb spasticity, changes in these measures may be small and they should be used in conjunction with other measures, such as GAS, to better capture clinical benefits [120]. A recent systematic review identified the Rivermead Mobility Index as a practical and clinically applicable self-reported measure of mobility that is reflective of real-life function and able to assess changes following focal rehabilitation and spasticity interventions in the lower limb in the context of stroke or brain injury [121, 122]. There was no measure identified that can evaluate passive function changes following spasticity intervention and management in the lower limb [121].

2.8. Spasticity management

2.8.1. Decision to treat spasticity

Decisions about whether and how to treat a patient’s spasticity are made on an individual basis following assessment by the treating team [6]. Factors to consider include chronicity, severity of spasticity, distribution of spasticity, degree of weakness, presence of contractures, development of compensatory strategies, severity of co-morbidities, availability of support and treatment goals [6]. Patients with spasticity may be treated if improvement in activity or participation (such as gait, independence in transfers, hygiene, dressing ability) or reduction in impairments (such as pain or contracture) can be realistically expected [21].
Spasticity management should be goal directed and these goals should address function [6, 21].

In some cases, the inappropriate treatment of spasticity may lead to loss of function, particularly when spasticity is counterbalancing the effects of paresis. On the other hand, spasticity may mask the return of selective movement in a paretic limb following stroke, and in some cases, relief of spasticity may facilitate the return of active movement. However, this cannot be guaranteed because underlying weakness will often persist, limiting functional gains to be made [76].

An overall algorithm for the treatment of spasticity is shown in Figure 2.2. Treatment should address exacerbating factors such as infection, pain, constipation and other nociceptive influences. Physical and pharmacological management approaches are discussed below.

![Algorithm for managing spasticity](image)

Adapted from Sheean 2010 [6] and Olver 2010 [98].

Figure 2.2. Algorithm for managing spasticity.

**2.8.2. Rehabilitation programs**

Stroke guideline recommendations specify that interventions to decrease spasticity (other than an early comprehensive therapy program) should not be routinely provided for people who have mild to moderate spasticity [22]. In stroke survivors who have persistent moderate to severe spasticity (i.e., spasticity that
interferes with activity or personal care), BoNT-A injections should be trialled in conjunction with rehabilitation therapy targeting clear treatment goals [22].

Currently, there are no modality-specific guidelines for treatment type, frequency or duration, but clinical practices for upper limb spasticity management in Australia [43] have been described. There is promising evidence that BoNT-A injections plus therapy and physical modalities may have sustained effects in spasticity reduction and functional outcomes in the upper limb [43, 123]. Reducing post-stroke spasticity alone – without addressing the negative components of the UMN syndrome – will limit meaningful recovery. Thus, a combination of rehabilitation techniques is needed to facilitate functional improvements [104].

### 2.8.3. Physical interventions and modalities

Although there is evidence suggesting that BoNT-A injections combined with physical therapies for the upper limb is more effective than BoNT-A injections alone, it is difficult to demonstrate an overall effect due to the heterogeneity of studies [35]. Most rehabilitation studies for spasticity management are limited to small RCTs [104]. Stroke guidelines support the use of electrical stimulation or electromyographic biofeedback as concomitant treatments to BoNT-A injections [22]. Other physical modalities for which there is supporting evidence include ergometer cycling, electrical stimulation, stretch (casting, splinting, taping, manual and exercise-induced), CIMT, task-specific motor training and exercise programs [35]. Additionally, physical interventions used clinically include therapeutic positioning and compensation training for functional activities [43]. Combinations of physical interventions are used to varying degrees in clinical practice to prevent and minimise the adverse effects of spasticity on function [43, 53].

There is less convincing evidence for physical treatments for lower limb spasticity [21], which is limited to possible effectiveness of stretching, taping, electrical stimulation and serial casting [124]. There is also emerging evidence for partial body weight support gait training and lower limb neuroprostheses improving gait speed, although evidence for use of an upper limb neuroprosthesis is better [104].
2.8.4. Botulinum toxin

BoNT-A is considered to be the gold-standard pharmacological treatment for focal spasticity [125].

**Pharmacology**

BoNT-A is injected intramuscularly to temporarily prevent the vesicle-dependent release of acetylcholine from the pre-synaptic nerve terminal, thereby blocking peripheral cholinergic transmission at the neuromuscular junction. BoNT-A cleaves synaptosome-associated protein (SNAP-25), a presynaptic membrane protein required for fusion of neurotransmitter-containing vesicles. BoNT-A is taken up by the neuromuscular junction within 12 hours with the clinical onset of spasticity reduction apparent at approximately seven days. BoNT-A interferes with neuromuscular transmission for about 12 to 16 weeks, at which point the neuromuscular junction is restored. Maximal effect occurs at approximately four weeks, and clinical benefits may last three to four months or longer [31].

Botulinum neurotoxins are produced by strains of the *Clostridium botulinum* bacteria with serotypes A to G. Only serotypes A and B are used in health care, and the biological activity units and dosing are unique to each BoNT preparation. Three BoNT-A products are available in Australia for clinical use: BOTOX (Allergan, Inc, Irvine, Canada), Dysport (Ipsen Pharmaceuticals, Slough, UK) and Xeomin (Merz Pharmaceuticals, Frankfurt, Germany).

**Adverse effects**

BoNT-A has a favorable safety and tolerability profile [126-128]. Potential adverse effects of BoNT-A may be injection site pain [127] or skin rash [129], and transient generalised muscle weakness or weakness observed beyond the site of local injection [130]. BoNT-A is contraindicated in those with pre-existing neuromuscular disorders such as myasthenia gravis and in pregnancy. Formation of neutralising antibodies to BoNT-A may reduce treatment efficacy and cause secondary treatment failure [131] by inactivating the biological activity of the toxin, although this is uncommon [132]. The presence of complexing proteins within botulinum neurotoxin agents increases the protein load and may exacerbate
an immune response[131]. The potential for antibody formation may be
minimised by injecting with the lowest effective dose given at the longest feasible
intervals between injections [133].

**Recommended use in stroke**

Stroke guidelines recommend the use of BoNT-A injections for moderate to
severe focal or multi-focal post-stroke spasticity [22]. The Australian
Pharmaceutical Benefits Scheme’s current criteria for therapy with BoNT-A
injections include treatment of moderate to severe spasticity (≥ 3 using the MAS)
of the upper limb in adults following a stroke when standard management (e.g.,
physiotherapy) has failed or as an adjunct to physical therapy. The maximum
number of interventions to be funded by the government is four per upper limb
per lifetime, with treatment delayed until three months in patients who do not
have severe contracture. Treatment with BoNT-A injections should be
discontinued if the patient does not respond after two interventions, as measured
by a decrease of MAS greater than one in at least one joint (www.pbs.gov.au).
Although there is no government funding for BoNT-A treatment for lower limb
post-stroke spasticity, it is still used when clinically indicated, but private or other
sources of funding are required.

**Injection techniques**

BoNT-A is injected using either nerve stimulation or electromyographic or
ultrasound guidance to locate the muscles to be injected. Determining which
muscles require injecting depends on patterns of spasticity, severity of spasticity,
motor function and goals of treatment [134]. Dosing of BoNT-A is determined by
previous responses to treatment, physician experience, muscle size, severity of
spasticity, residual function of the spastic muscles and risk of functional loss from
muscle weakness. Despite the clinical determinants for BoNT-A dosing and
muscle selection, injection practices seem to be guided by injector beliefs rather
than patient characteristics, spasticity severity or treatment goals [134]. Dose
ranging studies in the upper limb have shown that the optimal dose for a patient
with residual voluntary movement in the upper limb is from 500 to 1,000 units
Stroke patients with calf spasticity receiving Dysport 1,000 or 1,500 units have significant benefits [29].

**Benefits of BoNT-A in the upper limb**

Benefits of BoNT-A for upper limb post-stroke spasticity have been demonstrated in the areas of:

- attainment of goals [26, 33]
- improvement in impairments, such as tone [26, 129, 135-139], range of movement [136] and associated reactions [140]
- passive upper limb function [17, 27].

Goal achievement was greater in relation to impairments and body functions, such as tone and associated reactions, with lower performance in the goal domains representing activities and participation [33]. Goals related to passive function were more often achieved than goals relating to active upper limb functions such as dressing and eating [33].

Clinical experience seems to indicate that BoNT-A injections can, in selected patients with UMN syndrome, reduce spasticity and improve voluntary movement and active function. However, double-blind placebo-controlled trials have not shown active functional improvement, despite the clear ability of BoNT-A to reduce spasticity [129, 138, 141]. The evidence is less convincing as a result of the studies' methodologies, especially patient selection, injection protocols and the choice of outcome measures [59]. Improvement of quality of life has not been demonstrated following BoNT-A injections [26, 135]

Concurrent reduction in pain and spasticity from pharmacological treatments including BoNT-A [13, 142-145], intrathecal baclofen [146-148] and neurolytic blockade [149] suggests a causal relationship between the two [107]. In addition to paralytic effects, baclofen [150] and BoNT-A [144, 151] are thought to influence central pain mechanisms and the release of neurotransmitters that sensitise nociceptors.
Benefits of BoNT-A in the lower limb

Overall, there are fewer studies of spasticity in the lower limb than for spasticity in the upper limb, with less available data and fewer patients studied [152]. BoNT-A injections are recommended for use in adult lower limb post-stroke spasticity [21] to reduce spasticity [29], increase passive range of motion, reduce pain [29], improve gait quality [21, 153], and to treat associated reactions in the arm to improve gait speed [154]. Direct improvement in gait velocity following BoNT-A injections for lower limb spasticity has been difficult to demonstrate [30, 98]. The use of BoNT-A injections for lower limb post-stroke equinovarus-related spasticity is associated with a small, but statically significant, increase in gait velocity [15].

2.8.5. Other pharmacological treatments for post-stroke spasticity

Efficacy of oral antispasmodic drugs (e.g., baclofen, diazepam, dantrolene and tizanidine) is marginal at best [22, 155]. These drugs produce generalised muscle weakness, and in conjunction with their high levels of adverse reactions, their use is limited in post-stroke spasticity.

Intrathecal baclofen decreases severe spasticity, but adverse events such as infection and functional decline have been reported in a small proportion of cases [156, 157]. Intrathecal baclofen is currently uncommon for post-stroke spasticity [158]. Nerve blocks, such as with phenol and alcohol, are effective and widely used for post-stroke spasticity, but evidence for their effectiveness is limited [159]. Nerve blocks denature proteins in nerve membranes and axons leading to chemical denervation, with the effect of muscle weakness potentially lasting up to 12 months.

2.8.6. Surgical treatments for complications of post-stroke spasticity

In cases of established contracture, surgical release may correct deformity and facilitate better posture (e.g., standing) to prevent further spasticity. Procedures include split anterior tibial tendon transfer and Achilles tendon transfer for the lower limb, which may improve mobility and the ability to wear shoes [104]. Upper limb surgery (such as tendon transfers involving long finger flexors or
brachioradialis to the long finger extensors [160] and tendon lengthening of flexor pollicis longus) may assist with palmar access to maintain hygiene.

Chapter 3 describes the overall methodology for the thesis and the methodological frameworks to which the four studies apply.
Chapter 3. Methodology

This chapter describes the methodology used for the four studies. Important practical and methodological challenges are discussed along with the limitations associated with investigating complex interventions. Chapters 4 to 7 explain the methods for each of the studies in more detail.

3.1. Overview

The methods for the systematic Cochrane review of multidisciplinary rehabilitation following BoNT-A injections for post-stroke spasticity (Study 1, Chapter 4) followed the *Cochrane Handbook for Systematic Reviews of Interventions* [61]. The methods for Study 1 are summarised in Section 3.2 and a detailed description is given in Chapter 4. The other sections in this chapter relate to Studies 2, 3 and 4. Sections 3.3 to 3.5 outline the process for obtaining ethics approval, the recruitment of study subjects and the assessments conducted. Section 3.6 describes how four different methodological models guided the development of the studies in this thesis and helped to address the methodological challenges that arise when investigating complex interventions such as rehabilitation. Outcomes related to the objectives are discussed in Section 3.7.

3.2. Methods for systematic review

The aim of the Cochrane review was to assess the effectiveness of multidisciplinary rehabilitation following BoNT-A injections in adults and children with post-stroke spasticity. This was achieved by identifying the types of approaches that are effective (settings, intensities and modalities) and the outcomes that are affected. The Cochrane review was necessary to identify evidence for the interventions that are similar to that used in Study 2 (Chapter 5) and the methods used to evaluate those interventions.

The literature searches used for the electronic bibliographic databases are provided in Appendix 5. The MEDLINE search strategy was developed with the help of the Cochrane Stroke Group Trials Search Coordinator and adapted for the
other databases. In an attempt to identify other published, unpublished and ongoing trials, the searches were extended to include:

- reference lists of all retrieved articles, texts and other reviews on the topic
- journals related to spasticity research and treatment not already searched on behalf of the Cochrane Collaboration; this included searching journals such as the *Archives of Physical Medicine and Rehabilitation* (December 1995 to January 2012) using the search engine ScienceDirect and manually searching the *Journal of Rehabilitation Medicine* (January 2001 to January 2012)
- the PubMed related articles feature
- the Science Citation Index Cited Reference Search for forward tracking important articles
- Open Grey (formerly the System for Information on Grey Literature in Europe) at www.opengrey.eu
- contact with authors, researchers and experts in the field.

Included studies were RCTs that assessed the effectiveness of multidisciplinary (two or more disciplines in conjunction with medical input) rehabilitation programs following BoNT-A injections or other focal intramuscular treatment for upper limb or lower limb post-stroke spasticity. Studies were included if they used routinely available local services, lower levels of intervention or compared multidisciplinary rehabilitation programs of different types in different settings or at different intensities.

A qualitative synthesis of the best evidence was based on the GRADE levels of evidence (Table 4.2) taking into consideration the five factors that affect quality of evidence (Table 4.3) according to Section 12.2 of the *Cochrane Handbook for Systematic Reviews of Interventions* [61]. Meta-analysis was not possible due to the small number of clinically and methodologically heterogeneous studies.

A range of outcomes were used given the varied presentations of spasticity-related problems and goals of treatment related to stroke severity [33]. Primary outcomes reflected the level of activity limitation according to the ICF [12] (Figure 1.1) and included:
• passive function (e.g., Disability Assessment Scale [27] or Arm Activity Measure [115, 161])
• active function of the upper limb (e.g., MAL [162] or ARAT [163])
• active function of the lower limb with mobility measures including tests of walking speed, balance and gait pattern (e.g., 10 metre walk test [164]).

A measure of achievement of intended goals for treatment was included (e.g., GAS) [46] or other measure of goal achievement.

Secondary outcomes were measures of:
• symptoms and impairments (e.g., pain measured by verbal scores or visual analogue scales), measures of spasticity or tone such as the MAS [110] or the Tardieu Scale [112]
• restriction in participation and impact on caregivers (e.g., quality of life measures), reduction of caregiver strain and burden (e.g., Caregiver Strain Index [165]).

The following sections relate to Studies 2, 3 and 4 (Chapters 5, 6 and 7, respectively).

3.3. Ethics

The Melbourne Health HREC, in accordance with the National Statement on Ethical Conduct in Human Research 2007, approved the research (HREC number 2010.165). All participants received an information sheet and consent form written in plain English, which they signed after receiving a verbal explanation of the project from the primary investigator (MD) and an opportunity to ask further questions. Research data sheets were labelled with a unique study code for participant identification and kept in a locked office at the recruiting centre. Coded information was entered into a password-protected database.

3.4. Study participants

Community residing adults with post-stroke spasticity (diagnosed by a rehabilitation physician experienced in spasticity management) were recruited through a multidisciplinary spasticity management clinic at the Royal Melbourne
Hospital’s Royal Park Campus in Victoria, Australia. The clinic services metropolitan Melbourne and surrounding rural regions. Consecutive patients treated with BoNT-A for upper or lower limb post-stroke spasticity and eligible for rehabilitation (see inclusion criteria below) were invited to participate in the study. Inclusion criteria were: age 18 years or over; stroke diagnosis three or more months prior; upper or lower limb spasticity (MAS ≥ 2) interfering with function or causing a clinical problem, and no contraindications to BoNT-A injections. Patients were excluded if they: had treatment with BoNT-A within six months; had received intrathecal baclofen or other anti-spasticity medications; had undergone neurolysis or surgery to the affected limb; had concomitant neurological conditions; were pregnant; or were unable to participate in therapy due to cognitive or language impairment, psychiatric illness or medical illness. Screening was based on information collected from medical records, examining patients and verbal questioning.

Fifty-nine of 75 stroke survivors screened from January 2011 to June 2012 were recruited to the study, with 28 allocated to high-intensity rehabilitation programs and 31 allocated to lower intensity usual care rehabilitation programs (group allocation methods are described in Section 5.2.2). Of those excluded, 15 did not meet the inclusion criteria (the majority due to not having a clinical indication for treatment with BoNT-A injections) and one declined to participate. All but one participant (who was allocated to usual care low-intensity rehabilitation) completed the therapy program as per a priori 70% compliance with planned therapy sessions. This participant declined to continue therapy after the initial assessment. All participants were included in analyses. See Figure 5.1 for a study flow diagram.

Of the 59 participants recruited to the intervention study (Study 2, Chapter 5), therapy documentation forms [55, 62, 166] (Appendix 3) were completed by therapists for 47 participants, documenting 925 physical and occupational therapy sessions (Study 3, Chapter 6).
3.5. Assessments and data collection

3.5.1. Assessment procedures

Recruitment and study assessments were undertaken between January 2011 and June 2013 through the outpatient spasticity management clinic at the Royal Melbourne Hospital’s Royal Park Campus. Structured baseline assessments included data collection (relevant medical history, clinical status and demographics; MD, GA) and goal setting by a therapist experienced in using GAS [46] (JL; Appendix 2). Individualised BoNT-A injections in the affected limbs were administered at baseline by a rehabilitation physician (MD, GA) using neuromuscular stimulation, and referrals to community-based rehabilitation services were completed (JL).

A blinded assessor completed standardised outcome assessments (Section 3.7.1; see Appendix 6 for data collection sheets) at baseline and at six, 12 and 24 weeks. Figure 5.1 shows the study flow diagram.

Participants’ and therapists’ experiences during the program were assessed using questionnaires (Appendix 4). Following completion of rehabilitation programs and study assessments, participants were telephoned (MD) and invited to complete a brief verbal questionnaire (Appendix 4) regarding their experience with the therapy program. Thirty-five of the 59 participants agreed to participate and completed the questionnaire. Of those remaining, five were deceased, 12 were non-contactable and seven declined without providing reasons. Eight therapists completed questionnaires in the same manner.

3.5.2. Data collection

The mixed methods research involved collecting, analysing and integrating quantitative (e.g., experiment in Study 2) and qualitative (e.g., interviews in Studies 3 and 4) research. Qualitative research is primarily exploratory research that involves disciplined inquiry to gain an understanding of underlying reasons, motivations and opinions [167]. Quantitative research is used to quantify the problem by way of generating numerical data or data than can be transformed into useable statistics.
Variation in data collection leads to greater validity by answering the question from a number of perspectives and is useful when one methodology does not provide all the information required. Qualitative and quantitative research, in combination, provided a better understanding of the effectiveness of rehabilitation programs for post-stroke spasticity than either research approach alone. Outcomes of such interventions are not only influenced by the components of the interventions but the milieu in which rehabilitation is delivered. Qualitative methodology was appropriate for evaluating contextual factors that influence program implementation and effectiveness (e.g., social processes and participants’ and therapists’ attitudes and beliefs) and cannot be measured using quantitative evaluation tools.

Based on outcomes of importance related to spasticity management [6, 19, 21, 33], derived from the literature review (Chapter 2), suitable quantitative outcome measures to evaluate effectiveness of high-intensity rehabilitation programs compared with usual care (Study 2, Chapter 5) were chosen. Objective measures were combined with subjective or self-reported outcomes, which may be unreliable due to non-blinding of study participants [56]. Detail regarding the outcome measures used for Studies 2 to 4, in relation to the objectives of the thesis, is provided in Section 3.7.1. For baseline data collection sheets, see Appendix 6.

Therapists were asked to complete therapy documentation forms (Appendix 3) for each physical and occupational therapy session attended by participants. These forms were used to document time, in five-minute intervals, spent in each rehabilitation activity and the interventions (up to a maximum of five) used to facilitate these activities.

Qualitative questionnaires (Appendix 4) were used to assess the participants’ satisfaction with the rehabilitation programs (Studies 3 and 4) and the therapists’ experiences with implementing the programs and using the therapy documentation forms (Study 4, Chapter 7). The structured questionnaires included open questions and closed questions with a rating scale applied to them (Appendix 4). Further detail on the list of questions comprising the questionnaires is provided in Section 7.2.5. Semi-structured interviews or meetings with the Community Therapy Services manager aimed to identify issues related to implementation processes and organisational functioning (Section 7.2.4).
3.5.3. Assessment time points

The primary time point was three months post treatment because this is when the effect of spasticity reduction due to BoNT-A is expected to have worn off [31] and functional changes are expected after the maximal reduction in spasticity at four weeks [20]. The follow-up period of six months was selected to detect whether short-term changes persisted. Follow-up did not extend beyond six months as by this time point many patients require reinjection with BoNT-A or further episodes of rehabilitation, and for logistical reasons including limited funding and resources and prolonged study duration.

3.5.4. Intervention

Group allocation to rehabilitation programs was based on participants’ areas of residence to reflect real-life practices where service delivery protocols are determined by geographical catchment areas and proximity to services. Participants residing within a 12 kilometre radius of the investigating hospital received high-intensity therapy, while subjects outside of this geographical catchment underwent usual care, being lower intensity therapy at their local community or hospital rehabilitation service. Hence, a number of centres were involved in providing therapy in this study, predominantly tertiary hospital community therapy services.

Twenty-eight participants attended high-intensity ambulatory rehabilitation programs (three or more one-hour sessions per week for 10 weeks) provided by the Community Therapy Service at the Royal Melbourne Hospital’s Royal Park Campus. All achieved a priori compliance with outpatient treatment (attendance at more than 70% of scheduled therapy sessions). Thirty-one participants were allocated to usual care, low-intensity (two or fewer one-hour sessions per week). Intensity or amount of therapy has been described in a number of ways:

- frequency (number of hours during the week, calculated using session duration and number of sessions) and duration (number of weeks), which is considered to be applicable to clinical decisions [117, 168-170]
• subgroups defined by the total hours [171], calculated by multiplying number of weeks by the number of sessions per week by the session duration in hours [171, 172]
• mean daily therapy intensity (total therapy hours divided by length of stay) for inpatient rehabilitation [173].

Different calculations for the amount of therapy make it difficult to compare studies and can result in contradictory findings [169]. The first method described above [169] is used to define therapy intensity in this thesis due to clinical relevance.

Rehabilitation programs were individualised and goal-directed, with treating therapists determining appropriate therapy approaches and rehabilitation interventions to use.

3.5.5. Statistical analysis

Data was entered into a Microsoft Access database and exported into Stata version 12 (StataCorp, TX, USA) for analysis. Descriptive statistics are presented as mean and SD for continuous normally distributed data, as median and interquartile range for skewed or ordinal data and as number and percentage for categorical data.

3.6. Rationale for methodological methods and study design

The methodological models, frameworks and guidelines that contributed to the mixed methods design of this thesis are presented and discussed here. In general, quantitative methods aim for reliability and rely on standardised tools [174]. Qualitative methods are used to capture and evaluate the range of outcomes in a real-life clinical context.

Quantitative methods were used to investigate effectiveness in everyday practice and to determine whether BoNT-A injections combined with intensive ambulatory rehabilitation improves outcomes more than BoNT-A injections with usual care (Study 2, Chapter 5). Descriptive, quantitative and qualitative methods were used to evaluate the components (Study 3, Chapter 6) and the
implementation and delivery (Study 4, Chapter 7) of rehabilitation programs to address the following questions:

- What was the intervention?
- Was it implemented as planned?
- What short-term and long-term effects were achieved in terms of patient-centred outcomes?
- What were the patients’ and therapists’ experiences with the delivery and implementation of the rehabilitation programs?
- What were the barriers and enablers to implementation?

The following methodological models and theoretical frameworks supported the development of the thesis studies:

- A Taxonomy for Disease Management from the American Heart Association Disease Management Taxonomy Writing Group [175] (Studies 2 and 3; Section 3.6.1)
- Post-Stroke Rehabilitation Outcomes Project [36, 55] (Study 3; Section 3.6.2)
- ICF (WHO 2001; Studies 1, 2 and 3; Section 3.6.3)
- United Kingdom Medical Research Council Model (Studies 2, 3 and 4; Section 3.6.4)
- Reach, Effectiveness, Adoption, Implementation and Maintenance (RE-AIM) framework for program evaluation (Study 4; Section 3.6.5).

3.6.1. A taxonomy for chronic disease management

A taxonomy for chronic disease management (developed by the American Heart Association Disease Management Taxonomy Writing Group) provides a conceptual framework to describe critical attributes of multidisciplinary disease management programs in a way that can be used both to compare the diverse range of programs and to assist in identifying specific factors associated with effectiveness [175]. The Disease Management Taxonomy is a pragmatic but comprehensive approach to describing multidisciplinary community-based programs that can also be applied to rehabilitation programs. Chronic disease management programs provide long-term outpatient management of chronic illness, but are widely heterogeneous and lack a shared definition [175]. similar to
spasticity management in ambulatory rehabilitation settings. Hence, the framework was developed. The Disease Management Taxonomy includes the following eight domains to describe multidisciplinary programs, which were incorporated into Studies 2, 3 and 4 of this thesis (Figure 3.1) [175]:

1. *patient population* characterises risk status, demographic profile and level of comorbidity

2. *intervention recipient* describes the primary targets of disease management intervention and includes patients and caregivers, physicians and allied health care providers, and health care delivery systems

3. *intervention content* defines individual components, such as patient education

4. *delivery personnel* describes the network of health care providers involved in the delivery of disease management interventions

5. *method of communication* identifies a broad range of disease management delivery systems that may include face-to-face contact or some form of electronic or telecommunication technology

6. *intensity and complexity* distinguishes between the frequency and duration of exposure, and mix of program components.

7. *environment* defines the context in which disease management interventions are delivered such as hospital-affiliated outpatient programs which include community- or home-based programs.

8. *clinical outcomes* includes traditional, frequently assessed primary and secondary outcomes, patient-centred measures and caregiver burden.
Adapted from Krumholz 2006 [175]. Domains relevant to Studies 2*, 3+ and 4#.

Figure 3.1. Use of a Disease Management Taxonomy to classify rehabilitation programs for spasticity management in this thesis

Mixed methods and descriptive analyses were used to define and evaluate the program domains. A detailed cost–benefit analysis was beyond the scope of this thesis, but the direct cost of therapy was estimated based on hourly blocks.

Challenges associated with researching disease management programs, which are relevant to the thesis topic, include:

- limited generalisability of studies investigating similar interventions to larger patient populations because most are conducted at single sites [175]
- multidimensional nature of disease management programs with the essential program elements associated with efficacy yet to be established
- a lack of standardisation due to the variety of definitions of disease management and related models. Despite common core elements of disease management programs, such as coordination of care, evidence-based practice and outcomes evaluation, individual program components are highly variable in relation to key elements and
comprehensiveness. This variability causes difficulties in comparing models, programs, outcomes and effectiveness. Similarly, in spasticity management, clinical practices vary, as do the definitions of spasticity and what is being measured in the literature.

With these issues in mind, the Disease Management Taxonomy [175] was considered relevant to this thesis because its purpose is to provide a standardised system to classify these diverse elements and programs. This is a necessary step in advancing the field of spasticity management by building up an evidence base through the use of a common framework because future researchers may consider implementing a similar approach to enable comparisons of interventions across studies, and use of similar research methodology and outcome evaluation. This would assist in development of policies and guidelines that will improve effectiveness of care and service delivery.

3.6.2. Post-Stroke Rehabilitation Outcomes Project

The Post-Stroke Rehabilitation Outcomes Project is a large multicentre stroke rehabilitation study based in seven hospital-based rehabilitation centres in the United States (N = 6) and New Zealand (N = 1). The project provides an in-depth view of inpatient rehabilitation practice [36, 63]. The Post-Stroke Rehabilitation Outcomes Project’s main objective is to determine the impact that each stroke rehabilitation activity or intervention, both individually and collectively, has on patient outcomes at discharge, while controlling for each patient’s medical and functional differences [36]. To achieve this, it was necessary to first develop a taxonomy of inpatient stroke rehabilitation activities and interventions that could be used to document rehabilitation processes and content in detail for occupational and physical therapy [36, 55, 62, 176] (Appendix 3). This taxonomy provides sufficient detail for understanding rehabilitation programs at the individual level and how rehabilitation activities relate to patient’s spasticity management goals (Study 3, Chapter 6), whereas the American Heart Association’s taxonomy (Section 3.6.1) addresses broader elements. Describing rehabilitation programs in such detail is necessary to enable future studies to identify the components of therapy that are effective and allow for the
development of more comprehensive guidelines for spasticity management after BoNT-A injections.

Issues in stroke rehabilitation research that necessitated the Post-Stroke Rehabilitation Outcomes Project are similar to those in spasticity management and are addressed in this thesis; these include:

- variations in research methods limiting comparisons between studies and preventing establishment of a reliable evidence base [177]
- RCTs that are too small, have poor generalisability or are scientifically inadequate in providing guidance in establishing evidence-based practice [36, 177]; rigorous systematic reviews including all relevant trials are recommended [177] (Study 1, Chapter 4)
- interventions considered in isolation from the complex array of other rehabilitation-related interventions implemented in real-life clinical practice [55] (Study 2, Chapter 5)
- inadequate data collection on what happens between admission and discharge (i.e., details of rehabilitation programs and interventions used); thus the stroke rehabilitation process – the black box of rehabilitation – remains largely unknown [36, 63, 178-180] (Study 3, Chapter 6).

The clinical practice improvement methodology of the Post-Stroke Rehabilitation Outcomes Project allows for identification of promising therapeutic activities and interventions more quickly than conventional methods such as RCTs, which are also very expensive [36]. A better understanding of current practice assists in developing an evidence base. A limitation of the Post-Stroke Rehabilitation Outcomes Project was that the focus was at the patient level rather than addressing the organisational milieu and interdisciplinary team coherence and culture that influences therapists’ and patients’ moods and behaviours, and thus participation [36, 181].

In Study 3 (Chapter 6), therapists used the therapy documentation forms (for occupational and physical therapy rehabilitation activities) developed in the Post-Stroke Rehabilitation Outcomes Project to document each therapy session provided to participants. Therapists were also provided with definitions of terms [36] (Appendix 3). The Post-Stroke Rehabilitation Outcomes Project found that
there is overlap of activities across the different therapies. Thus, an integrated analysis is required to examine rehabilitation practice holistically across professional domains. Taking this into account, therapists using the therapy documentation forms in Study 3 were instructed that they could document activities on either form, rather than the form specific to their discipline, so as not to miss capturing activities that time was spent in.

### 3.6.3. The ICF framework

The ICF provides a unified and standard language and framework for the description of health and health-related states [12]. Table 3.1 outlines the main components comprising the ICF.
Table 3.1. Main components of the World Health Organization’s International Classification of Functioning, Disability and Health

<table>
<thead>
<tr>
<th>Parts</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td>Part 1. Functioning and disability</td>
<td>Body functions and structures</td>
</tr>
<tr>
<td></td>
<td>Activities and participation</td>
</tr>
<tr>
<td>Part 2. Contextual factors</td>
<td>Environmental factors</td>
</tr>
<tr>
<td></td>
<td>Personal factors</td>
</tr>
</tbody>
</table>

The ICF framework, Part 1, was useful in selecting the outcome measures used in this thesis to address the following recommendations in spasticity management:

- For studies to use outcomes related to activity and participation, not just impairments [6, 21].
- Use of a measure of goal attainment, such as GAS [46], to capture the range of individualised goals related to spasticity management. Goals can then be linked to categories related to the ICF (Study 2, Chapter 5). In contrast, many standardised outcome measures fail to capture the range of outcomes that are meaningful to patients and their caregivers [33].

Contextual factors (Part 2) influence the delivery and effectiveness of rehabilitation programs, although many are difficult to measure and quantify (e.g., patient motivation and self-efficacy, therapist–patient relationship and team coherence [181], behaviours and expertise of those delivering or receiving the intervention, patient’s educational level, cultural issues and therapy setting). Personal factors are often important barriers to, or facilitators of, this process. The interaction between each stroke survivor, his or her personal beliefs, coping abilities and behaviours, health care providers, and family members is complex and individualised, with all factors having a possible impact on a patient’s outcome [36]. Issues relating to personal factors often need to be explored, managed and adapted if possible, usually by the treating team, to optimise the rehabilitation process. These factors are discussed in Studies 1, 2 and 4 (Sections 4.8, 5.4 and 7.5, respectively) and evaluated where possible.

Although activities and participation are combined in the ICF, recommendations are to develop a distinct set of domains for each by dividing the
current classification into two mutually exclusive lists [12, 182]. Improved distinction between activity (the execution of a task or action by an individual or individual perspective of functioning [12]) and participation (involvement in a life situation or societal perspective of functioning [12]) is first required [182]. However, activities and participation are not always mutually exclusive [182]. This problem was evident in Study 2 (Chapter 5), where upper and lower limb goals often related to both activity and participation so these goals were combined into one category for classification.

Another limitation of the ICF is the lack of conceptualisation of participation and environment (the physical, social, and attitudinal environment in which people live and conduct their lives [12]), thus restricting their measurement [182]. It has been suggested that separate objective and subjective measures of participation are needed because there are methodologic difficulties inherent in measuring participation. Although a quality of life measure was used to measure participation (Section 3.7.1), there is debate about whether this is appropriate because the importance of the activity for the person is often not accounted for [182].

**3.6.4. Methodological challenges when investigating complex interventions: Medical Research Council framework (United Kingdom)**

**Complex interventions**

The Medical Research Council framework provided guidance in addressing challenges in researching complex interventions as discussed in Section 1.8.1. Complex interventions such as rehabilitation programs are described as such as they contain multiple interacting components with several dimensions of complexity that may relate to a range of possible outcomes, or due to their variability in the target population, as well as the number of elements in the intervention package itself [56]. It is important to understand the whole range of effects (i.e., how they vary among recipients of the intervention) [60]. Hence, use of a range of outcome measures is advised [60], which is particularly relevant when treating spasticity as goals are highly variable between individuals [33].
Study designs

In 2000, the Medical Research Council in the United Kingdom published the *Framework for the Development and Evaluation of RCTs for Complex Interventions to Improve Health* [183] to help researchers to recognise and adopt appropriate methods in the area of complex interventions. The original framework focused on the development and evaluation of RCTs for complex interventions [183], which are generally recognised as providing the highest grade of causal evidence [184]. Conventionally, RCTs involve parallel groups that are randomised to receiving and not receiving an experimental, therapeutic, preventative or diagnostic procedure and are then followed up to determine the outcome. However, robust methodology (such as RCTs within the Medical Research Council model), even with modifications, may not be feasible in certain areas of rehabilitation including spasticity management.

A review was conducted in 2006 extending the coverage in the guidance of non-experimental methods to help researchers to choose appropriate methods [60]. The new guidelines address other randomised designs if the conventional RCT design is not appropriate (e.g., individually randomised trials, cluster randomised trials and stepped wedge designs) [60]. The new guidelines also acknowledge that while experimental designs are preferred, they are not always practicable and observational designs may be necessary.

While randomised study designs were considered for this thesis, they were not deemed to be feasible or applicable due to organisational, service delivery, intervention and individual participant constraints. Phased implementations and wait list controls were also not considered suitable because BoNT-A provides a window of opportunity to remediate related problems with physical therapies so delaying treatment is not clinically appropriate [21].

Many practical and methodological difficulties needed to be overcome in the studies in this thesis while accepting certain limitations to study design. Although randomisation is the most robust method of minimising selection and information bias, controlling confounding and attempting to rule out chance [185], a RCT design was not suitable for Study 2 (Chapter 5) for the following reasons:

- A control group receiving no therapy was not feasible because
Based on recommendations in clinical guidelines [6, 19, 21], routine practice is to refer patients attending the Spasticity Management Clinic at the Royal Melbourne Hospital for therapy following BoNT-A injections.

Many patients receive therapy at the time of BoNT-A injection (N = 35/59, 59.3%) and it is considered unethical to withhold or stop therapy, despite the lack of robust evidence for its application in the study population.

- Not only is the intervention already in widespread use, but key decisions about how it is implemented have already been made based on organisational factors [56]. Practices may differ somewhat between rehabilitation centres and study investigators were unable to influence the nature of therapy programs (intensity, interventions and timing) delivered at rehabilitation services other than at the recruiting hospital. Hence, allocation to intervention was based on geographical catchment areas, as described in Section 3.5.2.

- Difficulty standardising the design and delivery of the interventions due to the following reasons
  - Rehabilitation programs are individualised, multifaceted and influenced by many personal factors (Section 3.6.3) and features of the local context (social, political, organisational setting within which an intervention is implemented) such as resource availability, resource allocation, infrastructure, policies and cultural influences [186]. These interventions are often defined pragmatically, according to local settings (which can vary nationally and internationally), rather than having a theoretical basis. The study protocol permitted flexibility and tailoring of the intervention consistent with real-life clinical practice and guideline recommendations for investigating complex interventions [60]. This adds another dimension of complexity to evaluating rehabilitation programs and limits generalisability.
Achieving consistency of intervention delivery by different staff to different patients on different days is unrealistic [177]. Training therapists to deliver similar interventions is costly and logistically challenging due to the time required, the number of therapists and regular staff changes in public hospitals, particularly when there is one recruiting hospital but the intervention is delivered by multiple services.

Documentation of the intervention in a detailed manner is required first to allow replication of the treatments evaluated [177].

To overcome some of these issues, a quasi-experimental or observational design may be considered where the intervention is already implemented [56] and where the effects of selection, allocation and other biases are relatively small. However, there is a significant limitation to the reliability of estimates of effect with these methods, and conclusive findings are often only found when interventions have rapid and large effects [60]. On the other hand, observational designs may contribute to the assessment of the feasibility of interventions (acceptability, compliance, implementation of interventions, recruitment and retention) and to the assessment of the effectiveness of interventions, although not without limitations.

An additional challenge in evaluating complex rehabilitation interventions is the length and complexity of the causal chains linking an intervention with an outcome, making RCT results subject to effect modification in different populations [187]. Post hoc adjustment is considered the best solution for dealing with external influences to the intervention, but its effectiveness is limited by measurement error in the confounding variables and inability to deal with unknown or unmeasured variables [60]. Multivariate logistic regression was used to estimate associations between the predictor variables and the GAS primary outcome in Study 2 (Chapter 5). The only measured variables included in the models were treatment allocation, age, gender, stroke localisation and time since stroke. Thorough process evaluation may also identify factors contributing to cause and effect relationships.
Evaluation in the real-life clinical setting

Trials of health care interventions are often described as either explanatory or pragmatic [188] where:

- Explanatory trials generally measure efficacy (i.e., the benefit a treatment produces under ideal conditions in a research clinic) often using carefully selected subjects to recruit as homogeneous a population as possible. Explanatory trials aim to further scientific knowledge.

- Pragmatic trials measure effectiveness (i.e., the benefit the treatment produces in routine clinical practice). The design of a pragmatic trial reflects the heterogeneity of patients in real-life, thus representing the population for whom the treatment is designed and ensuring generalisability of the results [188]. A key question in evaluating complex interventions, such as rehabilitation programs, is whether they are effective in everyday practice [60].

Program development and evaluation

Key steps in program development and evaluation [60] that are relevant to this thesis are depicted in Figure 3.2. Because it was not possible to influence the composition of intervention and how and when the intervention was implemented, the scope to undertake developmental work as part of this thesis was limited. Aspects that were addressed include:

- identifying the existing evidence base by conducting a systematic review to determine what is known about similar interventions and the methods used to evaluate them (Study 1, Chapter 4)
- developing a theoretical understanding of the process of change by drawing on existing evidence and theory enlightening the rationale for complex interventions, expected changes and how change is to be achieved (Chapter 2)
- modelling process and outcomes to inform the design of the intervention and evaluation (Studies 2, 3 and 4)
addressing components of feasibility including acceptability, compliance, delivery of the intervention, recruitment and retention, and understanding the context in which the intervention takes place (Studies 2, 3 and 4).

Widespread implementation and dissemination of intensive ambulatory rehabilitation programs (i.e., of greater intensity than usual care) is beyond the scope of this thesis.

Adapted from Craig 2008 [60].

Figure 3.2. Key elements of the development and evaluation process.

The updated Medical Research Council guidelines for the evaluation of complex interventions emphasise the importance of studies including a detailed description of the intervention to enable replication, evidence synthesis and wider implementation [60]. Studies of rehabilitation interventions for spasticity management and relevant guidelines lack detailed descriptions. Therefore, this was considered an important area to address in this thesis (Study 3, Chapter 6) by using standardised therapy documentation forms [55, 62, 63, 176] to capture detail.
3.6.5. RE-AIM framework for process evaluation

The RE-AIM framework informs the evaluation of implementation and delivery of the high-intensity rehabilitation program in Study 4 (Chapter 7) [189]. RE-AIM assesses the translatability and public health impact of interventions in a real-world setting and balances the emphasis on internal and external validity [190].

The review of the literature found that the important aspects to address in process evaluation are: sampling, recruitment, reach, acceptability and quality of the intervention, barriers and facilitators, and contextual influences [191-193]. Understanding these processes facilitates the interpretation of results and helps to explain discrepancies between expected and observed outcomes. The RE-AIM [194] process evaluation tool was selected for this study because it addresses these key areas and, importantly, encompasses mixed methods, which is the recommended approach for process studies [60, 192, 195].

Lack of impact may reflect program implementation failure rather than actual ineffectiveness. Thus, a thorough process evaluation is needed to identify implementation problems [56]. Process evaluation nested within a trial can be used to assess the fidelity and quality of implementation, clarify causal mechanisms and identify contextual factors associated with variation in outcomes [56].

The following five dimensions explore the individual- and organisational-level of impact:

1. reach (i.e., how well the intervention reaches the target population)
2. effectiveness
3. adoption by target staff or organisations. Widespread adoption is assessed by comparing the proportion, characteristics and representativeness of the rehabilitation centres that are willing to deliver the intervention and with the rehabilitation centres that were approached but unwilling to deliver the intervention and the rehabilitation centres in other communities in a larger geographic area or region.
4. implementation (i.e., consistency, costs and adaptions made during delivery). Implementation at the setting level refers to the therapist’s fidelity to the elements of an intervention’s protocol, including
consistency of delivery as intended and the time and cost of the intervention [190]. At the individual level, implementation refers to participants’ use of the intervention strategies [190].

5. maintenance refers to incorporation of the intervention program into routine practice and policy over time which is beyond the scope of this thesis. However, issues surrounding program delivery in the long-term are examined. Most decisions about maintaining a program are influenced not only by the overall impact of a treatment but also by its costs [21]. At the individual level, maintenance has been defined as the long-term effects of a program on outcomes six or more months after the most recent intervention contact [190].

3.7. Outcome evaluation

In this thesis, outcome evaluation comprises mixed methods. A quantitative approach is used to assess program effectiveness using standardised outcome measures described below. Quantitative and qualitative approaches are used to describe the program components and implementation.

3.7.1. How effective is the intervention? Outcomes evaluating effectiveness of BoNT-A injections and rehabilitation programs

A number of outcome measures were required because the rehabilitation intervention has an effect across a range of domains (function, satisfaction and caregiver burden) and the goals for treating upper [33] and lower limb [196] spasticity vary. The ICF framework (Figure 1.1) is used to classify outcome measures in terms of those related to impairments, limitation in activity and restriction in participation [12].

Primary outcome

GAS [46] is a method for rating individual goal achievement on a five-point scale (from –2 to 2), where a GAS score of 0 and above implies goal achievement (Section 1.3). Goals set at baseline by participants, caregivers and therapists experienced in using GAS relate to impairments, activity or participation. Up to
three goals for each injected limb were set for each participant at baseline. Goals were weighted by importance and difficulty, each graded on a scale of 0 to 3. The blinded assessor assigned the level of individual goal attainment according to the description in the statement of expected outcome (0 score) at follow-ups.

Appendix 2 shows examples of participant goals and scoring using GAS. The composite goal attainment score (T-score) is based on the aggregated weighted score of each participant’s goals. The T-score is calculated using a mathematical formula and is normally distributed with a mean of 50 and a SD of 10 [46].

GAS has been demonstrated to be a valid, reliable and responsive measure for evaluating focal intervention for spasticity in the upper [33, 34] and lower [196] limbs. GAS has been used for a number of different patient populations, including stroke [33, 197], cerebral palsy [49, 198-200], multiple sclerosis [47, 51], brain injury [34, 201], psychiatric [46] and geriatric [202]. GAS identifies outcomes of importance to the individual or caregivers that are not otherwise detected using standardised measures [33], particularly where patients form a heterogeneous group and goals of treatment are variable [11] such as the study cohort for this thesis. GAS also offers qualitative information regarding the goals that were set and achieved during the program [33].

A change in GAS T-score of at least 10 points is considered a clinically important change [34]. Participants who achieved 50% or more of their goals were considered to have responded to treatment and the proportion of participants achieving this outcome was calculated.

**Secondary outcomes: impairments, activity limitations and participation restriction**

The MAS [110, 116, 118] is a clinical measure of tone during passive joint movement. The single-item MAS is measured on a six-point scale from 0 (no increase in muscle tone) to 4 (affected part rigid in flexion or extension), with an additional point allocated at 1 (slight increase in muscle tone). The MAS therefore provides a single score to represent spasticity. The MAS has good inter- and intrarater reliability for use in the upper and lower limb over time [203-205]. A clinically significant response to treatment is defined as at least one point improvement from baseline scores [206].
The Arm Activity Measure [115, 161] is a self-reported (by patient or caregiver) measure of difficulty in passive and active arm function for application following focal interventions for spasticity (including BoNT-A and physical treatments). The Arm Activity Measure comprises a seven-item passive function subscale and a 13-item active function subscale. Each item is measured on a Likert scale from 0 (no difficulty) to 4 (unable to do task). The active and passive subscales are treated as separate constructs, with the passive function subscale scores ranging from 0 (high function) to 28, and the active function subscale scores ranging from 0 (high function) to 52 [161]. Both subscales are important for the achievement of clinically relevant goals [115].

Adequate psychometric properties for the Arm Activity Measure, including content validity, face validity [115], construct validity, reliability, responsiveness and feasibility have been demonstrated in patients with upper limb spasticity [161]. Preliminary findings suggest that a change of 2 to 3 on the passive function subscale represents a clinically important change, but further evaluation is required to quantify an clinically important change for the active function subscale, which was found to be less responsive for a group of patients tested [161].

The 10 metre walk test [164], where patients are asked to walk 10 metres independently at a comfortable speed using their usual shoes and gait aid, is timed with a stopwatch and used to calculate gait velocity. In patients one year post stroke, the 10 metre walk test has high within-assessment reliability but longer times for the first walk than for subsequent walks [164]. Participants who had lower limb injections therefore did a warm up walk first, then two timed walks that were averaged to determine gait velocity. Other studies investigating the effects of lower limb BoNT-A injections on gait have also used this outcome measure [30, 207, 208].

The Global Assessment Scale [126] assesses patient (and caregiver) perception of global improvement or worsening of symptoms or problems with the treatment. A score of −4 indicates very marked worsening, 0 indicates no change and 4 indicates very marked improvement. Treatment success is defined as a score of 1 or more.

Self-rated burden [209] for caregivers is a visual analogue scale with numerical ratings of caring for a patient that range from 0 (not hard at all) to 100
A higher score indicates higher subjective burden. Self-rated burden has been demonstrated to be a feasible and valid measure of subjective burden among informal caregivers of stroke patients [209].

World Health Organization Quality of Life (WHOQoL-BREF) [210] is a valid and reliable tool comprising 26 items that measure the following broad domains: physical health, psychological health, social relationships and environment. All items are rated on a five-point scale with higher scores indicating higher quality of life. The WHOQoL-BREF assesses the individual’s perceptions in the context of their culture, their value systems and their personal goals, standards and concerns. Although a previous study did not demonstrate change in quality of life following BONT-A injections for upper limb spasticity [26], there are limited other outcome measures relating to participation. Results for the WHOQoL-BREF are reported in Study 4 (Section 7.4.2).

3.7.2. What was the intervention? Evaluation of components of rehabilitation programs

The therapy documentation forms (Appendix 3) were used to collect quantitative data and descriptive analysis of the content of the rehabilitation programs provided in Study 2 (Chapter 5). Outcome measurement included:

- program and session data – median program duration (weeks); number and intensity of therapy sessions, in total and by discipline (occupational therapy and physiotherapy); therapy time (hours), in total and by discipline; mean session duration (minutes); and percentage of co-treatment and group sessions
- intervention content – percentage of total therapy time spent in each occupational and physical therapy rehabilitation activity and activity category, percentage of participants spending time in each activity and percentage of total sessions during which interventions were used to facilitate the three occupational and physical therapy activities that most time was spent in.
- therapists – discipline and level of expertise. Participant goals were categorised as described above and the percentage of total goals relating to each category, and upper or lower limb, was determined.
3.7.3. How well was the intervention implemented? Outcomes of process evaluation

The five dimensions of RE-AIM involved analysis of the following data:

1. Reach
   - The number of patients approached to participate in the program versus the number of patients who were eligible and the number of patients who agreed to participate.
   - Demographic information about participants including gender, age, educational level and living arrangements.

2. Effectiveness
   - Primary outcomes included the proportion of participants who achieved at least 50% of their total goals at 12 weeks, as measured by GAS process and change in GAS T-scores [46].
   - Secondary outcomes included measures of spasticity, upper and lower limb function, quality of life and caregiver burden (Section 3.7.1).
   - Participant and therapist experience and short- and long-term perceived benefits based on semi-structured questionnaires conducted one-on-one in person or over the phone (Appendix 4). Participants were asked to rate the degree to which the program addressed and contributed to goal achievement, translation of skills learnt in everyday life and overall satisfaction.

3. Adoption
   - The attitudes and beliefs of staff towards the intervention were explored using structured questionnaires (Appendix 4).
   - The percentage of participants who completed the rehabilitation program (attended at least 70% of planned therapy sessions).
   - Relevance and use of therapy documentation forms was evaluated by collecting data relating to therapist compliance with completing therapy documentation forms (number of forms completed verses number of therapy sessions attended) and the number of therapists who completed the forms as a proportion of those who provided...
therapy sessions to participants. Therapist experience in using the forms was explored using structured questionnaires (Appendix 4).

4. Implementation

- The time required for the intervention (mean number of sessions attended per week, program duration and mean duration of therapy sessions based on information collected using the therapy documentation forms) and the direct costs of the rehabilitation intervention.
- A qualitative evaluation of therapists’ experiences with program delivery to identify implementation information (Appendix 4). The extent to which therapists felt the therapy programs were implemented as planned and were relevant to participant goals, their satisfaction with delivery of the program and identification of barriers or enablers to program implementation were assessed using questionnaires.
- Detailed description of the contextual adaptations of the program.
- A qualitative evaluation of participants’ experiences with the rehabilitation program and use of strategies learnt in everyday life (Appendix 4).
- The types of treatments provided and the relationship between rehabilitation activities and treatment goals.

5. Maintenance

- Incorporation of the intervention program into routine practice and policy over time is beyond the scope of this thesis. Qualitative information obtained from the Community Therapy Service manager at the recruiting hospital via an open-ended interview explored the feasibility and sustainability of the rehabilitation program in the long-term.
- A qualitative evaluation of participants’ perceived long-term benefits.

The next chapter presents a systematic review that explores the current evidence base for multidisciplinary care following BoNT injections for post-stroke spasticity.
Chapter 4. Systematic review: Multidisciplinary rehabilitation following BoNT and other focal intramuscular treatment for post-stroke spasticity

This chapter presents the current evidence base for multidisciplinary care following BoNT injections and other focal intramuscular treatment for post-stroke spasticity, especially for outcomes related to activity limitation.

4.1. Background

4.1.1. Description of the condition

Following a stroke, spasticity typically develops over a few weeks due to abnormal patterns of supraspinal descending drive [64]. Spasticity is stiffness and abnormal posturing of the limb that results from a net imbalance of forces between agonist and antagonist muscles that affects static joint position and dynamic limb movement [80].

Spasticity is not always unwanted; in some instances, patients rely on spasticity to maintain function in an otherwise non-functional limb. Yet, spasticity should be treated when it interferes with activity or the ability to provide care to the stroke survivor, or when it causes pain or secondary complications. Spasticity often persists as a chronic neurological condition that requires long-term management and comprehensive multidisciplinary neurorehabilitation programs to address patient-centred problems.

4.1.2. Impact of spasticity and the WHO ICF

Spasticity-associated problems can be classified according to the WHO ICF [12] (Section 1.1.2). Understanding the impact of a disease on a person at different levels facilitates the planning of individualised, goal-directed and functionally orientated rehabilitation programs. Important patient-centred goals for the
treatment of post-stroke spasticity particularly relate to activity limitations affecting active function (the execution of a functional task by the individual) or passive function (provision of care to an affected limb).

### 4.1.3. Approaches to the management of spasticity

The two main approaches to the management of spasticity include pharmacological and physical interventions [211]. In clinical practice, these are often used in combination, but treatment tends to be piecemeal or not always provided as planned. One study reported that while the majority of people with spasticity received at least one concomitant treatment following BoNT injections, physiotherapy and occupational therapy were not given as planned in a significant proportion of patients [54].

Oral anti-spasmodic agents (e.g., baclofen) are commonly used for generalised spasticity, while BoNT injections or other focal intramuscular treatments such as phenol are increasingly used for focal or multi-focal post-stroke spasticity. BoNT injections are effective in reducing spasticity by causing temporary focal muscle weakness that lasts for three to four months [31]. Hence, BoNT injections can provide a window of opportunity to maximise the gains to be made during rehabilitation programs. BoNT injections can make it easier to stretch and lengthen muscles to prevent progression of contractures, and can allow strengthening of antagonist muscles, which may improve selective movement control. BoNT injections have been shown to reduce muscle tone and improve passive function, such as hand hygiene and caregiver burden [17, 25]. However, the effect of BoNT injections on active function remains unclear [59, 103].

Recent guidelines and consensus statements on spasticity management advocate a holistic multidisciplinary approach to increase the likelihood of treatment goals being achieved [18, 19, 21]. This includes physicians trained in spasticity management and integrated allied health services working together to enable appropriate evaluation, goal setting, outcome measurement, treatment and follow-up. Recommendations are based on expert opinion rather than research evidence.

Trials investigating non-pharmacological interventions for post-stroke spasticity have focused on single treatment modalities, such as casting [39], ankle
taping [212] or electrical stimulation [38, 124] following BoNT injections. Trials of BoNT effectiveness often allow concomitant routine therapy, which varies among centres and is rarely described in any detail [26]. There is no consensus on the optimal timing, type, duration and intensity of therapy. Similarly, the relationship between the types of rehabilitation therapies provided and patient outcomes is not known. While rehabilitation practices may be routine, they are often based on trial-and-error because they are difficult to characterise and standardise [55].

4.1.4. Description of the intervention

Following BoNT injections or other focal intramuscular treatment, multidisciplinary rehabilitation involves the provision of a coordinated program by a specialised team of health professionals from two or more disciplines (nursing, physiotherapy, occupational therapy, orthotists and others). Necessary elements of a multidisciplinary rehabilitation program, as discussed in Section 1.2.4, are [213]:

- an individualised patient-centred plan formulated by the patient and the rehabilitation team
- SMART goals that are developed and prioritised through a multidisciplinary process [44]
- patient participation to achieve the goals with improvement in the patient’s personal potential as a result
- outcomes demonstrating improvement in one or more domains of the ICF.

Unidisciplinary therapy (e.g., physiotherapy only) or single-treatment modalities (such as casting or functional electrical stimulation) used in isolation do not comply with the definition of multidisciplinary rehabilitation. Therefore, RCTs or other studies exploring single treatments were excluded.

4.1.5. How the intervention might work

Post-stroke spasticity can manifest in multiple ways with detrimental effects on function, quality of life and caregiver burden [16, 17]. Multidisciplinary rehabilitation uses a coordinated goal-directed treatment approach including allied
health and medical input. Multidisciplinary rehabilitation encompasses multiple therapeutic interventions aimed at improving patient experience at the level of impairment, activity or participation. Multidisciplinary rehabilitation also educates patients and caregivers in the ongoing self-management of spasticity. BoNT-A injections or other focal intramuscular treatments provide a window of opportunity to facilitate the gains to be made during rehabilitation and, in this context, they may be considered an adjunct to a multidisciplinary rehabilitation program rather than vice versa [18].

### 4.1.6. Why it is important to do this review

The effectiveness of multidisciplinary rehabilitation for neurological conditions such as multiple sclerosis [214], acquired brain injury [215] and stroke [216] has been proven. The effectiveness of multidisciplinary rehabilitation in managing post-stroke spasticity following BoNT injections or other focal intramuscular treatment has not been demonstrated. The general consensus is that following BoNT injections, optimal treatment of post-stroke spasticity requires a comprehensive multidisciplinary rehabilitation program [6, 21]. In practice, these programs are not always implemented and delivered as planned [43, 54].

Other reviews have focused on the effectiveness of BoNT injections [217] or individual physical interventions [35, 218] for spasticity management in stroke survivors. To date, no systematic review has evaluated the evidence for the effectiveness of multidisciplinary rehabilitation following BoNT injections or other focal intramuscular treatment for post-stroke spasticity. The optimal intensity, type and setting of rehabilitation programs and the effects on outcomes are unclear.

### 4.2. Objectives

This review aims to assess the effectiveness of multidisciplinary rehabilitation following BoNT injections or other focal intramuscular treatment in improving outcomes (symptoms and impairments, activity limitation, participation restriction, caregiver burden and quality of life) in adults and children with post-stroke spasticity. The specific questions asked by this review were:
• Does coordinated multidisciplinary rehabilitation achieve better outcomes than the absence of these services in persons with post-stroke spasticity?
• What type of rehabilitation programs are effective and in which setting?
• Does a greater intensity (time, expertise or both) of rehabilitation lead to better outcomes?

4.3. Methods: Criteria for considering studies for this review

4.3.1. Studies

The studies included in this review were (1) RCTs that compare the effectiveness of multidisciplinary rehabilitation programs following BoNT injections or other focal intramuscular treatment for upper or lower limb post-stroke spasticity, or both, with either routinely available local services or lower levels of intervention and (2) RCTs that compare multidisciplinary rehabilitation programs in different settings, of different types or at different intensities.

4.3.2. Participants

Included participants were children (aged less than 18 years) and adults (aged 18 years and over) with a confirmed diagnosis of stroke and upper or lower limb spasticity. A confirmed diagnosis of stroke fulfils the clinical criteria of the WHO ICF: ‘rapidly developed clinical signs of focal (or global) disturbances of cerebral function, lasting more than 24 hours or leading to death, with no other apparent cause than of vascular origin’ [66], with or without confirmation by computed tomography scan or magnetic resonance imaging. Stroke type may be ischaemic or haemorrhagic (subarachnoid, intraventricular or intracerebral haemorrhage).

Studies including participants with conditions other than stroke were not included unless stroke-specific data was provided separately or more than 75% of participants had a diagnosis of stroke. Where the proportion of the study population with stroke was less than 75%, study authors were contacted for data for stroke participants only.
4.3.3. Interventions

In this review, multidisciplinary rehabilitation was defined as any coordinated therapy program delivered by two or more disciplines (occupational therapy, physiotherapy, exercise physiology, orthotics, other allied health or nursing) in conjunction with medical input (neurologist or rehabilitation medicine physician) that aims to achieve patient-centred goals related to increasing activity and participation as defined by the ICF [12]. The term interdisciplinary was used in the initial submission to the Cochrane Stroke Group to describe the overlapping roles of the disciplines and the communication between team members. However, the Cochrane Stroke Group Editorial Review Board requested the use of the term multidisciplinary instead because the presence of processes distinguishing interdisciplinary care often cannot be determined when reviewing a study.

Rehabilitation programs may be delivered in:

- outpatient or day treatment settings located in private or public hospitals, community rehabilitation centres or specialist rehabilitation centres
- home-based settings in the patients’ own homes or local community
- inpatient rehabilitation settings where care is delivered 24 hours per day, including specialised medical rehabilitation units or hospital wards.

The actual content of multidisciplinary care may vary from patient to patient because rehabilitation programs are individualised. Any study that stated or implied that multidisciplinary care or rehabilitation was included, provided that it satisfied the definition above and included a control group for comparison.

Control groups were: no treatment, placebo or sham, or other interventions. Other interventions included lower levels or different types of intervention such as routinely available local services (e.g., medical care or physiotherapy only), minimal intervention (e.g., information only), waiting list conditions, interventions given in different settings and lower intensity (time) interventions.

RCTs that assessed the effectiveness of a unidisciplinary therapy (e.g., physiotherapy only) or a single intervention (e.g., stretching, casting, electrical stimulation or splinting only) were excluded. BoNT injections were administered using individualised or standardised protocols in intervention and control groups.
4.3.4. Outcome measures

Diverse outcomes were expected given the varied presentations of spasticity-related problems and goals of treatment related to stroke severity.

Primary outcomes

Primary outcomes reflected the level of activity limitation according to the ICF [12] and included:

- passive function (e.g., Leeds Arm Spasticity Impact Scale [219], Disability Assessment Scale [116] and Arm Activity Measure [115])
- active function of the upper limb (e.g., MAL [162] and ARAT [163])
- active function of the lower limb mobility measures including tests of walking speed, balance and gait pattern (e.g., 10 metre walk test [164]).

The measure of achievement of treatment goals (e.g., goal attainment scaling [46] or other measure of goal achievement) will be included. The assimilation of individualised goals for treatment is increasingly used as an overall measure of outcome for trials of multidisciplinary rehabilitation.

Secondary outcomes

Secondary outcomes were measures of:

- symptoms and impairments (e.g., pain measured by verbal scores or visual analogue scales, spasm frequency, joint range of movement, involuntary movements, and measures of spasticity or tone such as the MAS [110] or Tardieu scale [112])
- restriction in participation and impact on caregivers (e.g., quality of life measures such as the WHOQoL-BREF [210], caregiver strain and burden such as the Caregiver Strain Index [165]).

Adverse events that may have resulted from the intervention were considered. Serious adverse effects were defined as events that were life-threatening or required prolonged hospitalisation.
4.3.5. Timing of outcome measures

Outcome time points were divided into short-term (up to three months) and long-term (greater than three months).

4.4. Methods: Search methods for identification of studies

4.4.1. Electronic searches

The Cochrane Stroke Group Trials Register (last searched February 2012) and other electronic bibliographic databases were searched (Appendix 5). The MEDLINE search strategy was developed with the help of the Cochrane Stroke Group Trials Search Coordinator and was adapted for searching the other databases (Appendix 5).

4.4.2. Searching other resources

Searches included trials published in all languages. Attempts were made to identify other published, unpublished and ongoing trials by:

- searching ongoing trials registers (Appendix 5)
- searching the reference lists of all retrieved articles, texts and other reviews on the topic
- searching journals related to spasticity research and treatment not already searched on behalf of The Cochrane Collaboration, including the Archives of Physical Medicine and Rehabilitation (December 1995 to January 2012), using the search engine ScienceDirect, and the Journal of Rehabilitation Medicine (January 2001 to January 2012)
- using the PubMed related articles feature
- using the Science Citation Index Cited Reference Search for forward tracking important articles
- searching Open Grey (formerly System for Information on Grey Literature in Europe) at http://www.opengrey.eu/
- contacting authors, researchers and experts in the field.
4.5. Methods: Data collection and analysis

4.5.1. Selection of studies

Two authors (MD and SM) independently screened all titles and abstracts of publications identified from the searches of the electronic databases and excluded obviously irrelevant studies. The full texts of the remaining articles were obtained and assessed for inclusion and appropriateness based on the previously defined inclusion criteria for eligibility.

Once all potentially appropriate studies were obtained, two authors (MD and FK) independently evaluated each study for inclusion. Where there was no consensus about the possible inclusion or exclusion of a study, a final decision was made after discussion with a third author (LTS). Studies were not masked to the names of the authors, institutions or publication source at any level of this review.

4.5.2. Data extraction and management

Review authors (MD, LTS and CB) independently extracted data from each study that met the inclusion criteria. All studies that met the inclusion criteria were summarised using the Review Manager (version 5.1) software developed by the Cochrane Collaboration [220]. The summaries included the following information:

- publication details
- study design, study setting, inclusion and exclusion criteria, method of allocation and risk of bias
- patient population (e.g., age, sex, type of stroke and site of spasticity)
- details of interventions
- outcome measures
- withdrawals, length and method of follow-up, and number of participants followed up.

Where insufficient details were available, study authors were contacted and further information and clarification was obtained.
4.5.3. Assessment of risk of bias in included studies

Three authors (MD, LTS and CB) independently assessed the methodological quality of the included studies using the Cochrane Risk of Bias tool according to the Cochrane Handbook for Systematic Reviews of Interventions Section 8.5 [61]. The following domains were assessed: random sequence generation and allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessors (detection bias), attrition bias, reporting bias and other sources of bias. Each domain was scored as low risk of bias, high risk of bias or unclear risk of bias (Table 4.1).

Studies were considered to be of high methodological quality (high-quality studies) if the risk of bias for each domain item was low. Studies were rated to be of low methodological quality (low-quality studies) if there was an unclear or high risk of bias for one or more domains (Table 4.1). Any disagreements or lack of consensus were resolved with a fourth author (FK).

Table 4.1. Levels of quality of individual studies

<table>
<thead>
<tr>
<th>Judgement of risk of bias</th>
<th>Quality rating of study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk of bias of all domains low</td>
<td>High methodological quality = high-quality study</td>
</tr>
<tr>
<td>Unclear or high risk of bias for one or more domains</td>
<td>Low methodological quality = low-quality study</td>
</tr>
<tr>
<td>High risk of bias for most domains</td>
<td>Very low methodological quality = very low-quality study</td>
</tr>
</tbody>
</table>

4.5.4. Measures of treatment effect

It was not possible to pool data for quantitative meta-analysis due to the small number of included studies and the significant heterogeneity in the type and delivery of interventions, outcome measures, study designs (assessment time points and duration of follow-up) and participant characteristics. Therefore, a qualitative synthesis of best evidence was presented based on the GRADE levels of evidence (Table 4.2) taking into consideration the five factors that affect quality of evidence (Table 4.3) according to the Cochrane Handbook for Systematic
Reviews of Interventions Section 12.2 [61]. The GRADE approach specifies four levels of quality (Table 4.2) with the highest quality rating for RCT evidence. Evidence may be downgraded to moderate, low or very low quality depending on the presence of the five factors (Table 4.3).

Table 4.2. Levels of quality of a body of evidence in the GRADE approach

<table>
<thead>
<tr>
<th>Underlying methodology</th>
<th>Quality rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomised trials or double-upgraded observational studies</td>
<td>High</td>
</tr>
<tr>
<td>Downgraded randomised trials or upgraded observational studies</td>
<td>Moderate</td>
</tr>
<tr>
<td>Double-downgraded randomised trials or observational studies</td>
<td>Low</td>
</tr>
<tr>
<td>Triple-downgraded randomised trials, downgraded observational studies, case series or case reports</td>
<td>Very low</td>
</tr>
</tbody>
</table>

Table 4.3. Factors that may decrease the quality level of a body of evidence

1. Limitations in the design and implementation of available studies suggesting a high likelihood of bias
2. Indirectness of evidence (indirect population, intervention, control or outcomes)
3. Unexplained heterogeneity or inconsistency of results (including problems with subgroup analyses)
4. Imprecision of results (wide confidence intervals)
5. High probability of publication bias

4.5.5. Unit of analysis issues

The methodological quality of each included RCT was analysed using GRADE, as described in Chapter 12 of the Cochrane Handbook for Systematic Reviews of Interventions [61].

4.5.6. Dealing with missing data

Authors were contacted to obtain missing data.
4.5.7. Assessment of heterogeneity

Clinical heterogeneity was assessed by examining the characteristics of the studies and the similarity between the types of participants, the interventions and the outcomes, as specified in the criteria for included studies. Trial strengths and limitations were reported.

It was not possible to pool data to quantify statistical heterogeneity between studies using the $I^2$ statistic (where $I^2 > 50\%$ indicates substantial inconsistency) or conduct statistical analysis as described in the Cochrane Handbook for Systematic Reviews of Interventions [61].

4.5.8. Assessment of reporting biases

Publication bias was minimised by obtaining unpublished data where possible. Where data were not reported in full for certain outcomes, study authors were contacted to request the full data set or the reason for not publishing the data [168].

4.5.9. Data synthesis

Data synthesis was not possible.

4.5.10. Subgroup analysis and investigation of heterogeneity

Due to the small number of included studies it was not possible to perform subgroup analyses for:

- type of stroke and location
- site of spasticity (upper limb, lower limb or both)
- age (children, adults aged less than 65 years or adults aged 65 years or older)
- type of rehabilitation program (outpatient or home-based)
- intensity of treatment (high-intensity or low-intensity)
- time of treatment following stroke (acute – less than six weeks; subacute – six weeks to six months or chronic – more than six months).
Factors considered in assessing heterogeneity included the setting, type and intensity of multidisciplinary rehabilitation programs.

4.5.11. Sensitivity analysis

Due to the small number of included studies it was not possible to perform a sensitivity analysis to determine whether the overall results would be the same if studies outside different methodological cut-off points were analysed.

4.6. Results: Description of studies

4.6.1. Results of the search

Electronic and manual searches yielded a total of 877 titles and abstracts after removing duplicates. Of these, 33 were selected for closer scrutiny and resulted in three studies being included based on the review criteria. Figure 4.1 shows the study flow diagram.
Figure 4.1. Study flow diagram.
4.6.2. Included studies

The three included studies by Lai et al. [170], Sun et al. [117] and Weber et al. [168] investigated ambulatory rehabilitation programs following BoNT-A injections for upper limb spasticity in adults with chronic stroke. These were single centre RCTs that were underpowered because of their small sample sizes. The studies were conducted in the United States of America [168, 170] and Taiwan [117]. The characteristics of the three included studies are summarised in Table 4.4.

Table 4.4. Characteristics of included studies

<table>
<thead>
<tr>
<th>Lai et al. [170]</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Methods</td>
<td>Single-blind pilot RCT</td>
</tr>
<tr>
<td>Participants</td>
<td></td>
</tr>
<tr>
<td>• Included 36 adults (18 to 75 years) who were at least six months after stroke and had spasticity (MAS ≥ 2) involving elbow flexors and a range of movement deficit of more than 24% in elbow extension</td>
<td></td>
</tr>
<tr>
<td>• Thirty participants completed the study (six were excluded due to non-compliance)</td>
<td></td>
</tr>
<tr>
<td>• Intervention group: N = 15, mean age 49.1 (SD = 4) years and 53% female</td>
<td></td>
</tr>
<tr>
<td>• Control group: N = 15, mean age 55.6 (SD = 5) years and 33% female</td>
<td></td>
</tr>
<tr>
<td>Interventions</td>
<td></td>
</tr>
<tr>
<td>• All groups: BoNT-A (standard injections into biceps, brachialis and brachioradialis) and occupational manual therapy (two one-hour sessions weekly for 16 weeks) for moist heat, patient education, re-evaluation of symptoms, joint mobilisation, passive and active range of movement, proprio-neural facilitation, and therapeu tic exercise</td>
<td></td>
</tr>
<tr>
<td>• Intervention group: adjunctive dynamic elbow splinting with Elbow Extension Dynasplint® worn for six to eight hours during sleep and education in use of Elbow Extension Dynasplint® with change in tension prescribed twice a month</td>
<td></td>
</tr>
<tr>
<td>Outcomes</td>
<td></td>
</tr>
<tr>
<td>• Impairments: mean % change in active range of movement in elbow extension and MAS for elbow flexors</td>
<td></td>
</tr>
<tr>
<td>• Time points: before injection and 14 weeks after injection</td>
<td></td>
</tr>
<tr>
<td>Notes</td>
<td></td>
</tr>
<tr>
<td>• No outcomes of activity limitations (active or passive upper limb function) were used</td>
<td></td>
</tr>
<tr>
<td>• Physicians monitored adherence to wearing time of Elbow Extension Dynasplint® on a monthly basis</td>
<td></td>
</tr>
<tr>
<td>Risk of bias</td>
<td></td>
</tr>
<tr>
<td>Bias</td>
<td>Authors’ judgement</td>
</tr>
<tr>
<td>Bias</td>
<td>Risk</td>
</tr>
<tr>
<td>-----------------------------------------</td>
<td>-------</td>
</tr>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>High risk</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>High risk</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Low risk</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>High risk</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
</tr>
<tr>
<td>Other bias</td>
<td>High risk</td>
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</table>
### Sun et al. [117]

<table>
<thead>
<tr>
<th><strong>Methods</strong></th>
<th>• Single-blind RCT</th>
</tr>
</thead>
</table>
| **Participants** | • Included 32 adults (aged 18 to 80 years) at least one year after stroke with severe spasticity (MAS ≥ 3) in elbow, wrist or finger flexors; at least 10° active interphalangeal and metacarpal phalangeal extensions; and 20° active wrist extension (minimal motor criteria)  
• Twenty-nine participants completed the study (three dropouts)  
• Intervention group: N = 15, mean age 58.7 (SD = 9.9) years, 20% female, mean time since stroke 2.9 (SD = 1.5) years and 80% infarction  
• Control group: N = 14, mean age 61.5 (SD = 9.4) years, 21% female, mean time since stroke 2.9 (SD = 1.3) years and 78% infarction |
| **Interventions** | • All groups: BoNT-A (1,000 units Dysport®, standard injections into elbow, wrist and finger flexors) and physiotherapy and occupational therapy (two-hour sessions three times per week for three months) starting the day following injections  
• Intervention group: modified CIMT with the non-affected upper limb restrained for at least five hours per day. Therapy included massed practice, shaping (individualised task selection, graduated tasks difficulty and complexity, positive verbal feedback and physical assistance with movements), behavioural contract (activities to be done with restraint on and situations in which to remove it) and daily treatment diary. Participants were encouraged to use the affected upper limb during home activities.  
• Control group: neurodevelopmental therapy focusing on normalising tone and movement patterns, proximal upper limb control, restoration of stance, gait, dexterity and stamina training exercises with 40% of therapy time focused on upper limb exercises |
| **Outcomes** | • Primary outcome: MAS  
• Secondary outcomes: MAL amount of use and quality of movement (questionnaire for patient self-report) and ARAT  
• Other: patient’s global satisfaction with treatment (seven-point categorical scale from completely satisfied to completely dissatisfied) and adverse events  
• Time points: before injection, one, three and six months after injection  
• Exceptions: MAL not assessed at one month; patient satisfaction recorded at three and six months, and baseline ARAT performed twice, four weeks apart, with a mean score used |
Notes
- Baseline data were comparable
- Therapy adherence rates, assessed with daily exercise diaries, were high (93% and 87% for intervention and control groups, respectively)

<table>
<thead>
<tr>
<th>Risk of bias</th>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>• Central web-based randomisation; block randomisation in groups of four</td>
<td></td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>• Sealed opaque envelopes</td>
<td></td>
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</tbody>
</table>
| Blinding of participants and personnel (performance bias) | High risk | • Unblinded participants and therapists  
  • Therapy sessions conducted at different times to avoid contact between participants  
  • Unclear whether the injecting physician was blinded |
| Blinding of outcome assessment (detection bias) | Low risk | • Blinded outcome assessor  
  • MAL and patient global satisfaction were associated with a high risk of bias because participants were unblended |
| Incomplete outcome data (attrition bias) | High risk | • Low attrition rate 9.4% (3/32). Reasons for dropouts were provided (one in the intervention group relocated and two in the control group due to lack of transportation and a traffic accident).  
  • No intention to treat analysis or comparison of baseline characteristics between withdrawals and completers |
| Selective reporting (reporting bias) | Low risk | • All outcomes were reported |
| Other bias | High risk | • Single centre  
  • Small sample size and underpowered (16 participants were required in each group to achieve 90% power to detect differences between the groups of MAS ≥ 1 with SD ≤ 0.9 and accounting for 5% to 10% dropouts) |
**Methods**

- Single-blind pilot RCT

**Participants**

- Included 23 adults with unilateral spastic hemiparesis (MAS ≥ 2 for wrist or finger flexors) due to stroke or traumatic brain injury for at least six months and moderate or severe hand impairment (based on Chedoke–McMaster assessment ≥ 2 with ability to do at least one of the following stage-three tasks: active wrist extension greater than half range; active finger or wrist flexion greater than half range; or actively touch thumb to index finger when the hand was placed in supination with thumb fully extended).
- Exclusion criteria: no voluntary motion or severe fixed joint contracture of the affected arm.
- Eighteen participants completed the study.
- Intervention group: N = 8, mean age 54.0 (SD = 10.3) years, 70% female, 9.7 (SD = 8.6) years following cerebral event and 100% cortical insult.
- Control group: N = 10, mean age 41.2 (SD = 14.2) years, 62% female, 4.3 (SD = 2.5) years following cerebral event and 92% cortical insult.
- Traumatic brain injury participants comprised 39% of the control group and there were none in the intervention group.

**Interventions**

- All groups: BoNT-A (using individualised injections). Task practice therapy: six one-hour visits with the occupational therapist; one-hour home-based daily task practice (including four to five individualised functional tasks) for 12 weeks using a standardised protocol without restraining the unimpaired arm.
- Intervention group: H200 functional electrical stimulation device (Bioness®) with forearm-wrist-hand orthosis, worn during daily task practice activities to activate flexor and extensor muscles producing grasp and release at an individualised intensity. Additional one hour of occupational therapy to fit and train in use of H200 device. Subsequent visits to check functioning and use of functional electrical stimulation device and make adjustments.

**Outcomes**

- Primary outcome: How Well Scale of MAL-Observation for observational assessment of upper limb function during activities of daily living. Investigators standardised administration and scoring of each MAL item through observation and trained the blinded assessor to inter-rater reliability (intra-class correlation coefficient 0.97) with the occupational therapist researcher.
- Secondary outcomes: ARAT, MAL-Self-report.
- Time points: baseline (two weeks prior) and six and 12 weeks after injection.
Notes

- All traumatic brain injury participants were randomised to the control group (N = 5/13).
- The control group were significantly younger (p = 0.03), which may be related to the traumatic brain injury participants.
- Adherence to the task practice program, assessed through home diary records and an electronic log in the intervention group, was high in both groups.

### Risk of bias

<table>
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<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
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<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>• Random sequence of numbers; block randomisation in groups of four</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>High risk</td>
<td>• Author’s response: a master list of participants’ group assignment was kept by the treating therapist and used to determine whether or not to use the Bioness device’</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>High risk</td>
<td>• Unblinded participants and therapists; blinded injecting physician</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Low risk</td>
<td>• Blinded outcome assessor for primary outcome (MAL-Observation) and ARAT</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• MAL-Self-report associated with high risk of bias as participants unblinded</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>• High attrition rate (N= 5, 21.7%). Reasons for dropouts were provided (three in the control group and two in the intervention group discontinued the intervention or were lost to follow-up).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Intention to treat analysis (N = 23)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• No significant baseline differences between dropouts and completers</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Unclear risk</td>
<td>• MAS reported at baseline but not at follow-up. All other outcomes reported</td>
</tr>
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</table>
Other bias  High risk  

- Single-centre study
- Convenience sample
- Small sample size and underpowered
- Groups unmatched: all traumatic brain injury participants were randomised to the control group (N = 5/13) that was significantly younger (p = 0.03). Age was controlled for in analyses.
- No subgroup analysis for traumatic brain injury versus stroke participants in control group
- Authors’ conclusions related to results for entire cohort because there were no significant outcome differences between control and intervention groups

| ARAT, Action Research Arm Test; BoNT-A, botulinum toxin type A; CIMT, constraint-induced movement therapy; MAL, Motor Activity Log; MAS, Modified Ashworth Scale; RCT, randomised controlled trial; SD, standard deviation. |

**Participants**

A total of 91 adults were recruited, with 82 included in the analyses. Weber et al. [168] included participants with stroke as well as participants with traumatic brain injury, with almost 40% of the control group having traumatic brain injury (22% of the study population). This study was included because the intervention group consisted only of stroke patients. The five traumatic brain injury patients in the control group were matched to the intervention group for cognitive deficits and other neurological impairments.

Inclusion criteria for the studies (Table 4.4) were chronic stroke (greater than six months [117, 170] or one year [168] following event) and moderate or severe upper limb spasticity at specified joints (MAS ≥ 2 [168, 170] or MAS ≥ 3 [117]). Two studies included participants with voluntary upper limb motor activity [117, 168], using different criteria for inclusion. Sun et al. [117] based study inclusion on minimal motor criteria (10° active extension at metacarpophalyngeal and interphalyngeal joints and 20° extension at the wrist). Weber et al. [168] used the Chedoke–McMaster assessment of hand impairment [221] and the ability to do at least one of three upper limb tasks. Lai et al. [170] included participants with
a range of movement deficit greater than 24% in elbow extension, with no criteria reflecting whether the participants had functional or non-functional upper limbs.

**Rehabilitation interventions**

All of the included trials compared outpatient multidisciplinary rehabilitation programs in an intervention group with an active control situation (Section 4.3.3). The types of rehabilitation programs were diverse and were based on different therapy approaches and combinations of physical modalities. Lai et al. [170] included 36 participants (30 of whom completed the program) who had occupational, manual therapy combined with dynamic elbow splinting (Elbow Extension Dynasplint®) or occupational therapy alone. Sun et al. [117] included 32 participants (29 of whom completed the program) to compare modified CIMT (high intensity training of the affected upper limb while restraining the non-affected upper limb) with neurodevelopmental therapy. Weber et al. [168] included 23 participants (18 of whom completed the program) and compared task practice therapy, incorporating occupational therapy sessions and a home exercise program, with cyclic functional electrical stimulation to facilitate grasp and release, versus task practice therapy only.

Therapy protocols, for the intervention and control groups, differed in all three studies. Variables included: program duration, amount and frequency of therapist contact, time spent doing the program or other activity at home, and intensity (defined as total additional time spent doing the rehabilitation program, home exercises or other intervention [169]). Two studies investigated high-intensity versus lower intensity programs, with intervention groups receiving an additional 670 hours [170] and 490 hours [117] compared with controls.

All participants in Lai et al.’s study [170] received two hours of occupational therapy weekly for 16 weeks. The intervention group additionally had education in using the Elbow Extension Dynasplint® (worn six to eight hours daily during sleep) and fortnightly visits to adjust the device. In the study by Sun et al. [117], all participants had one hour of occupational therapy and one hour of physiotherapy thrice weekly for three months. The modified CIMT group had a higher intensity of upper limb training while the non-affected limb was restrained for at least five hours per day. In Weber et al.’s study [168], the control group
received six one-hour sessions and the intervention group received seven one-hour sessions of occupational therapy over 12 weeks. All participants were required to do a one-hour daily task practice home exercise program, during which the intervention group also wore the cyclic functional electrical stimulation device. The frequency of therapy sessions was high (more than two sessions per week) in the study by Sun et al. [117] and lower (less than or equal to two sessions per week) in the studies by Lai et al. [170] and Weber et al. [168].

Although the three studies all provided brief descriptions of the therapy programs, there was little detail or systematic analysis (conceptualising, measuring or counting) of interventions [55], such as quantification of time spent on specific therapeutic modalities [117, 170]. While the home exercise program (task-specific practice) was clearly described by Weber et al. [168], the interventions and treatments administered during occupational therapy sessions were not mentioned (see Table 4.4 for a description of the interventions).

Standardised protocols for upper limb BoNT-A injections (muscles and doses of BoNT-A injected) were used in two studies [117, 170], and one study used individualised protocols [168]. Two studies used electromyography for needle localisation [117, 168].

**Outcome measures**

A measure of activity limitation, the primary outcome for this review, was used in two studies (i.e., active upper limb function measured by the MAL and ARAT [117, 168]). Although both studies used the MAL, versions and administration varied. The MAL quality of upper limb use during activities of daily living was assessed observationally rather than being self-reported in the study by Weber et al. [168]. While the MAL was the primary outcome measure in the study by Weber et al. [168], an impairment measure (MAS) was the primary outcome in the study by Sun et al. [117]. Lai et al. [170] used impairment based outcome measures only (i.e., mean per cent change in active range of movement and MAS score at the elbow). Sun et al. [117] was the only study to assess patient satisfaction. None of the studies considered the impact on caregivers, and none used a measure of passive function or goal achievement such as the GAS (which has been shown to be a more sensitive outcome measure in this context) [33].
Different outcome time points were used across the studies: Lai et al. [170] 14 weeks; Sun et al. [117] one, three and six months; and Weber et al. [168] six and 12 weeks.

None of the included studies determined the minimal clinically important difference for the primary outcome measure. Power calculations were only provided by Sun et al. [117]. Lai et al. [170] stated that ‘the population of patients who completed this study (N = 30) was not adequate to power statistical analysis of variance.’ Sun et al. [117] required 16 participants in each group to adequately power the study, but only had 14 and 15 participants in the control and intervention groups respectively. Weber et al. [168] stated that ‘the group sizes in the present study were small (N = 13 in the control group and N = 10 and functional electrical stimulation group) … A larger sample size may have been more effective in detecting group differences between the two treatments.’

### 4.6.3. Excluded and ongoing studies

Thirty studies were excluded for the following reasons (Appendix 7):

- the intervention being compared was not consistent with the definition of multidisciplinary rehabilitation (Section 4.3.3) but rather was unidisciplinary or only a single modality treatment (N = 18)
- the comparison was BoNT-A versus placebo with both groups receiving the same rehabilitation programs (N = 12).

Two potentially relevant ongoing trials were identified [222, 223]. Table 4.5 shows the characteristics of the ongoing studies.
Table 4.5. Characteristics of ongoing studies

**Graham [222]**

<table>
<thead>
<tr>
<th>Study name</th>
<th>• Efficacy and safety study of botulinum neurotoxin A with rehabilitation versus botulinum neurotoxin A alone in treatment of post-stroke spasticity</th>
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</thead>
<tbody>
<tr>
<td>Methods</td>
<td>• RCT</td>
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</tbody>
</table>
| Participants | • Adults 18 years and above  
• Stroke (ischemic or haemorrhagic) at least six months prior  
• Upper limb focal spasticity at elbow, wrist, fingers and thumb; MAS ≥ 3 at wrist or fingers  
• Functional impairment secondary to spasticity (e.g., difficulty with hygiene, dressing, posture or pain) |
| Interventions | • BoNT-A with rehabilitation therapy for the duration of the study (up to two injections of BoNT-A) versus BoNT-A only |
| Outcomes | • Primary outcome measure: Fugl–Meyer upper extremity score  
• Secondary outcome measures: length of time to meet re-injection criteria; number of participants that do not meet re-injection criteria prior to completion of the study |
| Starting date | • January 2009                                                                                                                                 |
| Contact information | • Principal Investigator: Glenn D. Graham, New Mexico VA Health Care System Albuquerque, New Mexico, United States, 87108 |
| Notes | • Status: recruiting                                                                                                                                                                                   |

**Lannin [223]**

| Study name | • The effectiveness of best practice therapy after botulinum toxin A injections for adults diagnosed with neurological impairment and onset of spasticity |
| Methods    | • RCT                                                                                                                                                                                                |
| Participants | • Adults 18 years and above  
• Neurological injury (including stroke and brain injury) at least one month prior  
• Spasticity in at least one limb |
| Interventions | • Group A: Best practice therapy provided by an occupational or physical therapist including evidence-based protocols for casting, electrical stimulation, task-specific movement training and home practice. Total of 14 one-hour sessions of best-practice therapy provided over eight weeks (two weeks of casting for one session per week), followed by two weeks of thrice weekly therapy then two weeks of twice weekly therapy and finishing with two weeks of once weekly therapy)  
• Group B: Best practice therapy plus BoNT-A  
• Group C: BoNT-A only (i.e., without best practise therapy) |
|---|---|
| Outcomes | • Primary outcome measure: Goal Attainment Scaling T-score change score  
• Secondary outcome measures: Box and Block Test change score (hand dexterity); six-metre walk test change score and Tardieu Scale |
| Starting date | • September 2010 |
| Contact information | • Natasha Lannin, Alfred Health Clinical School Level 4 The Alfred Centre, 99 Commercial Road, Prahran Victoria 3181. Email: n.lannin@latrobe.edu.au. |
| Notes | • Status: recruitment completed |

4.6.4. Risk of bias in included studies

See Table 4.4 for risk of bias assessment. Figure 4.2 shows a risk of bias summary of author judgements about each risk of bias item for each included study. Figure 4.3 shows the risk of bias graph of review authors’ judgements about each risk of bias item presented as percentages across all included studies. All three studies had a high risk of bias and were graded as low quality based on the criteria in Table 4.1.
Figure 4.2. Risk of bias summary: review authors’ judgements about each risk of bias item for each included study.
Figure 4.3. Risk of bias graph: review authors’ judgements about each risk of bias item presented as percentages across all included studies.

**Allocation (selection bias)**

Because random sequence generation and allocation concealment were often not described, clarification was sought from study authors. Randomisation methods were adequate in all studies [117, 168, 170]. Allocation concealment was not possible in the studies by Weber et al. [168] and Lai et al. [170] because the treating therapist and physician had knowledge of upcoming assignment.

**Blinding (performance bias and detection bias)**

In all three included studies there was a high risk of performance bias (because both participants and therapists were unblinded) and a low risk of detection bias (because outcome assessors were blinded). Outcome assessors were not questioned to assess whether blinding was maintained throughout the follow-up period. In the study by Sun et al. [117], therapy sessions were conducted at different times in attempt to reduce the risk of performance bias. The injecting physician was blinded only in the study by Weber et al. [168].

**Incomplete outcome data (attrition bias)**

Attrition rates were moderate to high: 17% in Lai et al. [170] and 22% in Weber et al. [168], but only 9% in Sun et al. [117]. Reasons for dropouts were decline in health status (N = 2), personal factors (N = 2), non-attendance at follow-up (N = ...
1) [168], inability to attend therapy sessions due to practical reasons (N = 2) and car accident (N = 1) [117]. Six participants were excluded by Lai et al. [170] due to non-compliance with scheduled therapy sessions (which was not defined) and the time points of participant withdrawal were unclear. None of the included studies had fatal flaws (withdrawals of more than 40% of patients, total or nearly total non-adherence to the protocol, or very poor or non-adjusted comparability in the baseline criteria).

Only Weber et al. [168] performed intention to treat analysis and compared baseline differences between those who completed and dropped out of the study, with no significant differences reported. It is unknown whether dropouts or exclusions would have significantly affected the outcomes in Lai et al. [170] and Sun et al. [117].

Selective reporting (reporting bias)

Study outcomes were reported, except for the MAS at follow-up in the study by Weber et al. [168]. On enquiry, the authors stated that ‘the journal requested that the MAS not be reported’ but they did not provide data for this measure.

Other potential sources of bias

All studies were single centre with small sample sizes and were reported to be underpowered. The sample size calculation was only described in Sun et al. [117], with 16 participants required in each group to achieve 90% power to detect differences between the groups of at least one on the MAS with SD ≤ 0.9 and accounting for 5% to 10% dropouts. The authors’ conclusions must be considered in light of the studies being underpowered and other high risks of bias.

Lai et al. [170] did not report baseline data for time since stroke and other stroke characteristics (such as type and location). In the study by Weber et al. [168], the baseline data between the groups were not entirely comparable. The control group was significantly younger (p = 0.03) and 39% of the control group had a diagnosis of traumatic brain injury (versus no participants with a diagnosis of traumatic brain injury in the intervention group) because stratified randomisation by aetiology was not performed. Subgroup analysis for traumatic
brain injury versus stroke in the control group was not provided. Authors rationalised that the differences would not influence findings because there were similar baseline variables, cognitive function and program adherence for the traumatic brain injury and stroke participants, and age was controlled for in the analysis.

Weber et al. [168] reported no significant differences between the two groups for any outcome variable at any time point. Hence, the authors presented collapsed data for the entire cohort to show the benefit of task practice training for improved upper limb function. However, the confounder in this instance is the unknown influence of BoNT-A injections versus task practice therapy on outcomes because there was no BoNT-A injections only comparison group.

The study by Sun et al. [117] had a long follow-up period of six months (three months after completing the rehabilitation program). The other studies had shorter follow-up periods of 12 weeks (at the time of completion of the rehabilitation program) in Weber et al. [168] and 14 weeks (two weeks prior to completion of the therapy program) in Lai et al. [170] longer term effects could not be ascertained in these studies.

The results in the study by Lai et al. [170] had large standard deviations indicating that the data included a wide range of values (Section 4.7).

### 4.7. Results: Effects of interventions

See Table 4.6 for a description of the results of the included studies. A meta-analysis was not possible due to the clinical, methodological and statistical heterogeneity of the included studies.
### Lai et al. [170]

<table>
<thead>
<tr>
<th>Participants</th>
<th>• N = 36 (N = 30 in analysis)</th>
</tr>
</thead>
</table>
| Summary of Results | • Greater improvement in active range of movement elbow extension at 14 weeks in the intervention group compared with the control group. Median MAS scores for elbow flexors showed similar changes of 9.3% and 8.6% in the intervention and control groups, respectively.  
• Statistical analysis: trends and mean changes in outcomes were assessed using Microsoft Excel. |
| Results in favour of the intervention | • Active range of movement mean % change was 33.5 (SD = 29.6) in the intervention group versus 18.7 (SD = 48.7) in the control group |
| Authors’ conclusions | • This study confirmed the efficacy of BoNT-A injections in tone management and occupational therapy in contracture reduction. The study also showed the value of dynamic splinting in maintaining gains in range of motion. |

### Sun et al. [117]

<table>
<thead>
<tr>
<th>Participants</th>
<th>• N = 32 (N = 29 in analysis)</th>
</tr>
</thead>
</table>
| Summary of Results | • The median MAS score improved in both groups at four weeks and three months post injection, with no between-group differences. The median MAS score change was −2 in all cases, except at the elbow in the control group at three months where the median MAS score change was −1.5. At six months, there was a significant reduction in median MAS score at the elbow (p = 0.004), wrist (p = 0.003) and fingers (p < 0.001) in the intervention group (median MAS score change of −1). The benefit persisted only in the wrist flexors in the control group (p = 0.014).  
• The intervention group had statistically significant improvements compared with control group at: six months on the MAS at the elbow (p = 0.019), wrist (p = 0.019) and fingers (p < 0.001); on the ARAT at three months (p = 0.012) and six months (p < 0.001); and the MAL amount of use at three months (p < 0.001) and six months (p < 0.001), quality of movement at three months (p = 0.007) and six months (p < 0.001). Both groups improved on the ARAT at four weeks, with no between-group differences. Patient satisfaction was high in the intervention group at three and six months and declined in both groups at six months. |
• Statistical analysis: Mann–Whitney U tests, chi² tests or Fisher exact tests for baseline comparisons, Wilcoxon signed rank tests for within-group change from baseline, Mann–Whitney U test for between-group comparisons and p < 0.05 were statistically significant.

Results in favour of the intervention

- MAS at six months: greater reduction in MAS score for elbow (0.7 (95% CI = 0.1 to 1.3), p = 0.19), wrist (0.7 (95% CI = 0.2 to 1.2), p = 0.19) and fingers (1.2 (95% CI = 0.9 to 1.5), p < 0.001), median MAS score change = −1
- MAL amount of use at three months (1.1 (SD = 0.5) versus 0.1 (SD = 0.2), p < 0.001) and six months (1.2 (SD = 0.5) versus 0.1 (SD = 0.2), p < 0.001) and quality of movement at three months (0.9 (SD = 0.6) versus 0.3 (SD = 0.2), p < 0.007) and six months (1.0 (SD = 0.5) versus 0.1 (SD = 0.1), p < 0.001)
- ARAT at three months (7.3 (SD = 5.0) versus 3.1 (SD = 2.6), p = 0.012) and six months (7.9 (SD = 5.2) versus 1.2 (SD = 1.7), p < 0.001)
- Patient satisfaction at three months (93.3% versus 78.6%) and six months (86.7% versus 64.3%)

Authors’ conclusions

- Combined BoNT-A injections and modified CIMT produced significantly greater improvements in spasticity and upper extremity motor function than BoNT-A injections and conventional rehabilitation in chronic stroke patients with upper extremity spasticity, with benefits lasting up to six months. The combined therapy resulted in high patient satisfaction with no serious adverse events.

Weber et al. [168]

Participants

- N = 23 (all included in analysis)

Summary of Results

- No significant differences between intervention and control groups for any outcome variable over time. Positive but not statistically significant trends toward improvement for MAL-Observation, MAL-Self-report and ARAT for both groups from baseline to week six, and MAL-Self-report for intervention group from six to 12 weeks. The control group had a not statistically significant trend toward deterioration in MAL-Self-report from six to 12 weeks.
- The entire cohort had significant improvements in MAL-Observation (0.41 (95% CI = 0.24 to 0.58)), MAL-Self-report (0.64 (95% CI = 0.32 to 0.95))
ARAT (6.39 (95% CI = 3.38 to 9.4)) from baseline to week six. Improvements in MAL-Self-report (0.65 (95% CI = 0.33 to 0.97)) and ARAT (6.17 (95% CI = 2.31 to 10.03)) were sustained to week 12.

### Results in favour of the intervention
- Nil

### Authors’ conclusions
- BoNT-A injections and task practice therapy combined are effective in improving upper limb motor function and reducing spasticity in patients with chronic spastic hemiparesis. However, the cyclic functional electrical stimulation protocol used in this study did not increase the gains achieved.

ARAT, Action Research Arm Test; BoNT-A, botulinum toxin type A; MAL, Motor Activity Log; MAS, Modified Ashworth Scale; CIMT, constraint-induced movement therapy; SD, standard deviation; CI, confidence interval.

### Baseline data and demographics

In the three studies, the mean age of participants ranged from 49.1 years [170] to 58.7 years [117] in intervention groups and 41.2 years [168] to 61.5 years [117] in control groups. The lower mean age of the control group in the study by Weber et al. [168] may be due to inclusion of traumatic brain injury participants. Study populations had chronic stroke, with the mean duration following cerebral event being 2.9 years in both groups in the study by Sun et al. [117], and 4.3 and 9.7 years in the control and intervention groups, respectively, in the study by Weber et al. [168] but the time since cerebral event was not reported by Lai et al. [170]. Reporting of stroke characteristics varied in the studies by Sun et al. [117] and Weber et al. [168]). Stroke characteristics were unreported in Lai et al. [170].

Baseline mean (SD) ARAT scores for the intervention groups were 32.1 (12.7) and 19.5 (13.9) and for the control groups were 29.0 (14.1) and 25.8 (15.5) in the studies by Sun et al. [117] and Weber et al. [168], respectively.

### Interventions effects

Lai et al. [170] reported that occupational therapy in conjunction with dynamic elbow splinting (Elbow Extension Dynasplint®) resulted in a greater improvement in active range of movement elbow extension at 14 weeks for the...
intervention group (33.5% (SD = 29.6%) compared with the control group who had occupational therapy only (18.7% (SD = 48.7%)). The MAS (elbow flexors) score changes were similar in both groups. There were no measures of activity level (active or passive upper limb function), goal attainment, or patient or caregiver perspective. The authors concluded that BoNT-A injections are effective in facilitating tone management and occupational therapy in contracture reduction and that there is ‘value of dynamic splinting in maintaining gains in range of motion’ [170].

BoNT-A injection followed by modified CIMT was shown to improve spasticity and upper limb motor function in chronic stroke patients with residual voluntary upper limb motor activity. This improvement was more than that seen for BoNT-A injections followed by neurodevelopmental therapy program, and the benefits were maintained for up to six months [117]. Both groups had significant improvements in the MAS at four weeks and three months with no between-group differences. The modified CIMT group showed significantly greater improvements in elbow, wrist and finger spasticity than the control group (p = 0.019, p = 0.019 and p < 0.001, respectively) at six months. Compared with the control group, the modified CIMT group had greater improvements on the: MAL (amount of use and quality of movement) at three months (1.1 (SD = 0.5) versus 0.1 (SD = 0.2), p < 0.001 and 0.9 (SD = 0.6) versus 0.3 (SD = 0.2), p < 0.007) and six months (1.2 (SD = 0.5) versus 0.1 (SD = 0.2), p < 0.001 and 1.0 (SD = 0.5) versus 0.1 (SD = 0.1), p<0.001), and the ARAT at three months (7.3 (SD = 5.0) versus 3.1 (SD = 2.6), p = 0.012) and six months (7.9 (SD = 5.2) versus 1.2 (SD = 1.7) p < 0.001). Patient satisfaction was high following treatment with BoNT-A injections and modified CIMT up to three months (93.3% versus 78.6% in the control group), but was not sustained beyond this (86.7% versus 64.3% in the control group at six months).

Following BoNT-A injections, cyclic functional electrical stimulation in addition to task practice therapy did not improve upper limb motor function and spasticity up to 12 weeks more than task practice therapy alone [168]. When examining outcomes for the entire cohort, there were significant improvements in upper limb activity from baseline to week six for MAL-Observation (0.41 (95% CI = 0.24 to 0.58)), MAL-Self-report (0.64 (95% CI = 0.32 to 0.95)) and ARAT (6.39 (95% CI = 3.38 to 9.4)). There were also significant improvements in upper
limb activity to week 12 for MAL-Self-report (0.65 (95% CI = 0.33 to 0.97)) and ARAT (6.17 (95% CI = 2.31 to 10.03)). No significant adverse events were reported in any of the studies.

**GRADE methodology for best evidence synthesis**

All three studies were of low methodological quality (high risk of bias). Therefore, using GRADE methodology for best evidence synthesis (Table 4.2), there is:

- low-quality evidence that high-intensity training of the affected limb with modified CIMT, compared with a lower intensity neurodevelopmental therapy program, improves spasticity or tone (MAS) and active upper limb function (ARAT and MAL) and achieved high satisfaction in persons with residual motor function, with benefits maintained up to six months [117]

- very low-quality evidence that a high-intensity program of occupational therapy with additional dynamic elbow splinting (Elbow Extension Dynasplint®) assists in maintaining active range of movement at the elbow in the short-term, compared with occupational therapy only [170]

- no evidence that task practice therapy with cyclic functional electrical stimulation is superior to task practice therapy only in improving spasticity or tone (MAS) and upper limb motor function (MAL-Observation, ARAT and MAL-Self-report) in persons with residual motor function, at 12 weeks [168].

**4.8. Discussion**

**4.8.1. Summary of main results**

This review has evaluated the effectiveness of multidisciplinary rehabilitation following BoNT injections or other focal intramuscular treatment in improving activity level (primary outcome) and other outcomes (symptoms, impairments, participation restriction, caregiver burden and quality of life) in adults and children with post-stroke spasticity.
For chronic stroke survivors treated with BoNT-A injections for upper limb spasticity, there is low-quality evidence that modified CIMT improves upper limb function in the long term [117]. There is very low-quality evidence that occupational therapy with additional dynamic elbow splinting improves elbow tone and contractures [170]. There is no evidence that task practice therapy with cyclic functional electrical stimulation provides additional short-term benefit compared with task practice therapy alone [168]. The quality of the evidence is reduced by the methodological weakness of the included studies, which were underpowered and had a high risk of bias.

There was no available evidence for the benefits of multidisciplinary rehabilitation programs compared with the absence of such services in different settings (inpatient), for lower limb spasticity, in children with stroke or after focal intramuscular treatments for spasticity other than BoNT-A injections. Although results for intensity of therapy were presented wherever possible, it was difficult to categorise the studies based on this criterion alone. Subgroup analysis for type of stroke, location of stroke and acute versus chronic stroke was not possible. There was no evidence for the benefit of multidisciplinary rehabilitation interventions following BoNT-A injections for post-stroke spasticity on passive function, community participation, goal achievement, caregiver burden and quality of life.

4.8.2. Overall completeness and applicability of evidence

Despite some evidence for multidisciplinary rehabilitation interventions for upper limb spasticity in adults with chronic stroke, many aspects of multidisciplinary care for post-stroke spasticity remain to be investigated.

Gaps in the literature

It was not possible to identify evidence for multidisciplinary interventions for lower limb spasticity in this review because the available studies included single treatment modalities only (taping, casting or electrical stimulation [37, 38, 124]). Evidence for unidisciplinary interventions is presented elsewhere [218]. There were no identified studies that included multidisciplinary intervention in children or in those with an acute stroke.
The emerging evidence for the effectiveness of BoNT-A injections in stroke is in improving passive function and achieving individual goals [33]. However, none of the included studies addressed these outcomes. Two of the studies addressed active function in the subset of patients with residual upper limb function for which this is a realistic goal [117, 168].

The optimal intensity, duration and frequency of therapy that should be provided is unclear. Although high-intensity modified CIMT was considered to be superior to a lower intensity neurodevelopmental therapy program for those with voluntary upper limb activity [117], similar benefits could be achieved with less therapist contact time if patients are motivated. While other studies have shown benefits of CIMT in stroke survivors without significant spasticity, programs varied in terms of duration and frequency of therapy [169]. Further studies are needed to determine optimal protocols for CIMT in stroke survivors with spasticity.

**Clinical and research implications**

Applying the evidence in clinical practice is challenging. Firstly, evidence for ideal patient selection criteria for spasticity management is not available. Stroke survivors with upper limb spasticity have varied clinical presentations, whereas the study populations were restricted by strict inclusion criteria (e.g., degree of residual upper limb motor activity and chronicity of stroke). This may limit the relevance of the evidence to an individual patient and may mean that the evidence cannot be generalised to the heterogeneous stroke population. Furthermore, it is difficult to replicate study therapy protocols in real life due to the variability of available resources, need for specialised equipment (i.e., elbow extension Dynasplint® device), therapist time and expertise, consistency of therapy programs (intensity, duration, modalities) and other confounders (e.g., therapist–patient interaction).

Performing high-quality RCTs when investigating complex interventions such as multidisciplinary spasticity management is challenging in the real world. While high-quality RCTs are needed, other study designs such as clinical practice improvement methodology may assist in building on the current evidence. Data collected in the routine clinical setting can be used to identify the relative
contributions of specific interventions and therapies (the black box) to rehabilitation outcomes, while accounting for patient and environmental factors [55, 63]. This may assist clinicians in translating and generalising study findings to clinical practice. A better understanding of the processes of care in rehabilitation for spasticity management may then improve practice of care and ultimately patient outcomes.

Despite the gaps in the literature, development of integrated multidisciplinary rehabilitation teams – to provide a long-term comprehensive continuum of care to stroke survivors affected by spasticity – is clinically important for improving outcomes. This may be facilitated by training clinicians to set individualised SMART goals as well as appropriate evaluation and assessment of meaningful outcomes at the levels of the ICF for patients and their caregivers, for example using GAS. Use of item banks of standardised goals for spasticity management may be helpful where there is less expertise in goal setting [224].

4.8.3. Quality of the evidence

The quality of the evidence was limited because there were only three heterogeneous single-centre trials of low methodological quality, which prohibited the pooling of data for quantitative meta-analysis. The limitations affecting the quality of the evidence in this review include:

- inconsistent terminology and definitions for spasticity given that it is only one element of the UMN syndrome. In practice, rehabilitation interventions target various patterns of muscle overactivity, weakness, and contractures. When investigating spasticity there is ambiguity in what is being treated and measured, causing difficulty in the interpretation and application of evidence [57, 58]. Sun et al. [117] and Weber et al. [168] did not define spasticity, while Lai et al. [170] used multiple terms such as hypertonicity, tone and spasticity with interventions aiming to reduce contracture.
- inadequate allocation concealment [168, 170]
- high risk of performance bias due to non-blinding of treating therapists and participants (all studies). Additionally, patients may have revealed
information about the intervention to outcome assessors; however, this was not addressed to reduce risk of detection bias. In rehabilitation trials, blinding of participants and personnel can be particularly challenging.

- small sample sizes, underpowered studies and recruitment from single centres with strict inclusion and exclusion criteria
- the influence of significant attrition rates (16.7% in Lai et al. [170] and 21.7% in Weber et al. [168]), non-compliance affecting retention of participants and follow-up, excluding dropouts from analyses and outcome reporting
- differences in baseline characteristics between groups including age and aetiology [168]. Authors rationalised that the differences would not influence findings because there were similar baseline variables, cognitive function and program adherence for traumatic brain injury and stroke participants, and age was controlled for in analysis.
- difficulty controlling for personal factors that influence patient–therapist interaction, compliance and delivery of therapy, thus affecting outcomes. These were not assessed in any of the studies and include patient motivation, self-efficacy and activity level outside of therapy programs.
- selection of inappropriate outcome measures that do not show change following therapy and do not correlate with meaningful outcomes for patients and their caregivers. Impairment measures (such as the MAS range of movement) and other standardised measures (such as the ARAT) do not necessarily translate into improved function or benefits for patients and caregivers. These may be better captured through measures of passive function or individual goal attainment.

4.8.4. Potential biases in the review process

The authors accept that there may have been a degree of:

- selection bias from the literature search
• publication bias if trials have not been published due to small study populations and negative results, or effects of treatments in published trials have been exaggerated.

Although Weber et al. [168] included participants with traumatic brain injury in the control group without sub-analysis for stroke versus traumatic brain injury, excluding this study would have resulted in bias in the review because 78% of the participants had a diagnosis of stroke.

4.8.5. Agreements and disagreements with other studies or reviews

This review found insufficient evidence for the optimal type and intensity of multidisciplinary rehabilitation programs following BoNT-A injections for upper and lower limb spasticity. Thus, recommendations advocating integrated multidisciplinary rehabilitation programs following focal spasticity management are based on expert opinion only [6, 21].

The evidence for CIMT after BoNT-A injections for post-stroke upper limb spasticity, in improving active upper limb function [117] is also supported by a cohort study [225]. This study showed benefits of two weeks of CIMT compared with a home exercise program in participants more than 90 days following stroke. However, unlike the results of Sun et al. [117], the benefits diminished by 24 weeks. Other studies have shown that CIMT improves arm motor function in stroke survivors with benefits persisting up to one year [226], so future studies should consider follow-up periods beyond one year. Evidence for improvement in active upper limb function after BoNT-A injections is variable, being supported by some studies [227, 228] but not others [25, 59, 103].

4.9. Conclusions

4.9.1. Implications for practice

The limited evidence in this review and the lack of details in recent spasticity management guidelines do not allow the development of evidence-based optimal multidisciplinary therapy programs after BoNT-A injections. Hence, current clinical practice is based on professional judgement, expertise and trial-and-error. Further research is required to develop evidence-based recommendations.
4.9.2. Implications for research

Robust clinical trials are required to determine the optimal timing, types (combinations of therapy approaches and modalities) and intensities (frequency, amount and duration of therapy) of multidisciplinary rehabilitation programs to improve activity and participation after BoNT-A injections and other focal intramuscular treatments for post-stroke spasticity. Future trials may consider:

- better methodological quality including larger sample sizes, multicentre designs and internationally agreed data sets
- longer follow-up (beyond six months at least) to determine the benefits of an intervention (and whether the effects are maintained) because there may be a time lag between improvement in function and change in spasticity [20]
- development of appropriate outcome measures or consensus on a bank of measures that assess the activity (passive and active function) and participation and environmental factors domains of the ICF and translate into real-world functional abilities rather than focusing on impairments only. Other areas include addressing personal factors in the ICF that influence outcomes of rehabilitation interventions and using appropriate patient-centred outcomes with standardised measures to provide a more holistic picture.
- evaluation of the perspectives of patients and caregivers and the cost-effectiveness of rehabilitation programs
- investigating optimal and effective CIMT protocols
- investigating the contribution of individual components of rehabilitation programs to outcomes, individually and combined, to explore the black box of rehabilitation.

Chapter 5 examines the effect of therapy intensity on patient outcomes by comparing a high-intensity rehabilitation program with usual care low-intensity therapy following BoNT-A injections for upper and lower limb spasticity.
Chapter 5. Outcomes of ambulatory rehabilitation programs following BoNT-A for spasticity in adults with stroke

5.1. Introduction

The effectiveness of BoNT-A in reducing spasticity following stroke has been well established in the upper limb [17, 26, 27, 129] and the lower limb [29, 30]. A multimodal rehabilitation approach to spasticity management achieves long-term functional improvement after spasticity reduction [20]. An appropriate rehabilitation management program should ideally be in place prior to BoNT-A treatment and should continue thereafter [229] as the effects of BoNT-A are temporary and functional changes usually take longer to become apparent. While spasticity management guidelines advocate a multidisciplinary approach [6, 21] recommendations are based on expert opinion rather than scientific evidence. The guidelines lack details on optimal therapy programs and patient selection as discussed in Chapter 1.

Physical therapies used in rehabilitation following BoNT-A injections may include electrical stimulation [38], stretching [124], casting [39], CIMT [41, 117] and task-specific practice [168]. The Cochrane review found limited and low quality evidence for the effectiveness of multidisciplinary rehabilitation following BoNT-A for post-stroke spasticity (Study 1, Chapter 4) [230]. The few included studies had methodological limitations including small sample sizes and use of outcome measures that do not necessarily translate into improved function or benefits for patients and caregivers. As highlighted in Chapters 1 and 4, studies of physical interventions following BoNT-A have tended to focus on single treatment modalities or unidisciplinary therapy, rather than the complex array of interventions delivered in real-life rehabilitation settings. The optimal types (modalities, therapy approaches and settings) and intensities of therapies for achieving meaningful patient outcomes following BoNT-A remain unclear, causing these elements to be described as the black box of rehabilitation [55].
Post-stroke spasticity contributes to a diversity of patient-centred problems [11] as outlined in Section 2.6. As spasticity affects individual stroke survivors differently, so treatment goals are variable. Hence, the use of functional outcome measures, such as GAS, that identify outcomes of importance to the individual and caregivers are recommended [11, 26, 33, 34].

Stroke patients are often told their recovery stabilises within six to 12 months [98]. These plateaus may be due to patient physiological or psychological adaptation to rehabilitation exercises, rather than reduced capacity for motor recovery [99], as explained in Section 2.5.5. Adjusting the rehabilitation approach (modifying intensity or modalities) and challenge of therapeutic exercise allows positive neuromuscular adaptations to occur [99]. Additionally, there is often a time lag between peak spasticity reduction following BoNT-A and maximal functional gain [20, 34]. These factors emphasise the need for comprehensive rehabilitation and longer follow up periods to ensure that the benefits of treatment are not missed and to determine whether effects are maintained after treatment cessation.

This study examined the effectiveness of a high-intensity ambulatory multidisciplinary rehabilitation program versus lower intensity usual care, as measured by goal achievement and other outcomes up to 24 weeks, in Australian adult stroke survivors receiving BoNT-A injections for upper and lower limb spasticity.

5.2. Methods

This study is a prospective single centre, controlled clinical trial.

5.2.1. Participants and setting

The study was conducted at a multidisciplinary, tertiary referral spasticity management service. Following ethics committee approval (HREC number 2010.165), consecutive adult patients treated with BoNT-A for upper and lower limb post-stroke spasticity and eligible for rehabilitation were invited to participate in the study. Inclusion criteria were: age 18 years or above, stroke diagnosis at least three months prior to recruitment; upper or lower limb spasticity (MAS ≥ 2) interfering with function or causing a clinical problem, and no
contraindications to BoNT-A injections. Patients were excluded if they had:
treatment with BoNT-A within six months; had received intrathecal baclofen or
anti-spasticity medications; had undergone neurolysis or surgery to the affected
limb; had concomitant neurological conditions; were pregnant; or were unable to
participate in therapy due to cognitive or language impairment, psychiatric illness
or medical illness.

5.2.2. Procedures

Group allocation

This trial was designed to reflect real-life clinical practice in an ambulatory
rehabilitation service in Australia. In this context, therapy is delivered based on
accessibility to services, treating team assessments and service delivery protocols
determined by geographical catchment areas. Thus, allocation to rehabilitation
programs was based on participants’ areas of residence. Those residing within a
12 kilometre radius of the investigating hospital received high-intensity
ambulatory rehabilitation programs, while subjects outside of this geographical
catchment underwent usual care, being lower intensity therapy at their local
community or hospital rehabilitation service. Participants were not informed of
allocation within the trial.

Assessments

Structured assessments were completed in the hospital clinic. Baseline data that
was collected and documented in data collection sheets (Appendix 6) included:
demographic data, stroke related impairments (based on history, review of
medical records and clinical examination) and details of prior BoNT-A
administration. Up to three individualised, SMART [44] goals for each treated
limb (to a maximum of six goals if both limbs were treated) were negotiated
between participants, caregivers and the clinic therapist (JL). Using the GAS
process [46], a defined statement of expected outcome was determined for each
goal at 12 weeks following BoNT-A injections (Appendix 2). Participants were
referred to ambulatory rehabilitation services based on geographical catchment
areas and details of treatment goals were provided. A blinded assessor completed
standardised outcome assessments at baseline, six, 12 and 24 weeks (Section 5.2.4).

5.2.3. Treatment schedules

BoNT-A injections

All participants received individualised BoNT-A injections in the affected limbs, as determined by clinical factors, spasticity patterns, injector preference and treatment goals [6, 21]. Injections were administered at baseline by a rehabilitation physician (MD or GA) using neuromuscular stimulation for muscle localisation.

Rehabilitation programs

A high-intensity ambulatory rehabilitation program comprised of three or more one-hour sessions per week for approximately 10 weeks. This protocol was more intensive than the usual care provided for spasticity management in local tertiary hospital community-based rehabilitation services. Usual care was a lower intensity rehabilitation program (a maximum of two one-hour sessions per week). Therapy settings included tertiary hospital community-based rehabilitation services or community health centres, depending on service accessibility and availability as per routine service delivery. A priori compliance with outpatient treatment was attendance in more than 70% of scheduled therapy sessions.

All participants received goal-directed, individualised rehabilitation programs, consistent with real-life rehabilitation practices in Australia. Therapy was based on neurodevelopmental techniques and other therapy approaches as deemed clinically relevant by treating therapists. Interventions targeting relevant impairments included: task specific practice, motor learning, strengthening, postural awareness, balance training, aerobic and conditioning exercises, range of movement, stretching, adaptive or compensatory strategies (environmental adaptation, one handed skills) and sensory training. The main activities focussed on were gait or upper extremity control in relation to activities of daily living such as dressing and feeding. Others included transfer practice, sitting balance, trunk control, and functional mobility. Participants received education in self-
management and home exercise programs. Therapists documented details of therapy sessions (discipline, date, duration, activities and interventions) using standardised forms (Appendix 3) [55].

5.2.4. Outcome measurement

A blinded assessor completed investigator-observed and participant (or caregiver) reported outcome measures at baseline, six, 12 (primary outcome time-point), and 24 weeks. Results were recorded in the study data collection sheets (Appendix 6).

**Primary outcome measures**

Primary outcome measures were: (1) the proportion of participants who at 12 weeks achieved at least 50% of their total goals, as measured by GAS process, and (2) change in GAS T-scores [33, 34, 46] determined using methods described in Section 1.3.2. Goals were identified using the goal-setting procedure and weighted by importance and difficulty (each graded on a 0 to 3 scale) of achieving the goal. Baseline goal scores were -1 (or -2 if participants could not have been at a worse level). Goal attainment was rated using a five-point scale (-2 to 2), where a GAS score of 0 and above implies goal achievement. The blinded assessor assigned the level of individual goal attainment according to the description in the statement of expected outcome (0 score) at follow-ups. The composite goal attainment score (T-score), based on the aggregated weighted score of each participant’s goals, was calculated [46] as a variable normally distributed around a mean of 50 and with a standard deviation of 10 points [33].

**Secondary outcome measures**

The MAS [110] assessed muscle tone during passive range of movement of the joints associated with injected muscle groups in the treated limbs on a six-point scale from 0 (no increase in muscle tone) to 4 (rigid flexion or extension). A score of 1+ was assigned the value of 1.5. Change in mean MAS scores for treated limbs, and upper and lower limbs separately, were calculated.

The Arm Activity Measure [115] assessed difficulty in passive arm function (seven-items, Section A) and active arm function (13-items, Section B) for
participants who had upper limb BoNT-A injections. Participants or their caregivers rated the difficulty in performing each function, based on activity over the preceding seven days, using a five-point ordinal scale (0 = no difficulty, 1 = mild, 2 = moderate, 3 = severe, 4 = unable to do).

The 10-metre walk test [164] where participants are asked to walk 10 metres independently at a comfortable speed using their usual shoes and gait aid, was used to calculate gait velocity (metres per second, m/s) for participants who had lower limb injections. The mean of two tests was used.

Global assessment scale [126] rated participants’ subjective improvement or worsening of symptoms and satisfaction following treatment from -4 (very marked worsening) to 4 (very marked improvement) with 0 indicating no change. At least one point increase indicated treatment success.

Self-rated burden [209] for caregivers used a visual analogue scale with numerical ratings in response to the question how burdensome do you feel caring for your partner is at the moment from 0 (not hard at all) to 100 (much too hard).

5.2.5. Power calculation and statistical analysis

A change in GAS-T score of at least 10 points is associated with clinically important change [34]. Sample size was estimated by assuming a difference in GAS T-score change score of 10 (SD = 12) points between high-intensity and usual care groups. Allowing for a 15% dropout rate, 27 participants were required in each group to detect the difference with 80% power.

Data was entered into a Microsoft Access database and exported into Stata version 12 (StataCorp, TX, USA) for analysis. Descriptive statistics were presented as mean and SD for continuous normally distributed data, median and interquartile range (IQR) for skewed or ordinal data and N (%) for categorical data.

Data analysis was performed using intention-to-treat principles with Last Observation Carried Forward for missing data. Continuous normally distributed variables were analysed using Student t-test and skewed or ordinal data were analysed using Wilcoxon rank-sum test. Change scores were calculated as follow-up minus baseline scores. Categorical variables were analysed using chi² or Fisher’s exact tests. Multivariate logistic regression (generalised linear model)
was used to determine variables associated with participants achieving at least 50% of their goals and the change in GAS T-score. Variables of interest included in models were: treatment allocation, age, gender, stroke localisation (cortical versus subcortical) and time since stroke (one year or less versus more than one year). P-values less than 0.05 indicated statistical significance for all tests.

5.3. Results

5.3.1. Study flow

Fifty-nine of 75 stroke survivors screened from January 2011 to June 2012 were recruited to the study, with 28 allocated to high-intensity rehabilitation programs and 31 to lower intensity usual care (Figure 5.1). There were no losses to follow up or adverse events.

Figure 5.1. Study flow diagram.
5.3.2. Baseline characteristics

Demographic and clinical factors for both groups are summarised in Table 5.1. Participants had a median age of 61 (IQR = 48 to 68) years and a median time since stroke diagnosis of 2.5 (IQR = 1.1 to 5.0) years. Over 70% (N = 42) were male. A greater proportion of usual care participants had cortical strokes (p = 0.036) though there were no differences in the proportion of participants with cortical and cognitive impairments on assessment between the two groups. The high-intensity group had lower Arm Activity Measure active function score and GAS T-score (p = 0.027 and 0.053, respectively).

Table 5.1. Baseline characteristics of high-intensity and usual care groups

<table>
<thead>
<tr>
<th></th>
<th>High-intensity (N = 28)</th>
<th>Usual care (N = 31)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic factors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex male, N (%)</td>
<td>19 (67.9)</td>
<td>23 (74.2)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>60.6 (48.6 - 65.9)</td>
<td>61.4 (47.8 - 68.6)</td>
</tr>
<tr>
<td>Range</td>
<td>20.3 - 83.1</td>
<td>37.4 - 78.5</td>
</tr>
<tr>
<td>Time since stroke (years)</td>
<td>2.3 (1.1 - 5.5)</td>
<td>2.5 (1.1 - 5.0)</td>
</tr>
<tr>
<td>Range</td>
<td>0.4 - 15.3</td>
<td>0.3 - 12.0</td>
</tr>
<tr>
<td>Education, N (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary</td>
<td>1 (3.6)</td>
<td>6 (19.4)</td>
</tr>
<tr>
<td>Secondary</td>
<td>18 (64.3)</td>
<td>14 (45.2)</td>
</tr>
<tr>
<td>Tertiary / other</td>
<td>9 (32.1)</td>
<td>11 (35.5)</td>
</tr>
<tr>
<td>Living arrangements, N (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>With family/ friends</td>
<td>25 (89.3)</td>
<td>27 (87.1)</td>
</tr>
<tr>
<td>Alone</td>
<td>1 (3.6)</td>
<td>3 (9.7)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (7.1)</td>
<td>1 (3.2)</td>
</tr>
<tr>
<td>Caregivers, N (%)</td>
<td>21 (75.0)</td>
<td>26 (83.9)</td>
</tr>
<tr>
<td><strong>Clinical characteristics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke aetiology, N (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infarct</td>
<td>20 (71.4)</td>
<td>25 (80.6)</td>
</tr>
<tr>
<td>Haemorrhage/ mixed</td>
<td>8 (28.6)</td>
<td>6 (19.4)</td>
</tr>
<tr>
<td>Stroke localisation, N (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cortical</td>
<td>20 (71.4)</td>
<td>29 (93.5)*</td>
</tr>
<tr>
<td>Subcortical</td>
<td>8 (28.6)</td>
<td>2 (6.5)</td>
</tr>
</tbody>
</table>
### Left cerebral lesion, N (%)  
16 (57.1) 17 (54.8)

### Dominant side affected, N (%)  
18 (64.3) 15 (48.4)

**Dependent variables**

<table>
<thead>
<tr>
<th>Variable</th>
<th>All (N = 59)</th>
<th>Upper limb (N = 40)</th>
<th>Lower limb (N = 37)</th>
<th>ArmA (N = 21)</th>
<th>Section A</th>
<th>Section B</th>
<th>Gait speed, m/s*</th>
<th>GAS T-score</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAS treated limb/s</td>
<td>2.4 (2.0 - 2.7)</td>
<td>2.4 (2.0 - 2.7)</td>
<td>2.3 (2.0 - 3.0)</td>
<td>2.4 (6 - 13)</td>
<td>10.5 (6 - 15)</td>
<td>49.5 (46 - 51)*</td>
<td>0.37 (0.29 - 0.74)</td>
<td>31.3 (26.9 - 36.1)</td>
</tr>
<tr>
<td>Gait speed, m/s*</td>
<td>(N = 16)</td>
<td>(N = 20)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Prior treatments**

| Therapy program pre-existing and continued, N (%) | 18 (64.3) 17 (54.8) |
| BoNT-A > 6 months prior to recruitment | 16 (57.1) 15 (48.4) |
| Number of cycles | 1.0 (1 - 3) 2.5 (1 - 4) |

Results are median (interquartile range, IQR) unless otherwise specified. *P-value < 0.05. GAS, Goal Attainment Scaling; MAS, Modified Ashworth Scale (mean score for treated muscle groups in limbs, scoring = 1, 1.5, 2, 3, 4); ArmA, arm activity measure (Section A passive arm function and Section B active arm function) for participants receiving upper limb injections; BoNT-A, botulinum toxin type A. *Gait speed, metres per second (m/s) for participants receiving lower limb injections. **One participant was unable to complete the 10 metre walk test.
5.3.3. Details of BoNT-A injection

Forty participants received upper limb injections (21 in the high-intensity and 19 in the usual care groups) and 37 received lower limb injections (16 in the high-intensity and 21 in the usual care groups). Nine participants in each group had both limbs injected. There were no significant differences in the proportions of participants who had upper and lower limb injections in each group (p = 0.40 and 0.26 respectively). Fifty-four participants were injected with Dysport® and five with BOTOX®. Mean doses of BoNT-A (Dysport®) injected in a limb were 766 (SD = 244) in the high-intensity and 673 (SD = 314) in the usual care groups, (p = 0.19). There were no significant differences between upper and lower limb doses between groups (p = 0.19 and 0.94 respectively). Elbow flexors and long finger flexors were most commonly injected in the upper limb, and gastrocnemius and soleus were injected in over 90% of those receiving lower limb injections (Table 5.2).
Table 5.2. Number of participants injected in the various upper and lower limb muscle groups.

<table>
<thead>
<tr>
<th>Muscle Group</th>
<th>High-intensity (N = 28)</th>
<th>Usual care (N = 31)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Upper limb injections</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shoulder muscles: pectoralis, latissimus dorsi and corachobrachialis</td>
<td>4 (19.0)</td>
<td>5 (26.3)</td>
</tr>
<tr>
<td>Elbow flexors: biceps, brachialis and brachioradialis</td>
<td>12 (57.1)</td>
<td>11 (57.9)</td>
</tr>
<tr>
<td>Pronators: pronator teres and pronator quadratus</td>
<td>8 (38.1)</td>
<td>2 (10.5)</td>
</tr>
<tr>
<td>Wrist flexors: flexor carpi ulnaris and flexor carpi radialis</td>
<td>14 (66.7)</td>
<td>6 (31.6)</td>
</tr>
<tr>
<td>Finger flexors: flexor digitorum superficialis and flexor digitorum profundus</td>
<td>15 (71.4)</td>
<td>13 (68.4)</td>
</tr>
<tr>
<td>Thumb: flexor pollicus longus, adductor pollicus, flexor pollicus brevis and opponens pollicus</td>
<td>11 (52.4)</td>
<td>8 (42.1)</td>
</tr>
<tr>
<td><strong>Lower limb injections</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quadriceps: vastus lateralis, vastus intermedius, vastus medialis and rectus femoris</td>
<td>3 (18.8)</td>
<td>5 (23.8)</td>
</tr>
<tr>
<td>Plantarflexors: gastrocnemius medial, gastrocnemius lateral and soleus</td>
<td>15 (93.8)</td>
<td>20 (95.2)</td>
</tr>
<tr>
<td>Invertors: tibialis posterior and tibialis anterior</td>
<td>6 (37.5)</td>
<td>4 (19.0)</td>
</tr>
<tr>
<td>Toe flexors: flexor hallucis longus, flexor hallucis brevis, flexor digitorum brevis and flexor digitorum longus</td>
<td>2 (12.5)</td>
<td>4 (19.0)</td>
</tr>
</tbody>
</table>

Data are N (%), where N is the number of participants injected in at least one of the muscles in the muscle group and calculated as a percentage of those injected in the upper or lower limb for high-intensity versus usual care groups. The total is more than 100% as participants had injections in multiple locations.
5.3.4. Details of rehabilitation programs

Therapy commenced within 14 days of BoNT-A injections for the majority of participants. Participants in the high-intensity group attended a mean of 3.2 one-hour therapy sessions per week (SD = 0.6, range 2 to 4), and the usual care group a mean of 1.2 (SD = 0.5, range 0.7 to 2.2). Mean duration of therapy programs was 11 weeks (SD = 3.3, range 7.9 to 19.4) for the high-intensity group and 10 weeks (SD = 3.9, range 1 to 20.3) for the usual care group. Participants in the high-intensity group attended a mean total of 35.2 one-hour therapy sessions and the usual care group a mean total of 12 one-hour therapy sessions. All participants attended hospital community-based rehabilitation services for therapy programs, except for three in the usual care group who attended community health centres (N = 2) and a private therapist (N = 1). Rehabilitation programs included physiotherapy (96% of high-intensity and 87% of usual care participants), occupational therapy (64% of high-intensity and 48% of usual care participants respectively) or at least two disciplines (64% of high-intensity and 48% of usual care participants respectively). A priori compliance was achieved in all but one participant (allocated to the usual care group) who declined to participate in therapy after one session.

5.3.5. Details of treatment goals

There were 93 goals set in the high-intensity and 96 in the usual care groups (mean 3 goals per participant, range 1 to 6), with the majority of goals related to the ICF domains of activity and participation rather than symptoms and impairments (Table 5.3).
Table 5.3. Categories of upper and lower limb goals for high-intensity and usual care groups

<table>
<thead>
<tr>
<th>Goal categories</th>
<th>High-intensity</th>
<th>Usual care</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Upper limb goals, N (%)</strong></td>
<td>High-intensity</td>
<td>Usual care</td>
</tr>
<tr>
<td>Impairments and symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain or discomfort</td>
<td>4 (7.1)</td>
<td>6 (13.6)</td>
</tr>
<tr>
<td>Range of movement and prevent contracture</td>
<td>6 (10.7)</td>
<td>3 (6.8)</td>
</tr>
<tr>
<td>Involuntary movements</td>
<td>6 (10.7)</td>
<td>7 (15.9)</td>
</tr>
<tr>
<td>Activity and participation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active function</td>
<td>21 (37.5)</td>
<td>12 (27.3)</td>
</tr>
<tr>
<td>Passive function</td>
<td>18 (32.1)</td>
<td>15 (34.1)</td>
</tr>
<tr>
<td>Mobility</td>
<td>1 (1.8)</td>
<td>1 (2.3)</td>
</tr>
<tr>
<td>Total upper limb goals, N</td>
<td>56</td>
<td>44</td>
</tr>
</tbody>
</table>

| Lower limb goals, N (%)                  | High-intensity | Usual care |
| Impairments and symptoms                |                |            |
| Pain or discomfort                       | 1 (2.7)        | 6 (11.5)   |
| Involuntary movements                   | 0 (0.0)        | 2 (3.8)    |
| Activity and participation              |                |            |
| Active function                          | 34 (91.9)      | 44 (84.6)  |
| Passive function                         | 1 (2.7)        | 0 (0.0)    |
| Other                                    | 1 (2.7)        | 0 (0.0)    |
| Total lower limb goals, N               | 37             | 52         |

*Percentage of upper or lower limb goals out of the total number of goals set for high-intensity and usual care groups.
5.3.6. Primary outcomes

The majority of participants in the high-intensity and usual care groups achieved at least 50% of their goals at 12 weeks (75% and 77% respectively, p = 0.99) and 24 weeks (79% and 61% respectively, p = 0.17). GAS T-scores improved significantly (p < 0.001) at all time points in both groups. When considering all goals, median change in GAS T-score from baseline to 24 weeks approached statistical significance favouring the high-intensity versus usual care group (20.1 (IQR = 10.4 to 25.5) versus 12.3 (IQR = 5.8 to 18.7) respectively, p = 0.071) (Table 5.4). Analysing goal attainment by upper and lower limb GAS revealed a strong statistical trend towards participants with upper limb injections achieving more goals at 24 weeks in the high-intensity compared to the usual care group (median 3 (IQR = 1 to 3) versus 1 (IQR = 1 to 2), p = 0.052), with no observed difference for those who had lower limb injections.

5.3.7. Secondary outcomes

The high-intensity group showed greater reduction in mean upper limb MAS score compared with the usual care group at six (p = 0.005) and 12 (p=0.015) weeks, and overall mean MAS score at 12 weeks (p = 0.033) (Table 5.4). The usual care group had a greater reduction in lower limb MAS score at 24 weeks (p = 0.004). Overall, MAS scores trended towards baseline at 12 and 24 weeks. Participant satisfaction with treatment, measured using the global assessment scale, improved throughout the study in both groups (Table 5.4). There were no significant differences in change scores for secondary measures of activity and participation (Arm Activity Measure, gait speed, Global Assessment Scale and Self Rated Burden) at any time point. There were no differences in secondary outcomes for participants receiving upper or lower limb injections in either group.
Table 5.4. Summary of analysis of outcomes of high-intensity rehabilitation programs and usual care: change scores from baseline at six, 12 and 24 weeks.

<table>
<thead>
<tr>
<th></th>
<th>6 weeks</th>
<th>12 weeks</th>
<th>24 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary outcomes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Participants</td>
<td>19 (67.9)</td>
<td>20 (64.5)</td>
<td>21 (75.0)</td>
</tr>
<tr>
<td>achieving ≥ 50%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>of goals, N (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GAS T-score</td>
<td>12.9 (7.7 - 19.9)</td>
<td>12.4 (4.6 - 9.1)</td>
<td>13.4 (11.6 - 25.6)</td>
</tr>
<tr>
<td>Secondary outcomes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MAS, mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>UL and LL</td>
<td>-1.0 (0.7)</td>
<td>-0.7 (0.6)</td>
<td>-0.6 (0.6)*</td>
</tr>
<tr>
<td>UL (N = 40)</td>
<td>-1.2 (0.7)*</td>
<td>-0.6 (0.5)</td>
<td>-0.8 (0.7)*</td>
</tr>
<tr>
<td>LL (N = 37)</td>
<td>-0.7 (0.7)</td>
<td>-0.7 (0.7)</td>
<td>-0.4 (0.5)</td>
</tr>
<tr>
<td>ArmA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(N = 21)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Section A</td>
<td>-4 (-6 - 0)</td>
<td>-2 (-5.5 - 0)</td>
<td>-3 (-6 to -1)</td>
</tr>
<tr>
<td>Section B</td>
<td>-2 (-5 - 0)</td>
<td>-1 (-2.5 - 0.5)</td>
<td>-2 (-5 - 0)</td>
</tr>
<tr>
<td></td>
<td>6 weeks</td>
<td>12 weeks</td>
<td>24 weeks</td>
</tr>
<tr>
<td>------------------------</td>
<td>---------</td>
<td>----------</td>
<td>----------</td>
</tr>
</tbody>
</table>
| Gait speed m/s
g | (N = 16) | (N = 20) | (N = 16) | (N = 20) | (N = 16) | (N = 20) |
|                        | 0.03 (-0.01-0.16) | 0.06 (0.00-0.10) | 0.05 (0.01-0.10) | 0.03 (0.01-0.08) | 0.04 (-0.01-0.11) | 0.02 (-0.02-0.12) |
| Global Assessment Scale | 2 (1 - 3) | 2 (2 - 3) | 2 (2 - 3) | 2 (1 - 3) | 2 (1 - 3) | 2 (1 - 3) |
| SRB | (N = 21) | (N = 26) | (N = 21) | (N = 26) | (N = 21) | (N = 26) |
|                | 0 (-10 - 0) | -10 (-20 - 0) | -10 (-20 - 0) | -10 (-20 - 0) | -10 (-20 - 0) | 0 (-10 - 10) |

All scores calculated as change from baseline and median (interquartile range, IQR) unless otherwise specified. *P-value < 0.05. GAS, goal attainment scaling; MAS, Modified Ashworth Scale (change in mean score for treated muscle groups in limbs); SD, standard deviation; UL, upper limb; LL, lower limb; ArmA, arm activity measure, Section A passive arm function and Section B active arm function (for participants receiving upper limb injections); SRB, self rated burden (caregivers). # Gait speed (metres per second, m/s) for participants receiving lower limb injections.
5.3.8. Factors contributing to effect size

Gender, time since stroke and stroke localisation (cortical versus sub-cortical) did not correlate with goal achievement outcomes. Older participants had less change in GAS T-score at 12 weeks ($\beta = -0.27, 95\% \text{ CI} = -0.45 \text{ to } -0.08, \text{ p} = 0.005$) and 24 weeks ($\beta = -0.26, 95\% \text{ CI} = -0.45 \text{ to } -0.07, \text{ p} = 0.009$). Participants who achieved at least 50% of their goals at six weeks were more likely to do so at 12 weeks (crude odds ratio = 3.7, 95% CI = 1.1 to 12.8, p = 0.04; adjusted odds ratio = 4.1, 95% CI = 1.1 to 15.6, p = 0.04) and 24 weeks (crude odds ratio = 5.6, 95% CI = 1.7 to 18.6, p = 0.005; adjusted odds ratio = 6.4 (95% CI = 1.7 to 23.9, p = 0.005). At six weeks, the chance of achieving at least 50% of goals was 3.5 times higher with one point decrease in MAS score (95% CI = 1.2 to 8.9, p = 0.03). However, this correlation was not found at other time points.

5.4. Discussion

5.4.1. Summary of results

In this pragmatic controlled trial, a high-intensity ambulatory rehabilitation program (mean 3.2 one-hour sessions per week for approximately 10 weeks) following BoNT-A injections for post-stroke upper and lower limb spasticity was compared against a lower intensity, usual care program (mean 1.2 one-hour weekly sessions). Both groups improved significantly in terms of goal achievement and participant satisfaction up to 24 weeks. There was a strong trend towards upper limb-injected participants in the high-intensity therapy group achieving more goals at 24 weeks compared with usual care. This effect was not observed for lower limb goals. Demographic and clinical characteristics of study participants were similar to those of other studies including: age [26, 27, 129], time following stroke [30] and proportion of male participants (72% compared with 58 to 63%) [17, 26, 29, 129]. Although the usual care group had more cortical strokes, there were no differences in cortical and cognitive deficits on assessment, and regression analysis did not show any effect of this variable on outcomes. Lower baseline GAS T-scores in the high-intensity group implies participants started at a lower level. Although gender, time since stroke and stroke...
localisation (cortical versus sub-cortical) did not correlate with goal achievement outcomes, older participants showed reduced benefit at 12 weeks.

5.4.2. Patient-centred benefits: goal achievement

Benefits relating to goal achievement were maintained up to 24 weeks post-injection, even after cessation of therapy and despite the effects of BoNT-A on spasticity wearing off. Other studies have demonstrated a similar delay between spasticity reduction and improved upper limb function [20, 33], suggesting that motor relearning continues after muscle tone is returning to baseline and supporting the need for BoNT-A to be used with active rehabilitation [20]. Most trials of physical interventions or single treatment cycles of BoNT-A for spasticity rarely extend beyond four months [25, 230]. The longer follow-up in this study ensured that the benefits of therapy and their maintenance after completion of the intervention could be identified. At six weeks, spasticity reduction was related to a greater chance of achieving at least 50% of goals, but this relationship did not continue after six weeks. The prolonged benefits of combined BoNT-A and therapy are more likely to result from factors other than spasticity reduction such as ongoing neuroplasticity; particularly as the study cohort were a median of 2.5 years post-stroke. This finding supports other literature on chronic (more than one year post) stroke, where long-term motor improvement after participation in novel rehabilitation protocols or therapy modalities were observed due to neuromuscular adaptive changes [99].

5.4.3. Rehabilitation programs: is higher-intensity therapy better than usual care?

Participants in both groups improved in terms of goal achievement and satisfaction up to 24 weeks, beyond the duration of spasticity reduction by BoNT-A. This study showed a statistical trend suggesting a benefit of goal-directed higher intensity therapy over usual care following BoNT-A injections to the upper limb. Comparison of the study findings with other studies is limited due to the lack of literature investigating the influence of therapy intensity on outcomes after BoNT-A injections for post-stroke spasticity. Instead, studies have tended to compare single treatment modalities such as stretching, taping or electrical
stimulation [38, 124], or qualitatively different therapy approaches such as CIMT and neurodevelopmental therapy [117]. While the optimal type and amount of therapy has not been determined, rehabilitation programs have been suggested to play an important role in improving outcomes following BoNT-A treatment [117, 231, 232]. A feasibility study showed that neurological patients receiving therapy (comprising of serial casting and movement training) with or without BoNT-A, versus BoNT-A alone, had greater improvement in GAS scores [231]. A limited impact of higher intensity rehabilitation programs (inpatient and outpatient) on functional outcomes after stroke has been found in other studies [233-235], partially supporting the findings of this study. As both study groups received individualised ambulatory rehabilitation programs in similar settings, the current study suggests that while therapy is important, more intensive therapy in late stroke may have a differential capacity to modulate patient outcomes following upper and lower limb BoNT-A injections. The black box of rehabilitation requires further investigation as spasticity management guidelines lack details on optimal therapy approaches [6, 21]. In particular, it may be that provision of goal-directed therapy is more important than the amount of therapy, although further exploration is required.

5.4.4. Limitations

Limitations of research design have the potential to contribute to the findings of this study. As both groups received active rehabilitation following BoNT-A injections there may have been insufficient variation of intensity of therapy. However, the high-intensity group received almost three times as many therapy sessions compared with the usual care group. In comparison, other studies have reported an intensity differential of up to two times the control intervention [233, 235]. As the provision of a rehabilitation program in conjunction with BoNT-A injections is considered best practice [6, 21], it was not ethically possible to have a non-therapy control group. More than 50% of participants were receiving therapy at the time of recruitment, which may have influenced the results as some of the benefit of rehabilitation may have already been realised. Furthermore, participants may have been undertaking informal therapy, particularly for the lower limb in the form of walking, that may have been much greater in extent than
the difference between formal therapy. The different locations of therapy provision between the groups may have been a confounder as therapy approaches may have differed between sites.

Other factors external to therapy intensity may have impacted on the outcomes of this study. At the participant level, these include their activity levels outside of therapy, personal factors such as motivation, self-efficacy, attitudes, beliefs, and participation in study assessments [234] including formal goal setting procedures. At the therapist level, potential confounders include those factors that influence the patient-therapist interaction, compliance and delivery of therapy.

This trial highlights the challenges of investigating complex rehabilitation interventions in the real-life clinical setting. It was not possible to design the study as an RCT due to the nature of service delivery, limitations in resources and those reasons outlined above. Although the outcome assessor was blinded, it was not possible to blind therapists. Participants were not informed of study design related to intensity of therapy; however, it is unclear whether this was maintained throughout the study period. Demonstrating functional benefits following focal spasticity management can be difficult as standardised outcome measures are often insensitive [59], particularly with a small sample size and heterogeneous stroke population as in this study. Measurement of goal attainment using GAS sought to overcome some of these issues. GAS assessment has greater responsivity to the effects of BoNT-A than other standardised person-centred or global outcome measures [26, 33, 34] and acknowledges the diversity of individualised spasticity management goals. The methodological limitations of this study indicate the need for a larger RCT to establish the role of therapy in achieving patient-centred outcomes after BoNT-A treatment and determining which patients benefit from rehabilitation, particularly comparing upper and lower limb outcomes.

5.5. Conclusions

In this study, a statistical trend towards better patient-centred outcomes was observed for the attainment of upper limb goals following more intensive ambulatory rehabilitation following BoNT-A injections for spasticity management. Therapy intensity did not modify post-injection outcomes for the
lower limb. This finding leaves open the role of therapy intensity as a post-injection modifier of the black box of rehabilitation, at least for the upper limb. Furthermore, overall goal achievement was maintained up to 24 weeks post-injection, even after cessation of therapy and despite the effects of BoNT-A on spasticity wearing off. Despite the lack of literature on the optimal therapy protocols, therapy is routinely provided following BoNT-A injections at a significant cost to health care services. In light of this and the study findings, further research to determine the optimal types, intensities and timing of multidisciplinary therapy programs following BoNT-A injections and ideal patient selection is warranted.

Chapter 6 examines the black box by demonstrating use of a stroke rehabilitation taxonomy to describe the fundamental components of rehabilitation programs provided in the current study, including an in-depth analysis of activities and interventions (Study 3).
Chapter 6. More than a black box of rehabilitation: Characterising therapy programs following BoNT-A injections for spasticity in adults with stroke

A stroke rehabilitation taxonomy is used to describe the therapeutic activities and interventions that therapists prescribed during the rehabilitation programs provided to the study cohort in Study 2 (Chapter 5). Thereby, the black box of rehabilitation for post-stroke spasticity is characterised.

6.1. Introduction

An integrated multidisciplinary rehabilitation program [18, 229] in conjunction with BoNT-A aims to achieve individualised patient and caregiver goals [33]. However, rehabilitation in this setting remains a black box. Although guidelines recommend multidisciplinary management [6, 21], the details of therapy content, and optimal therapy types (activities, interventions, therapy approaches) and settings are unclear and highly variable [230]. Studies rarely describe details of rehabilitation programs beyond duration, frequency and generic broad therapy terms [26, 41, 117] making replication in a clinical setting difficult. Additionally, therapy interventions are often investigated in isolation rather than in the milieu of the complex array of rehabilitation interventions provided in everyday clinical practice during rehabilitation programs [230].

Extensive work has been done in opening and examining the black box of stroke rehabilitation programs [36] during occupational therapy [62, 178, 236] and physiotherapy [176, 236]. However, no such studies have investigated the therapy components provided following BoNT-A for post-stroke spasticity, although rehabilitation is often routinely provided. These complex rehabilitation interventions are difficult to standardise and define, and measuring what actually works in rehabilitation is a challenge. Standardised approaches to documenting therapy interventions are a step towards bridging this gap. A general model for
describing critical attributes of disease management programs for chronic conditions has been developed allowing for comparisons across interventions [175]. At a more detailed level, use of a taxonomy to characterise the complex array of therapy activities and interventions systematically provides a means for capturing what actually happens in stroke rehabilitation programs [36, 55] and determining how therapy prescription relates to patients’ goals. Patient factors and specific therapy activities associated with better outcomes can then be identified [55], improving patient selection, service delivery and effectiveness. Stroke rehabilitation in inpatient [62, 166, 176, 178] and day hospital settings [236] has been defined in such a way. This is yet to be described specifically for multidisciplinary rehabilitation programs following BoNT-A for post-stroke spasticity.

Using a standardised taxonomy [36, 55, 166], this study describes the therapeutic activities and interventions prescribed within multidisciplinary ambulatory rehabilitation programs for stroke survivors receiving BoNT-A for upper and lower limb spasticity. How rehabilitation content differs as categorised by the limbs injected or the goals selected is investigated.

6.2. Methods

6.2.1. Study design and participants

Adult stroke survivors recruited from a multidisciplinary, tertiary referral, spasticity management service in Victoria, Australia, participated in ambulatory rehabilitation programs following BoNT-A for problematic upper and lower limb spasticity (Study 2, Chapter 5). Ethics approval was obtained from the relevant ethics committee (HREC number 2010.165).

All participants received individualised BoNT-A injections in the affected limbs, as determined by clinical factors, spasticity patterns and treatment goals [6, 21]. Individualised SMART (specific, measurable, achievable, realistic and timed) [44] goals were negotiated between participants, caregivers and the clinic therapist (JL) using the GAS process [46]. Baseline data included demographic and clinical characteristics such as stroke aetiology and localisation.
Following BoNT-A injections participants were referred to ambulatory rehabilitation services determined by geographical catchment areas [237]. Details of treatment goals were provided to treating therapists. Therapy programs were individualised and goal-directed following treating team assessments, where interventions and therapy approaches were determined.

### 6.2.2. Stroke rehabilitation taxonomy: standardised therapy documentation forms

Treating therapists used a stroke rehabilitation intervention classification system (comprising two forms; physical therapy and occupational therapy) [55, 62, 166, 176] to document rehabilitation activities and interventions used during each physiotherapy and occupational therapy session for the program duration (Appendix 3). Sixteen occupational and 11 physical therapy activities of variable complexity comprise the key structure of the classification system, in addition to 31 interventions classified by targeted body systems. To complete the documentation grid, therapists recorded the duration of each therapeutic activity in five-minute intervals and codes for the interventions (to a maximum of five) used to facilitate performance of these activities. A category for other interventions was used if needed. Additional information recorded included the therapist’s discipline and level of experience (i.e., therapist, assistant or student), the session duration and the amount of time spent in formal assessment, co-treatment with other disciplines or in a group. Therapists were provided with written and verbal instructions in completing the forms, reference [55] and definitions of terms [55] (Appendix 3). Therapists could use either form depending on relevance.

To categorise rehabilitation activities and goals the classification system used in studies describing occupational therapy stroke rehabilitation [62, 166] was modified for the purposes of this study. The four activity categories used in this study were: (1) performance skill deficits or body structure or function impairments [62, 166] (e.g., pre-functional activity, transfers, upper extremity control, wheelchair, pre-gait, and sitting balance or trunk control); (2) gait; (3) personal care tasks or home management; and (4) community participation (community mobility and community integration) or leisure (Box 1).
Box 1 Rehabilitation activities and interventions comprising physical and occupational therapy standardised documentation forms

<table>
<thead>
<tr>
<th>Physical therapy activities</th>
<th>Pre-gait*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-functional activity*</td>
<td>Gait†</td>
</tr>
<tr>
<td>Bed mobility*</td>
<td>Advanced gait†</td>
</tr>
<tr>
<td>Sitting*</td>
<td>Community mobility#</td>
</tr>
<tr>
<td>Transfers*</td>
<td>Intervention not related to functional activity</td>
</tr>
<tr>
<td>Sit-to-stand*</td>
<td></td>
</tr>
<tr>
<td>Wheelchair mobility*</td>
<td></td>
</tr>
</tbody>
</table>

**Categories and examples of physical therapy interventions**

**Neuromuscular**: balance training, postural awareness, motor learning, proprioceptive neuromuscular facilitation, neurodevelopmental therapy, involved upper extremity addressed, CIMT

**Musculoskeletal**: strengthening, mobilisation, passive range of movement and stretching, manual therapy, motor control

**Cardiopulmonary**: breathing, aerobic and conditioning exercises

**Cognitive/ Perceptual/ Sensory**: cognitive, perceptual, visual and sensory training

**Education**: patient, family, caregiver, staff

**Equipment**: prescription, selection, application, fabrication, ordering

**Modality**: electrical stimulation, biofeedback, ultrasound

**Assistive device**: ankle dorsi flex assist, cane, crutches, parallel bars, swiss ball, walker, wheelchair

**Area involved**: upper extremity, lower extremity, trunk, head and neck
<table>
<thead>
<tr>
<th>Occupational therapy activities</th>
<th>Home management‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-functional activity*</td>
<td>Community integration#</td>
</tr>
<tr>
<td>Dressing‡</td>
<td>Leisure performance#</td>
</tr>
<tr>
<td>Bathing‡</td>
<td>Upper extremity control*</td>
</tr>
<tr>
<td>Grooming‡</td>
<td>Wheelchair management*</td>
</tr>
<tr>
<td>Toileting‡</td>
<td>Sitting balance and trunk control*</td>
</tr>
<tr>
<td>Feeding and eating‡</td>
<td>Intervention not related to functional activity</td>
</tr>
<tr>
<td>Transfers*</td>
<td></td>
</tr>
<tr>
<td>Bed mobility*</td>
<td></td>
</tr>
<tr>
<td>Functional mobility</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Categories and examples of occupational therapy interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Neuromuscular</strong>: Balance training, postural awareness, motor learning, proprioceptive neuromuscular facilitation, neurodevelopmental therapy, CIMT</td>
</tr>
<tr>
<td><strong>Adaptive or compensatory</strong>: one handed skills, energy conservation, environmental adaption, adaptive equipment</td>
</tr>
<tr>
<td><strong>Musculoskeletal</strong>: strengthening, mobilisation and manual therapy, passive range of movement and stretching, oedema control</td>
</tr>
<tr>
<td><strong>Cardiopulmonary</strong>: breathing, aerobic and conditioning exercises.</td>
</tr>
<tr>
<td><strong>Cognitive/ Perceptual/ Sensory</strong>: cognitive, perceptual, visual and sensory training</td>
</tr>
<tr>
<td><strong>Equipment</strong>: prescription/ selection, application, fabrication (serial casts, splints), ordering</td>
</tr>
<tr>
<td><strong>Modality</strong>: electrical stimulation, biofeedback, hot or cold therapy</td>
</tr>
<tr>
<td><strong>Education</strong>: patient, family, caregiver, staff</td>
</tr>
<tr>
<td><strong>Assistive device</strong>: cane, crutches, parallel bars, swiss ball, tray table, walker, wheelchair</td>
</tr>
<tr>
<td><strong>Area involved</strong>: upper extremity, trunk</td>
</tr>
</tbody>
</table>

Adapted from De Jong 2004 [55]. CIMT: constraint induced movement therapy. Activities relating to: (1) *performance skill or body structure and function; (2) ‡gait; (3) †personal care tasks and home management; and (4) #community participation and leisure.
Concordance between the total number of sessions for which therapy documentation forms were completed and the total number of occupational therapy and physiotherapy sessions attended according to the hospital computerised health management system was determined.

6.2.3. Evaluating participant experience

Participants’ experiences with the rehabilitation programs were assessed using questionnaires. Participants were asked to rate the degree to which the program addressed and contributed to goal achievement, translation of skills learnt in everyday life and overall satisfaction.

6.2.4. Outcome measurement

Information provided in the therapy documentation forms was used to determine the following:

1. program and session data: median program duration (weeks); number and intensity of therapy sessions in total and per discipline (occupational therapy and physiotherapy); therapy time (hours) in total and per discipline, mean session duration (minutes), and percentage of co-treatment and group sessions
2. intervention content: percentage of total therapy time spent in each occupational and physical therapy rehabilitation activity and activity category, percentage of participants spending time in each activity and percentage of total sessions during which interventions were used to facilitate the three occupational and physical therapy activities that most time was spent in
3. therapists: discipline, level of expertise (e.g., qualified therapist, assistant, or student).

Participant goals were categorised as described above and the percentage of total goals relating to each category, and upper or lower limb, was determined.

6.2.5. Data Analysis

Data was entered into Microsoft Excel database and exported into Stata version 12 (StataCorp, TX, USA) for analysis. Descriptive statistics were presented as mean
and SD for continuous normally distributed data, median and IQR for skewed or ordinal data and N (%) for categorical data. P-values < 0.05 indicated statistical significance. Sub-analysis was carried out for groups based on the limb or limbs injected (i.e., upper and lower limb, upper limb and lower limb).

Program duration (weeks) was calculated by dividing the number of days from first and last session, inclusive, by seven. Therapy intensity was defined as the number of sessions divided by program duration (sessions per week). The total amount of therapy time for each activity (addition of time spent in the activity by each participant) and activity category was converted to a percentage of total therapy time across all participants and sub-groups.

6.3. Results

6.3.1. Participants and baseline data

Of the 59 participants recruited to the larger study [237], between January 2011 to June 2012, therapy documentation forms were completed for 47 participants (median age 60.7 years and 2.0 years post stroke) (Table 6.1), documenting 285 occupational therapy sessions and 640 physiotherapy sessions (total 925 sessions). The only significant baseline difference was a shorter median time since stroke (1 (IQR = 0.5 to 1.7) year) in the lower limb group compared with other groups (p = 0.004) (Table 6.1). While this group received more physiotherapy sessions in total (p = 0.019), there was no significant difference in program duration and total number of therapy sessions (Table 6.2).
Table 6.1. Baseline characteristics of all participants and sub-groups based on limbs injected with BoNT-A

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All  (N = 47)</th>
<th>ULLL (N = 15)</th>
<th>UL  (N = 19)</th>
<th>LL  (N = 13)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic factors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex male, N (%)</td>
<td>34 (72.3)</td>
<td>10 (71.4)</td>
<td>13 (68.4)</td>
<td>11 (78.6)</td>
</tr>
<tr>
<td>Age (years), median (IQR)</td>
<td>60.7 (47.5–68.3)</td>
<td>59.3 (47.5–69.5)</td>
<td>61.9 (45.9–68.3)</td>
<td>59.9 (50.7–65.2)</td>
</tr>
<tr>
<td>Time since stroke (years), median (IQR)</td>
<td>2.0 (1.1–4.0)</td>
<td>3.0 (1.4–5.4)</td>
<td>2.5 (1.8–7.2)</td>
<td>1.0 (0.5–1.7)*</td>
</tr>
<tr>
<td><strong>Clinical characteristics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke aetiology, N (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infarct</td>
<td>34 (73.90)</td>
<td>12 (85.7)</td>
<td>10 (55.6)</td>
<td>12 (85.7)</td>
</tr>
<tr>
<td>Haemorrhage/mixed</td>
<td>12 (25.5)</td>
<td>2 (14.3)</td>
<td>8 (44.4)</td>
<td>2 (14.3)</td>
</tr>
<tr>
<td>Stroke localisation, N (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cortical</td>
<td>38 (80.9)</td>
<td>12 (85.7)</td>
<td>14 (73.7)</td>
<td>12 (85.7)</td>
</tr>
<tr>
<td>Subcortical</td>
<td>12 (25.5)</td>
<td>4 (28.6)</td>
<td>6 (31.6)</td>
<td>2 (14.3)</td>
</tr>
<tr>
<td>Dominant side effected, N (%)</td>
<td>29 (61.7)</td>
<td>10 (71.4)</td>
<td>9 (47.4)</td>
<td>10 (71.4)</td>
</tr>
<tr>
<td>Living arrangements, N (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Friends or family</td>
<td>41 (87.2)</td>
<td>12 (85.7)</td>
<td>16 (84.2)</td>
<td>13 (92.9)</td>
</tr>
<tr>
<td>Alone</td>
<td>2 (4.3)</td>
<td>1 (7.1)</td>
<td>1 (5.3)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Other</td>
<td>4 (8.5)</td>
<td>1 (7.1)</td>
<td>2 (10.5)</td>
<td>1 (7.1)</td>
</tr>
</tbody>
</table>

*P-value > 0.05. BoNT-A, botulinum toxin type A; UL, upper limb; LL, lower limb; ULLL, upper and lower limb; IQR, interquartile range.
6.3.2. Completion of therapy documentation forms

Concordance between the number of sessions for which therapists’ completed therapy documentation forms and those actually attended by a sample of 22 participants was 68.8%.

6.3.3. Program and session characteristics

Table 6.2 shows program and session characteristics using data from the therapy documentation forms. The upper limb group received significantly more occupational therapy and the lower limb group more physiotherapy per participant compared with other groups (Table 6.2).
Table 6.2. Program and session characteristics per participant

<table>
<thead>
<tr>
<th></th>
<th>All (N = 47)</th>
<th>ULLL (N = 15)</th>
<th>UL (N = 19)</th>
<th>LL (N = 13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Program duration, weeks</td>
<td>10.0 (8.0 - 12.7)</td>
<td>10.0 (8.0 - 12.7)</td>
<td>9.6 (7.9 - 10.9)</td>
<td>12.7 (9.0 - 14.1)</td>
</tr>
<tr>
<td>Total sessions</td>
<td>17.0 (10.0 - 26.0)</td>
<td>17.0 (10.0 - 26.0)</td>
<td>18.0 (9.0 - 30.0)</td>
<td>17.0 (13.0 - 26.0)</td>
</tr>
<tr>
<td>Total number of sessions by discipline</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occupational therapy</td>
<td>3.0 (0 - 10.0)</td>
<td>4.0 (0 - 9.0)</td>
<td>8.0 (3.0 - 18.0)*</td>
<td>0* (0 - 0)</td>
</tr>
<tr>
<td>Physiotherapy</td>
<td>12 (7.0 - 18.0)</td>
<td>12.0 (7.0 - 16.0)</td>
<td>10.0 (6.0 - 17.0)</td>
<td>17.0 (13.0 - 25.0)*</td>
</tr>
<tr>
<td>Sessions per week</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>1.5 (1.0 - 2.2)</td>
<td>1.4 (1.2 - 2.4)</td>
<td>1.7 (1.0 - 2.0)</td>
<td>1.5 (1.0 - 2.2)</td>
</tr>
<tr>
<td>Occupational therapy</td>
<td>0.4 (0 - 1.3)</td>
<td>0.3 (0 - 0.9)</td>
<td>1.4 (1.0 - 1.7)*</td>
<td>0 (0 - 0)</td>
</tr>
<tr>
<td>Physiotherapy</td>
<td>1.2 (0.8 - 1.7)</td>
<td>1.1 (0.7 - 1.7)</td>
<td>1.0 (0.7 - 1.6)</td>
<td>1.5 (1.0 - 2.1)</td>
</tr>
<tr>
<td>Total therapy time, hours</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occupational therapy</td>
<td>2.5 (0 - 9.0)</td>
<td>2.5 (0 - 9.0)</td>
<td>7.5 (3.0 - 17.7)*</td>
<td>0 (0 - 0)</td>
</tr>
<tr>
<td>Physiotherapy</td>
<td>11.8 (6.9 - 18.5)</td>
<td>11.5 (6.3 - 15.7)</td>
<td>9.5 (4.3 - 16.7)</td>
<td>18.5 (13.3 - 24.6)*</td>
</tr>
<tr>
<td>Occupational therapy and physiotherapy</td>
<td>16.3 (9.6 - 30.8)</td>
<td>15.8 (9.6 - 25.7)</td>
<td>16.3 (7.8 - 30.4)</td>
<td>18.5 (13.3 - 24.8)</td>
</tr>
<tr>
<td>Duration of sessions, mins</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occupational therapy</td>
<td>50.9 (9.6)</td>
<td>49.9 (9.8)</td>
<td>53.0 (16.6)</td>
<td>42.5 (10.6)</td>
</tr>
<tr>
<td>Physiotherapy</td>
<td>56.8 (6.6)</td>
<td>56.3 (8.4)</td>
<td>54.9 (6.3)</td>
<td>59.7 (2.8)</td>
</tr>
</tbody>
</table>

Data are either median (IQR) or mean (SD). *P < 0.05. ULLL, upper and lower limb; UL, upper limb; LL, lower limb; IQR, interquartile range; SD, standard deviation. #Two participants who had lower limb botulinum toxin type A injections had occupational therapy.
6.3.4. Intervention content

Rehabilitation activities

Figure 6.1 shows the proportion of total therapy time all participants and subgroups spent in the various physical and occupational therapy activities. For all participants most time was spent in upper extremity control, followed by physical therapy activities including interventions not related to functional activity, gait and pre-functional activity (Figure 6.1). Following upper extremity control, the next most common occupational therapy activities were interventions not related to functional activity and pre-functional activity. In the upper limb, and upper and lower limb groups most time was spent in upper extremity control activities (Figure 6.1), and 88.5% and 44% of goals related to the upper limb respectively, and the remainder to gait.
Figure 6.1. Percentage of total therapy time spent in various physical and occupational therapy rehabilitation activities for all participants and sub-groups

ULLL, upper and lower limb; UL, upper limb; LL, lower limb.

*Total therapy time defined as total time spent in physiotherapy and occupational therapy across each group.

PhysT, physical therapy; OT, occupational therapy.

Note. Activities performed for 2% or less of total therapy time in all groups were classified as:

*Other physical therapy activities (i.e., sitting and wheelchair mobility).

#Other occupational therapy activities (i.e., bathing, dressing, grooming, toileting, transfers, functional mobility, bed mobility, community integration, wheelchair management, and sitting balance and trunk control).
Rehabilitation activities and treatment goals

Table 6.3 shows the percentage of total therapy time and goals related to the activity categories for all participants and sub-groups. Most time was spent in performance skill or body structure and function impairment activities, with more than a third of goals for all groups except lower limb relating to this activity category (Table 6.3). There was a higher percentage of total therapy time and goals related to gait activities in those who had the lower limb injected (Table 6.3). Minimal time was spent in community participation and leisure activities (Figure 6.1 and Table 6.3). A small proportion of goals, except in the lower limb group (mostly related to community mobility), related to this activity category (Table 6.3). While little time was spent in personal care activities and home management, a large proportion of goals in all but the lower limb group were associated with these tasks (Table 6.3).

Table 6.3. Percentage of total therapy time and goals related to each of the activity categories for all participants and sub-groups

<table>
<thead>
<tr>
<th>Activity and goal categories</th>
<th>All (N = 47)</th>
<th>ULLL (N = 15)</th>
<th>UL (N = 19)</th>
<th>LL (N = 13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Performance skill, body structure &amp; function</td>
<td>% time</td>
<td>% goals</td>
<td>% time</td>
<td>% goals</td>
</tr>
<tr>
<td></td>
<td>53.6</td>
<td>34.5</td>
<td>45.9</td>
<td>38.7</td>
</tr>
<tr>
<td>Gait</td>
<td>16.8</td>
<td>33.8</td>
<td>22.2</td>
<td>40.3</td>
</tr>
<tr>
<td>Personal care tasks and home management</td>
<td>5.1</td>
<td>19.6</td>
<td>6.8</td>
<td>19.4</td>
</tr>
<tr>
<td>Community participation and leisure</td>
<td>2.4</td>
<td>12.2</td>
<td>4.4</td>
<td>1.6</td>
</tr>
</tbody>
</table>

ULLL, upper and lower limb; UL, upper limb; LL, lower limb.
Note. Percentage of total therapy time spent in interventions not related to functional activity and formal assessment were not included.
Rehabilitation activities and limbs injected

Table 6.4 shows the percentage of participants participating in occupational and physical therapy activities for the group and sub-groups. More than 50% of all participants participated in upper extremity control activities and the upper limb was injected more often.

Table 6.4. Proportion of participants participating in occupational and physical therapy activities

<table>
<thead>
<tr>
<th></th>
<th>All (N = 47)</th>
<th>ULLL (N = 15)</th>
<th>UL (N = 19)</th>
<th>LL (N = 13)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Occupational therapy activities</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-functional activity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bathing</td>
<td>1 (2.1)</td>
<td>0 (0.0)</td>
<td>1 (5.3)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Dressing</td>
<td>5 (10.6)</td>
<td>1 (6.7)</td>
<td>3 (15.8)</td>
<td>1 (7.7)</td>
</tr>
<tr>
<td>Grooming</td>
<td>2 (4.3)</td>
<td>0 (0.0)</td>
<td>2 (10.5)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Toileting</td>
<td>3 (6.4)</td>
<td>2 (13.3)</td>
<td>1 (5.3)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Feeding and eating</td>
<td>7 (14.9)</td>
<td>0 (0.0)</td>
<td>*6 (31.6)</td>
<td>1 (7.7)</td>
</tr>
<tr>
<td>Transfers</td>
<td>7 (14.9)</td>
<td>1 (6.7)</td>
<td>4 (21.1)</td>
<td>2 (15.4)</td>
</tr>
<tr>
<td>Bed mobility</td>
<td>4 (8.5)</td>
<td>0 (0.0)</td>
<td>3 (15.8)</td>
<td>1 (7.7)</td>
</tr>
<tr>
<td>Functional mobility</td>
<td>11 (23.4)</td>
<td>1 (6.7)</td>
<td>7 (36.8)</td>
<td>3 (23.1)</td>
</tr>
<tr>
<td>Home management</td>
<td>6 (12.8)</td>
<td>2 (13.3)</td>
<td>3 (15.8)</td>
<td>1 (7.7)</td>
</tr>
<tr>
<td>Community integration</td>
<td>1 (2.1)</td>
<td>1 (6.7)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Leisure performance</td>
<td>1 (2.1)</td>
<td>1 (6.7)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Upper extremity control</td>
<td>25 (53.2)</td>
<td>8 (53.3)</td>
<td>*16 (84.2)</td>
<td>1 (7.7)</td>
</tr>
<tr>
<td>Wheelchair management</td>
<td>3 (6.4)</td>
<td>2 (13.3)</td>
<td>1 (5.3)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Sitting balance and trunk control</td>
<td>13 (27.7)</td>
<td>4 (26.7)</td>
<td>7 (36.8)</td>
<td>2 (15.4)</td>
</tr>
<tr>
<td>Intervention not related to functional activity</td>
<td>17 (36.2)</td>
<td>7 (46.7)</td>
<td>9 (47.4)</td>
<td>*1 (7.7)</td>
</tr>
<tr>
<td></td>
<td>All  (N = 47)</td>
<td>ULLL (N = 15)</td>
<td>UL  (N = 19)</td>
<td>LL  (N = 13)</td>
</tr>
<tr>
<td>------------------------------</td>
<td>--------------</td>
<td>--------------</td>
<td>--------------</td>
<td>--------------</td>
</tr>
<tr>
<td><strong>Physical therapy activities</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-functional activity</td>
<td>34 (72.3)</td>
<td>10 (66.7)</td>
<td>13 (68.4)</td>
<td>11 (84.6)</td>
</tr>
<tr>
<td>Bed mobility</td>
<td>22 (46.8)</td>
<td>6 (40.0)</td>
<td>8 (42.1)</td>
<td>8 (61.5)</td>
</tr>
<tr>
<td>Sitting</td>
<td>22 (46.8)</td>
<td>5 (33.3)</td>
<td>9 (47.4)</td>
<td>7 (53.8)</td>
</tr>
<tr>
<td>Transfers</td>
<td>23 (48.9)</td>
<td>8 (53.3)</td>
<td>9 (47.4)</td>
<td>5 (38.5)</td>
</tr>
<tr>
<td>Sit-to-stand</td>
<td>32 (68.1)</td>
<td>12 (80.0)</td>
<td>10 (52.6)</td>
<td>10 (76.9)</td>
</tr>
<tr>
<td>Wheelchair mobility</td>
<td>4 (8.5)</td>
<td>1 (6.7)</td>
<td>1 (5.3)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Pre-gait</td>
<td>37 (78.7)</td>
<td>13 (86.7)</td>
<td>11 (57.9)</td>
<td>12 (92.3)</td>
</tr>
<tr>
<td>Gait</td>
<td>39 (83.0)</td>
<td>14 (93.3)</td>
<td>*12 (63.2)</td>
<td>13 (100)</td>
</tr>
<tr>
<td>Advanced gait</td>
<td>20 (42.6)</td>
<td>6 (40.0)</td>
<td>4 (21.1)</td>
<td>*10 (76.9)</td>
</tr>
<tr>
<td>Community mobility</td>
<td>11 (23.4)</td>
<td>3 (20.0)</td>
<td>1 (5.3)</td>
<td>*7 (53.8)</td>
</tr>
<tr>
<td>Intervention not related to functional activity</td>
<td>33 (70.2)</td>
<td>12 (80.0)</td>
<td>10 (52.6)</td>
<td>11 (84.6)</td>
</tr>
<tr>
<td><strong>Formal Assessment</strong></td>
<td>25 (53.2)</td>
<td>9 (60.0)</td>
<td>10 (52.6)</td>
<td>7 (53.8)</td>
</tr>
</tbody>
</table>

Data are N (%). *P < 0.05. ULLL, upper and lower limb; UL, upper limb; LL, lower limb.

**Rehabilitation interventions**

Tables 6.5 and 6.6 show the percentage of total sessions during which interventions were used to facilitate the three occupational and physical therapy activities, respectively, in which most time was spent. Overall, 87% of participants and their caregivers received some educational intervention during at least one session (range 1 to 21) relating to any of the rehabilitation activities.
Table 6.5. Occupational therapy interventions used to facilitate the most common activities: percentage of total sessions*

<table>
<thead>
<tr>
<th>Occupational Therapy Activities</th>
<th>Pre-functional activity (N %)</th>
<th>Upper extremity control (N %)</th>
<th>Intervention not related to functional activity (N %)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Occupational Therapy Interventions</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neuromuscular</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Balance training</td>
<td>0.1</td>
<td>0.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Postural awareness</td>
<td>0.8</td>
<td>1.2</td>
<td>1.0</td>
</tr>
<tr>
<td>Motor learning</td>
<td>1.5</td>
<td>2.8</td>
<td>0.0</td>
</tr>
<tr>
<td>Neurodevelopmental therapy and Bobath</td>
<td>1.7</td>
<td>4.2</td>
<td>0.0</td>
</tr>
<tr>
<td>Adaptive or compensatory</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>One-handed skills</td>
<td>1.0</td>
<td>0.5</td>
<td>0.0</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strengthening</td>
<td>2.2</td>
<td>5.1</td>
<td>1.4</td>
</tr>
<tr>
<td>Mobilisation, manual therapy</td>
<td>2.1</td>
<td>3.6</td>
<td>1.1</td>
</tr>
<tr>
<td>Passive range of movement and stretching</td>
<td>4.9</td>
<td>8.8</td>
<td>0.9</td>
</tr>
<tr>
<td>Educational</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient</td>
<td>1.2</td>
<td>3.5</td>
<td>1.8</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exercise prescription</td>
<td>2.8</td>
<td>5.8</td>
<td>0.6</td>
</tr>
</tbody>
</table>

Data are N % of total therapy sessions. Only interventions used during at least 1.0% of total sessions and for at least one activity are included. *Total sessions: occupational therapy and physiotherapy sessions.
Table 6.6. Physical therapy interventions used to facilitate the most common activities: percentage of total sessions

<table>
<thead>
<tr>
<th>Physical Therapy Interventions</th>
<th>Pre-functional activity (N %)</th>
<th>Gait (N %)</th>
<th>Intervention not related to functional activity (N %)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Neuromuscular</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Balance training</td>
<td>3.6</td>
<td>8.1</td>
<td>3.1</td>
</tr>
<tr>
<td>Postural awareness</td>
<td>4.1</td>
<td>6.3</td>
<td>1.6</td>
</tr>
<tr>
<td>Motor learning</td>
<td>3.9</td>
<td>13.3</td>
<td>2.2</td>
</tr>
<tr>
<td>Proprioceptive neuromuscular facilitation</td>
<td>1.3</td>
<td>0.1</td>
<td>0.0</td>
</tr>
<tr>
<td>Neurodevelopmental therapy</td>
<td>9.5</td>
<td>8.6</td>
<td>1.5</td>
</tr>
<tr>
<td>Involved upper extremity addressed</td>
<td>7.0</td>
<td>1.3</td>
<td>4.1</td>
</tr>
<tr>
<td><strong>Musculoskeletal</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strengthening</td>
<td>13.4</td>
<td>5.8</td>
<td>9.4</td>
</tr>
<tr>
<td>Mobilisation</td>
<td>2.9</td>
<td>0.3</td>
<td>4.4</td>
</tr>
<tr>
<td>Passive range of movement / stretching</td>
<td>8.0</td>
<td>1.1</td>
<td>4.9</td>
</tr>
<tr>
<td>Manual therapy</td>
<td>1.8</td>
<td>0.1</td>
<td>0.3</td>
</tr>
<tr>
<td>Motor control</td>
<td>8.3</td>
<td>5.2</td>
<td>2.2</td>
</tr>
<tr>
<td><strong>Cardiopulmonary</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aerobic exercise</td>
<td>0.2</td>
<td>4.4</td>
<td>8.3</td>
</tr>
<tr>
<td><strong>Educational</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient</td>
<td>0.6</td>
<td>2.5</td>
<td>5.0</td>
</tr>
<tr>
<td>Family and caregiver</td>
<td>0.6</td>
<td>0.6</td>
<td>3.4</td>
</tr>
<tr>
<td><strong>Modality interventions</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Electrical stimulation</td>
<td>1.6</td>
<td>0.0</td>
<td>0.9</td>
</tr>
<tr>
<td><strong>Assistive devices</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemirail</td>
<td>0.0</td>
<td>1.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Walker four wheel</td>
<td>0.0</td>
<td>1.6</td>
<td>0.0</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other interventions*</td>
<td>0.4</td>
<td>1.5</td>
<td>9.4</td>
</tr>
</tbody>
</table>

Data are N % of total therapy sessions. Only interventions used during at least 1.0% of total sessions and for at least one activity are included. *Total sessions - occupational therapy and physiotherapy sessions. *Other interventions: exercise prescription, hydrotherapy, exercise bike, wobble board and pilates.
6.3.5. Delivery personnel

Of all participants 94% received physiotherapy and 62% received occupational therapy. The majority of participants in the upper and lower limb, and upper limb group received occupational therapy (N = 11/15 (73%) and N = 16/19 (84%) respectively) compared with the lower limb group (N = 3/13 (23%), p = 0.002). All participants who had lower limb BoNT-A injections had physiotherapy. Over 25% of all participants were also seen by other disciplines including orthotists, podiatrists, exercise physiologists, social workers and dieticians.

Qualified occupational therapists and physiotherapists delivered the majority of rehabilitation sessions. Allied health assistants provided a small number of sessions (ranging from 1 to 12 sessions) in occupational therapy (N = 2/47 participants) and physiotherapy (N = 11/47 participants). Group sessions accounted for just over 20% (N = 186/925) of all sessions, involving 17 participants. Co-treatment with two disciplines (occupational therapy and physiotherapy) occurred in almost 9% (N = 82/925) of sessions, all of which were group sessions, and involved over 20% (N = 10/47) of participants.

6.3.6. Environment: therapy settings

The majority of participants (N = 46/47) attended government funded, community-based rehabilitation services, while one saw a private therapist. Rehabilitation programs were centre-based except for two participants who received home-based therapy. All sessions were face-to-face contact.

6.3.7. Participant experience

Of the participants who completed questionnaires (N = 35/47), most reported that the program addressed their goals (71%) and helped to contribute to their goals being achieved (74%) to a great deal or extreme amount. Over 70% reported being able to use skills learnt during the program in everyday life to an extreme amount or great deal, up to six months but only 20% did so beyond this time frame. Overall 91% reported being very satisfied or satisfied with the rehabilitation program.
6.4. Discussion

Therapeutic activities and interventions (physical and occupational therapy) comprising individualised ambulatory rehabilitation programs following BoNT-A for spasticity in stroke survivors were explored using a standardised taxonomy [55]. This is the first study to explore current rehabilitation practices for post-stroke spasticity in such detail.

6.4.1. Overview of results

The 47 chronic (more than one year) stroke survivors had a similar median age to those in other studies [166, 178]. While the lower limb group had a significantly shorter median time since stroke at baseline, they did not receive more therapy compared with other groups. Long-term motor improvement has been shown in chronic stroke following rehabilitation [99]. In order to determine effectiveness of rehabilitation programs, the therapeutic components need to be identified.

Program characteristics varied depending on the limb injected. The upper limb group received significantly more occupational therapy and the lower limb group more physiotherapy. These results may reflect the tendency in Australia for occupational therapists to treat the upper limb and physiotherapists to treat mainly the lower limb; however there is crossover. Therapy allocation may also be influenced by availability of services and resource allocation.

The rehabilitation activities that most therapy time was spent in reflected the limbs injected, and goals to some extent; particularly in the upper limb group in relation to upper extremity control and those who had the lower limb injected where therapy and goals focused on gait activities. Minimal therapy time was spent in personal care tasks, despite a moderate proportion of goals being related to such tasks in those receiving upper limb injections. Perhaps this is because these skills are often addressed in inpatient rehabilitation programs [62, 166]. In addition, little therapy time was spent addressing community participation and leisure activities, contrary to what may be expected for ambulatory rehabilitation programs. Focal spasticity may not have resulted in significant limitation in community participation in the study cohort, except in the lower limb sub-group where over a third of goals related to community mobility. As the majority of
sessions were centre- rather than home-based, this factor in conjunction with resource limitations may have restricted the therapists’ focus on community activities. Nonetheless, translation of skills learnt in rehabilitation to the home and community environment is important in improving activity level and participation. Further studies are needed to explore how rehabilitation activities relate to goal categories [33] in this group, as diverting resources to relevant therapeutic activities may improve outcomes such as goal achievement.

A large proportion of therapy time in all groups was spent in remediating performance skills or body structure and function impairments, particularly upper extremity control, with passive range of motion being the intervention most frequently used to facilitate such activities, similar to other studies of occupational therapy in stroke rehabilitation [166, 178]. More than one-third of goals in all but the lower limb group related to performance skills or body structure and function impairments. The importance of addressing performance skill deficits and motor preparation may be due to the window of opportunity after BoNT-A to normalise motor patterns, which have previously been inhibited by spasticity, before translation into functional activities, particularly as optimal reduction of spasticity occurs before the maximum change in function [20]. Research into how therapeutic activities vary over the course of rehabilitation programs following BoNT-A and their relationship to long-term functional outcomes is warranted.

6.4.2. Use of a standardised stroke rehabilitation taxonomy to describe components of rehabilitation programs

The therapy documentation forms used in this study [36, 55, 166] combine documentation of therapeutic activities and corresponding interventions allowing the multidimensional nature and complexity of therapy to be described, whereas other tools record activities only [236]. Further studies to assess the relevance of the current taxonomy to describing similar rehabilitation programs would be beneficial. The forms, however, have inherent limitations. Firstly, they do not allow for recording of rest or inactive time, so do not reflect how intensely participants participated in therapy. This data is important in determining therapy effectiveness as greater intensity of therapy has been suggested to result in increased recovery of motor function to a varying degree [238-240] and greater
upper limb goal achievement following BoNT-A [237] after stroke. Stroke inpatients have been found to spend approximately one-third of therapy time in rest or inactivity [241], so it is also important to capture this time in ambulatory settings. In addition, the forms rely on therapists’ estimating activity time rather than an objective measure of accuracy. Therapists have been found to be inaccurate in their estimations of the time patients spend engaged in active task practice during therapy sessions [242, 243], overestimating active time by 28% and underestimating rest time by 36% [242]. Objective measures for recording therapy activity time include simple counting of repetitions of tasks or exercises [244] or using activity monitors such as accelerometers [245, 246], which also capture activity level out of therapy time in community-dwelling patients. This would be useful in determining the contribution of formal therapy time compared with home-based activity to patient outcomes.

Although the therapists who completed the therapy documentation forms received instructions and written definitions of terms, reporting reliability was not assessed due to resource limitations. Thus, interventions and activities may have been incorrectly classified. Intervention not related to functional activity was defined as activities not in direct contact with participants; however therapists recorded interventions that involved contact with participants in this section but were not related to any of the functional activities (e.g., strengthening, aerobic and conditioning exercises). Video recording of sessions and completion of forms by trained external therapists or an observer therapist [166, 247] would have enabled comparisons of accuracy of documentation. Information obtained from these methods may also have assisted in determining whether the forms capture details and multidimensionality of the rehabilitation programs and applicability to this outpatient group. This would assist in determining whether adequate information is obtained to enable effectiveness research.

Lastly, particular rehabilitation activities may have related to more than one activity (e.g., upper extremity control may have been addressed during dressing or grooming tasks). As it is not possible to categorise more than one activity per five-minute period [62], time spent in particular activities may have been underestimated.
6.4.3. Study limitations

The small number of rehabilitation centres and sample size limit the generalisability of the study findings. Due to small numbers, time spent in rehabilitation activities was examined as a percentage of the total therapy time added up for all participants and each sub-group rather than per participant, and sub-group analysis was not included for the rehabilitation interventions used. A much larger sample size would allow for analysis of all rehabilitation activities and interventions used in order to determine patterns of therapy approaches. Sub-analysis was performed based on the limb injected, rather than comparing the high-intensity versus usual care group (Study 2, Chapter 5), as the relationship between therapy components and the limb injected is more useful for clinicians and service providers.

As this study was conducted in the real-life clinical setting with limited funding, factors that influence therapy delivery such as organisational and cultural differences between the centres, and availability of resources, were not addressed.

6.5. Conclusions

This study demonstrates that a stroke rehabilitation taxonomy [55] assists in describing therapeutic interventions and activities comprising ambulatory rehabilitation programs following BoNT-A for spasticity in stroke survivors. Future larger, multicentred studies may use this approach to determine the relationship between activities and interventions and treatment goals, to identify which facets of therapy improve outcomes. Evidence-based spasticity management guidelines can then include detailed guidance on effective rehabilitation interventions after BoNT-A treatment to improve clinical practices and service delivery. Health care providers, and other funding bodies, can then be better informed about the benefits of costly rehabilitation programs in promoting greater community independence [36].
Chapter 7. Implementing and evaluating rehabilitation programs following BoNT-A injections for post-stroke spasticity: a mixed methods process evaluation study

Mixed methods, process evaluation activities nested into program implementation inform on the effectiveness, delivery and quality of implementation of high-intensity ambulatory rehabilitation programs following BoNT-A injections. A detailed description of the content of the rehabilitation programs is provided in Chapter 6 and is not repeated here.

7.1. Introduction

The development, implementation and evaluation of complex health interventions require careful consideration of not only the outcomes but also of the processes involved [192]. Process evaluation is recommended to improve understanding of underlying mechanisms related to clinicians, patients, context and intervention delivery that may affect a program results and its potential for transfer into practice [190]. Process evaluation can be defined as the scientific study of strategies to promote the systematic, widespread, sustainable and continuous adoption of clinical research findings in routine practice [192]. Ascertaining how to enhance the effectiveness, feasibility and sustainability of complex interventions is the process of implementation [248].

Process evaluations investigate the implementation, receipt and setting of an intervention and assist in determining the true implications of interventions in practice [195, 249]. Lack of impact may reflect program implementation failure rather than ineffectiveness of the program. Thus, a thorough process evaluation is needed to identify implementation problems [56]. Process evaluation can also be used to assess fidelity and quality of implementation, clarify causal mechanisms and identify contextual factors associated with variation in outcomes [56].
Process evaluation entails both qualitative and quantitative research methods. It is often the richness of qualitative methods that provides the more detailed in-depth language, context and relationships between ideas that best informs program process [250]. Strategies used to collect process-level information may include interviews, where open-ended questions regarding feelings, knowledge, opinions, experiences and perceptions are used and data recorded from focus groups and forums.

A good process evaluation plan will include a number of indicators that can be linked to program and service inputs and program and service outputs [250]. Each of the process indicators maps directly back onto the program logic model and key process evaluation questions. A program logic is a visual representation that describes a sequence of steps that need to occur for a project to meet its desired outcomes. This generally consists of identifying the inputs, activities, outputs and outcomes. Examples of service inputs include [250]:

- participants – number, health status and demographic background
- the setting where services are provided (e.g., rural or urban)
- quality of services
- intervention delivery – quantity, fidelity to plan.

Examples of service outputs (Study 3, Chapter 6) include [250]:

- units of service and service completion – quantity and type
- intervention – dosage received and satisfaction.

Program logic is a useful planning, communication and evaluation tool that articulates what the program is, what it expects to do and how success will be measured. Program logic is useful for checking the proposed program design for adequacy of cause and effect, and the reasons or assumptions behind this.

The review of the literature found that the important aspects to address in process evaluation are: sampling, recruitment, reach, acceptability and quality of the intervention, barriers and facilitators, and contextual influences [191-193]. Understanding these processes facilitates the interpretation of results and helps to explain discrepancies between expected and observed outcomes. The RE-AIM framework [194], a process evaluation tool, was selected for this study because it addresses these key areas and importantly encompasses mixed methods, which is the recommended approach for process studies [60, 192, 195]. RE-AIM has been
used to translate research into practice and to help plan programs and improve their chances of working in real-world settings [190]. RE-AIM assists in understanding the relative strengths and weaknesses of health programs by evaluating five key domains (Figure 7.1). The overall goal of the RE-AIM framework is to encourage program planners, evaluators, funders and policymakers to focus on essential program elements (including external validity) that can improve the sustainable adoption and implementation of effective, generalisable and evidence-based interventions [190]. Programs must reach a diverse and representative sample of the population at risk, must be realistic to adopt in relevant clinical settings and must be able to be implemented as planned [192].

![Figure 7.1. Five steps of program evaluation using the Reach, Effectiveness, Adoption, Implementation and Maintenance framework.](image)

Adapted from Estabrooks 2016 [190].

In this study, using qualitative and quantitative analyses, the RE-AIM framework informs the evaluation of processes relating to the effectiveness and implementation of a high-intensity ambulatory rehabilitation program compared with usual care. The main objective of this study is to identify implementation and process issues that may influence effectiveness and outcomes of rehabilitation programs following BoNT-A injections for adults with spasticity.
7.2. Methods

7.2.1. Study design

This is an observational, descriptive process study comprising quantitative and qualitative methods.

7.2.2. Participants and setting

Participants (N = 59) were recruited from a Spasticity Management Clinic, as described in Study 2 (Section 5.2.1) and participated in ambulatory rehabilitation programs following BoNT-A injections (Sections 5.2.2 and 5.2.3). Rehabilitation programs were described in detail for participants for whom therapists completed therapy documentation forms for (N = 47; Study 3). After completion of study assessments, therapists and participants were contacted by phone and invited to complete a brief verbal questionnaire to assess their experiences with the programs (Appendix 4).

7.2.3. Program logic

Figure 7.2 outlines the program logic for ambulatory rehabilitation programs including the program inputs, activities and impacts. The program logic was developed and reviewed at different times in the program cycle: before the program started, during implementation and as part of the program evaluation.
Figure 7.2. Program logic diagram.
7.2.4. Data collection methods: Key process (RE-AIM) evaluation questions

Quantitative and qualitative data collection methods are discussed in Section 3.5.2. Quantitative and qualitative data were collected relating to the following processes:

- **Reach** – the absolute number, proportion, and representativeness of individuals who are willing to participate in a given initiative [190] and participant recruitment.
- **Effectiveness** – the impact of an intervention on important outcomes (including potential negative effects, quality of life and economic outcomes [190]) and detail of what the intervention comprised. Refer to Section 5.2.2 for details of outcome assessment procedures and Section 5.2.4 for details of patient-centred outcome measures (Study 2). Refer to Section 6.2 for procedures relating to completion of therapy documentation forms and Section 6.2.4 for outcome measures to describe components of rehabilitation programs (Study 3).
- **Adoption** – the absolute number, proportion representativeness of settings and staff who are willing to initiate a program; adherence and attitudes of staff to the intervention; and participant recruitment, adherence levels and drop outs.
- **Implementation** – the therapist’s attitudes and fidelity at the setting level to the various elements of an intervention’s protocol, including consistency of delivery as intended, the time and cost of the intervention, and adaptations made during delivery [190]. At the individual level, implementation refers to participants’ use of the intervention strategies and attitudes to the intervention [190].
- **Maintenance** – the extent to which a program or policy becomes part of the routine organisational practices and policies [190]. At the individual level, maintenance is the long-term effects of a program on outcomes six or more months after the most recent intervention contact [190].
Table 7.1 summarises the key evaluation questions for which data was collected in this study.

Table 7.1. Process evaluation questions related to RE-AIM domains and associated data collection tools

<table>
<thead>
<tr>
<th>RE-AIM domains</th>
<th>Key evaluation questions</th>
<th>Data collection tools</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reach</td>
<td>How is the targeted population reached with the intervention?</td>
<td>Description of recruitment methods (Study 2)</td>
</tr>
<tr>
<td></td>
<td>How well did the intervention reach all those who are potentially eligible for the intervention?</td>
<td>Screening and recruitment data and dropout rates (Study 2)</td>
</tr>
<tr>
<td>Effectiveness</td>
<td>Did the program achieve its intended objectives (i.e., improve patient-centred outcomes)?</td>
<td>Quantitative outcome measures (Study 2)</td>
</tr>
<tr>
<td></td>
<td>Was the program responsible for the outcomes that actually occurred?</td>
<td>Participant and therapist interviews on the phone or in person (qualitative questionnaires; Study 4)</td>
</tr>
<tr>
<td></td>
<td>What intervention activities took place?</td>
<td>Therapy documentation forms to capture types of treatments (activities and interventions; Study 3)</td>
</tr>
<tr>
<td></td>
<td>Who conducted the intervention activities?</td>
<td>Descriptive data on therapist discipline and expertise (Studies 2 and 3)</td>
</tr>
<tr>
<td>RE-AIM domains</td>
<td>Key evaluation questions</td>
<td>Data collection tools</td>
</tr>
<tr>
<td>----------------</td>
<td>------------------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Adoption</td>
<td>What were the attitudes and beliefs of staff towards the intervention?</td>
<td>Interviews on the phone or in person (qualitative questionnaires; Study 4)</td>
</tr>
<tr>
<td></td>
<td>Was the intervention adopted by treating clinical staff?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>How relevant and useful were the therapy documentation forms?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Was the intervention adopted by participants?</td>
<td>A priori compliance with outpatient treatment, (i.e., attendance in over 70% of scheduled therapy sessions; Study 2)</td>
</tr>
<tr>
<td></td>
<td>What were the attitudes and beliefs of participants towards the intervention?</td>
<td>Interviews on the phone or in person (qualitative questionnaires; Study 4)</td>
</tr>
<tr>
<td>Implementation</td>
<td>To what extent was the intervention implemented as planned (i.e., expected therapy intensity, and session and program duration as per protocol)?</td>
<td>Mean (SD) number of one-hour sessions per week and program duration in weeks (Study 2; N = 59)</td>
</tr>
<tr>
<td></td>
<td>Was the program relevant (i.e., goal directed and useful)?</td>
<td>Data collected using therapy documentation forms (Study 3) to calculate: total therapy time (hours, median, interquartile range) provided per participant (N = 47) and duration of therapy sessions (minutes, mean (SD)) including time spent in rehabilitation activities</td>
</tr>
<tr>
<td></td>
<td>What were the barriers and enablers to program delivery?</td>
<td>Therapy documentation forms to capture types of treatments (activities and interventions) provided and relationship with goals (Study 3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Interviews on the phone or in person (qualitative questionnaires; Study 4)</td>
</tr>
<tr>
<td>RE-AIM domains</td>
<td>Key evaluation questions</td>
<td>Data collection tools</td>
</tr>
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<td>----------------</td>
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<td>-----------------------</td>
</tr>
<tr>
<td></td>
<td>Were there adaptations made during program delivery?</td>
<td>questionnaires) to evaluate participant and therapist opinions on relevance of therapy to treatment goals, barriers and enablers to implementation, program adaptations and strength and weakness of rehabilitation programs</td>
</tr>
<tr>
<td></td>
<td>What were the strengths and weaknesses of the programs and areas that need improvement?</td>
<td>Calculation of direct costs for provision of rehabilitation programs</td>
</tr>
<tr>
<td></td>
<td>How did participants experience the programs?</td>
<td>Interview (face-to-face) with Community Therapy Services manager at the recruiting hospital interviews (qualitative)</td>
</tr>
<tr>
<td></td>
<td>What were the treatment costs?</td>
<td>Interview (face-to-face) with Community Therapy Services Manager at the recruiting hospital</td>
</tr>
<tr>
<td></td>
<td>What inputs or resources were allocated or mobilised for program implementation?</td>
<td>Refer to Figure 7.2</td>
</tr>
<tr>
<td></td>
<td>How did external factors influence program delivery?</td>
<td></td>
</tr>
<tr>
<td>Maintenance</td>
<td>Is long-term implementation feasible?</td>
<td>Interview (face-to-face) with Community Therapy Services manager at the recruiting hospital</td>
</tr>
<tr>
<td></td>
<td>Was the data used to change practice?</td>
<td>Participant questionnaires to identify long-term perceived benefits (Section 7.3.4)</td>
</tr>
<tr>
<td></td>
<td>What were the long-term benefits for participants?</td>
<td></td>
</tr>
</tbody>
</table>
7.2.5. Data collection: questionnaires and interviews

Questionnaires (Appendix 4) comprised both open-ended questions and closed questions where interviewees were asked to rate the degree of impact using descriptive numerical rating scales.

Participants were asked to rate the degree to which the program addressed and contributed to their goal achievement and translation of skills learnt in everyday life in the short- and long-term (up to 12 months) on a scale of 1 (not at all) to 5 (extreme amount), and their overall satisfaction on a scale of 1 (very dissatisfied) to 5 (very satisfied). An open-ended question was used to assess whether any difficulties were encountered with the program.

Similarly designed therapist questionnaires (using the same scales described for the participant questionnaires) assessed the extent to which the therapists felt that the therapy programs were implemented as planned, were relevant to participant goals, to what extent participants benefited given the resources allocated and the therapist’s satisfaction with the delivery of the program. Open-ended questions were used to determine strengths and weaknesses of the programs, barriers or enablers to program implementation, their attitudes and beliefs towards the intervention, and any recommendations for changes to implementation processes.

The usefulness of therapy documentation forms was evaluated using questionnaires to determine to what extent the forms captured program details, relevance to the study population, degree of burden and limitations (Appendix 4).

Face-to-face meetings were conducted in the planning and implementation phases with the Community Therapy Services manager at the recruiting hospital (where the high-intensity rehabilitation was provided) to discuss issues related to implementation and maintenance.

7.2.6. Data analysis

Data analysis methods for outcomes relevant to Studies 2 and 3 are described in Section 5.2.5 and Section 6.2.5, respectively. Qualitative analysis of participants’ and therapists’ experiences with the intervention and perceived benefits was based on the semi-structured questionnaires (Appendix 4). The proportions of
participants and therapists who provided the most common responses to the numeric scales were calculated.

7.3. Results: participants and setting

Demographic and clinical data for the whole study population (N = 59) is shown in Table 5.1 (Chapter 5). There were no significant differences between the usual care and high-intensity therapy group, in terms of gender, age, educational level, and living arrangements. This was despite the high-intensity rehabilitation program being implemented only at the recruiting hospital, while other centres provided the usual care. All participants attended government-funded community-based rehabilitation services, except for one who attended a private practice.

Almost 60% (N = 35/59) of the participating patients completed questionnaires to evaluate process factors (Appendix 4); these were conducted one-on-one either in person or over the phone. Of those remaining, five were deceased, 12 were non-contactable and seven declined without providing reasons. High-intensity rehabilitation programs were completed by 57% (N = 20/35) and usual care low-intensity programs by 43% (N = 15/35) of the participants who completed questionnaires.

Five of a potential nine therapists at the recruiting hospital were interviewed; the remaining four therapists were not contactable due to overseas travel, leaving the service or changing jobs. Three therapists who provided low-intensity usual care therapy completed questionnaires.

7.4. Results: RE-AIM framework

7.4.1. Reach: how well did the intervention reach the target population?

The target population was community-based stroke survivors with a spasticity-related clinical problem. Recruitment occurred at a spasticity management clinic in metropolitan Melbourne, where many of the participants were already attending, while others were new referrals from therapists, general practitioners or specialists. To increase awareness of the program (Study 2, Chapter 5) and to facilitate study recruitment through new referrals to the clinic, the principal
investigator (MD) conducted information presentations to therapists at the recruiting hospital and surrounding rehabilitation centres. Letters were sent to potential referring doctors informing them of the research being conducted and to clinic patients inviting them to participate.

Almost 80% of patients screened were recruited (N = 59/75; Study 2). Need for treatment with BoNT-A was determined by a rehabilitation physician who was experienced in spasticity management. Of those screened, 15 did not meet the study inclusion criteria, mostly due to not having a clinical indication for BoNT-A injections at the time of assessment, and one declined to participate because they resided in a rural area and did not want to attend additional appointments (see Figure 5.1 for study flow diagram). Non-English speaking people were included in the study. Given the high participation rate the study sample was representative (defined as the similarity or differences between those who participate and those who are eligible but do not [190]) of the defined population. The reach of the intervention to the eligible population was excellent based on the participation rate.

7.4.2. Effectiveness: what was the impact of the intervention on important outcomes?

Patient-centred outcomes

Effectiveness of high-intensity rehabilitation programs compared with usual care has been considered in detail in Chapter 5 (see Table 5.4 for results). In brief, benefits in terms of goal achievement (the primary outcome) were demonstrated in both groups, with the high-intensity group achieving more upper limb goals at 24 weeks compared with the usual care group. Participant satisfaction with treatment improved throughout the study in both groups. No significant differences between groups were demonstrated for secondary measures of activity and participation at any time point. Nor were there any benefits in terms of quality of life (measured using the WHO-QOL BREF) in either group (Table 7.2). The reasons for failing to demonstrate a significant difference between high- and low-intensity intervention groups has been discussed in Chapter 5. Reasons include: both groups had received an active intervention and the therapy difference
between groups may have been small; almost 50% of participants were engaged in a therapy program at recruitment so effects may have already been realised; the potential influence of activity outside formal therapy and potential confounding from variations in therapy approaches between rehabilitation centres.

Table 7.2. Quality of life: Change in WHOQoL-BREF score from baseline to six, 12 and 24 weeks

<table>
<thead>
<tr>
<th></th>
<th>High-intensity N = 28</th>
<th>Low-intensity N = 31</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 weeks</td>
<td>0.01 (−0.02 to 0.06)</td>
<td>0.01 (−0.05 to 0.06)</td>
<td>0.6</td>
</tr>
<tr>
<td>12 weeks</td>
<td>0.01 (−0.01 to 0.07)</td>
<td>0.02 (−0.05 to 0.05)</td>
<td>0.6</td>
</tr>
<tr>
<td>24 weeks</td>
<td>0.01 (−0.05 to 0.06)</td>
<td>0.02 (−0.05 to 0.05)</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Data are median (interquartile range). WHOQoL-BREF, World Health Organization Quality of Life.

Early on, spasticity reduction was related to a greater chance of achieving at least 50% of goals, suggesting that BoNT-A played a significant role. But this relationship did not persist beyond six weeks when benefits were likely to be related to the effects of therapy programs in both groups.

Of the participants who completed questionnaires, most reported that the program addressed their goals (N = 25/35, 71%) and helped to contribute to their goals being achieved (N = 26/35, 74%) to a great deal or an extreme amount. Responses were similar for the high-intensity and usual care groups.

**Relevance of therapy to treatment goals**

The rehabilitation programs are described in detail in Chapter 6. Most time was spent in upper extremity control activities. A large proportion of therapy time was spent in activities remediating performance skills or body structure and function impairments for all groups. This activity category was related to 39% of goals in the upper and lower limb group, 46% of goals in the upper limb group, but less than 10% of goals in the lower limb group. This suggests that the therapy provided was goal directed, as it ideally should be, at least for the upper limb. This may explain why the high-intensity group achieved more upper limb goals.
than the usual care group. Little time was spent in community participation and leisure activities for all groups, while over one-third of lower limb group goals related to this category. Reasons for this are resource limitations in conjunction with the therapy setting being centre based, as discussed in Chapter 6. The findings imply that, for those who had lower limb BoNT-A injections, the therapy may not always have been directly relevant to their community mobility goals.

**Personnel**

The characteristics of the therapists, such as their discipline, are provided in Section 5.3.4 (Study 2) and Section 6.3.5 (Study 3). All tertiary hospital-affiliated services have similar resources in terms of therapist disciplines.

**7.4.3. Adoption: how well was the intervention adopted by staff, participants and services?**

**Adoption by staff**

Therapists at the recruiting hospital stated that they were positive about providing high-intensity therapy, despite the increased resources and time required. The therapists felt that it would be beneficial for the patients’ outcomes and a favourable research finding may facilitate more funding for Community Therapy Services. The therapists were very motivated to ensure that participants received the required intensity of therapy and implemented strategies to overcome barriers to implementation (Table 7.3).

One therapist commented that there was ‘significant benefit as increased therapy allowed more one-on-one contact with the patient especially when the patient needed clinically relevant therapy techniques by a therapist rather than group setting’. Another therapist felt that compliance with home exercise programs might have been reduced due to the increased frequency of therapy sessions. The overall positive attitude of therapists towards the intervention suggests that it was well adopted.
Adoption by participants

The rehabilitation program was completed by 98% of participants as per a priori compliance (attend at least 70% of planned therapy sessions), which is an extremely high adoption rate. This was despite a few participants expressing concerns that it would be challenging to attend sessions three times per week.

Adoption by settings

Widespread implementation of high-intensity therapy was beyond the scope of this thesis. As previously discussed, only the recruiting rehabilitation centre provided high-intensity therapy. However, almost all participants attended government-funded hospital or community-based rehabilitation services for therapy programs, while one attended a private therapist. The majority of services were located in western and metropolitan Melbourne. If an intervention is in widespread use but differential adoption exists, comparisons between services that do and do not adopt the intervention should be made on basic information such as resource availability, setting size or location, and interventionist expertise.

Relevance and use of therapy documentation forms

Therapists’ completion rate for the therapy documentation forms was 69% of total sessions conducted, based on a sample of 22 participants (Section 6.3.2), and over 70% (N = 11/15) of therapists completed the forms. Therapists’ experiences in using the forms varied with respect to how burdensome the forms were to complete for each therapy session, with time taken ranging from a small amount to great deal. Therapists reported that the therapy documentation forms captured details of the program to a moderate amount or great deal and were relevant to the study group to a moderate amount. Limitations in using the forms for the study participants were not being able to capture the positions the exercises were performed in and inability to capture techniques that are not as prescriptive, such as facilitation and documenting interventions that were relevant to multiple activity categories (e.g., pre-functional activity and upper extremity control). A suggestion was made to devise a way that information could be obtained from
routine therapy progress notes and clinical statistics to reduce duplication of documentation tasks.

Therapists rated the degree to which the therapy documentation forms captured the details (activities and interventions) of the program as a moderate amount (N = 6/8, 75%) or great amount (N = 2/8, 25%) and they rated applicability to the patient group a moderate amount (N = 8/8). Most therapists found the forms were burdensome to complete for each session to a great extent because they were time consuming. Limitations to using the forms were difficulty in determining which category to put the interventions under because often interventions were such that they could be placed within multiple categories (e.g., pre-functional activities versus upper extremity control) and limited ability to capture interventions that are not as prescriptive, such as facilitation and the position that exercises are done in.

7.4.4. Implementation: to what extent was the intervention implemented as planned?

Therapy amount (intensity, session and program duration) as per protocol

Therapy was found to have been prescribed at the appropriate intensity of three or more one-hour sessions per week for 10 weeks (Study 2, Section 5.3.4) because participants in the high-intensity group (N = 28) attended a mean of 3.2 (SD 0.6, range 2 to 4) sessions per week for a mean duration of 11 weeks (SD 3.3, range 7.9 to 19.4); participants in the usual care group attended a mean of 1.2 (SD 0.5, range 0.7 to 2.2) sessions per week for a mean duration of 10 weeks (SD 3.9, range 1 to 20.3).

Staff time spent in direct contact with participants during therapy was thoroughly examined in Study 3 (Table 6.2) and was based on data from completed therapy documentation forms, which did not capture every session provided. The mean durations of therapy sessions, based on time spent in rehabilitation activities, assessment and evaluation, were 56.8 (SD 6.6) minutes for physiotherapy and 50.9 (SD 9.6) minutes for occupational therapy (Table 6.2). Therapist time spent on patient care outside therapy time, including tasks such as
Therapist fidelity

Because the rehabilitation programs were individualised, providing consistent therapy to all participants was not prescribed in the protocol. Most therapists (N = 4/5, 80%) claimed that the high-intensity therapy programs were implemented as planned, in terms of consistency and time, to a great extent; as did the therapists who provided usual care (N = 3/3). Overall, all the therapists were satisfied or very satisfied with the delivery of the therapy programs.

Attitudes and beliefs of therapists towards the intervention (Section 7.3.3) may also affect quality of implementation. Given the resources allocated to the high-intensity program, therapists perceived that the patients benefited to a moderate (N = 2/5, 40%) or great amount (N = 3/5, 60%).

Quality of the intervention

The relevance of rehabilitation activities prescribed to treatment goals (Section 7.4.2) also reflects the quality of the intervention. The results of analyses in Study 3 show that rehabilitation activities reflected treatment goals to some extent, but more so for those who had the upper limb injected because a significant amount of therapy time was spent in upper extremity control. Therapists reported that the high-intensity therapy programs were relevant to the patients’ goals to a great extent (N = 3/5, 60%) or extreme amount (N = 2/5, 40%). Two of the therapists who provided usual care felt that the programs were relevant to the patients’ goals to a great extent or to an extreme amount.

The intensity at which participants participated in therapy sessions (i.e., active therapy time versus rest) is another dimension of quality of therapy sessions. However, this data was not captured using the therapy documentation forms, although recommended methods for measuring this in future research are made in Section 6.4.2.
Barriers and enablers and contextual adaptations

Potential barriers to implementing high-intensity therapy and contextual adaptations were discussed at two pre-implementation meetings between the principal investigator (MD), the Rehabilitation Medicine Director (FK) and the Community Therapy Services Manager at the recruiting hospital. Further meetings were conducted during the study to ensure service provision was being met. Table 7.3 shows strategies used to overcome the barriers to implementation identified at these meetings and during participant and therapist interviews.

Table 7.3. Program implementation barriers: strategies and contextual adaptations to overcome key issues

<table>
<thead>
<tr>
<th>System</th>
<th>Barriers</th>
<th>Enablers: implementation strategies and contextual adaptations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Administration</td>
<td>Funding constraints and lack of evidence of cost-benefit for the intervention.</td>
<td>Education provided to management staff regarding the importance of the research and potential implications.</td>
</tr>
<tr>
<td></td>
<td>Difficulty scheduling appointments to match with other therapy sessions to get the intensity or frequency and lack of appointment availability.</td>
<td>Appointment times were blocked off for study participants.</td>
</tr>
<tr>
<td>Resources – therapists</td>
<td>Competing clinical priorities and difficulty allocating therapists’ time to enable provision of at least three sessions per week.</td>
<td>An increased number of group sessions was provided and more participants attended group therapy than usual. Regular contact with therapists to provide support, ensure their commitment to providing the intervention and address any implementation issues.</td>
</tr>
<tr>
<td></td>
<td>Shortage of occupational therapists due to staffing changes and lack of resources impacting on</td>
<td>Physiotherapists provided an increased number of therapy sessions in the first four months of recruitment.</td>
</tr>
<tr>
<td>System</td>
<td>Barriers</td>
<td>Enablers: implementation strategies and contextual adaptations</td>
</tr>
<tr>
<td>--------</td>
<td>----------</td>
<td>---------------------------------------------------------------</td>
</tr>
<tr>
<td></td>
<td>participants with upper limb spasticity.</td>
<td>Study participants were prioritised to commence therapy within 14 days of BoNT-A injection.</td>
</tr>
<tr>
<td></td>
<td>Risk of overburdening the service causing delays in programs commencing for study participants and other patients and inability to provide three sessions per week.</td>
<td>Recruitment rate was controlled where possible to ensure no more than two participants were recruited per week.</td>
</tr>
<tr>
<td></td>
<td>Staff changes during the study period and requirement for therapists skilled in spasticity management.</td>
<td>Two permanent senior neurophysiotherapists were allocated to providing therapy for study participants and supervision of junior staff. Education sessions provided to new staff on completion of therapy documentation forms.</td>
</tr>
<tr>
<td>Participants and caregivers</td>
<td>Time commitment for participants who were not keen or able to attend therapy three times per week.</td>
<td>A priori compliance was attendance at over 70% of scheduled therapy sessions.</td>
</tr>
<tr>
<td></td>
<td>Accessibility - logistics and costs of parking and transport.</td>
<td>Funding for taxi transport and parking was made available.</td>
</tr>
</tbody>
</table>

Strengths of the high-intensity program identified by therapists were: ‘the opportunity to spend more time with participants, particularly one-on-one rather than group’, which was interesting considering there were more group sessions provided than in the usual care group; ‘ability to provide interventions otherwise not prioritised such as ankle foot orthosis provision and training’, and having ‘clear guidance with goal setting’.
Individual level

Over 70% (N = 25/35) of participants who completed questionnaires reported being able to use the skills learnt during the program in everyday life to an extreme amount or great deal up to six months after BoNT-A injection, but only 20% did so beyond this time frame. Of those, 80% (N = 15/20) who did high-intensity rehabilitation programs and 67% (N = 10/15) who received usual care reported being able to use the skills learnt during the program in everyday life to an extreme amount or great deal up to six months after BoNT-A injection. Overall, 91% reported being satisfied or very satisfied with the rehabilitation program.

Cost

It was not within the scope of the study to undertake a cost-effectiveness study. However, direct costs of providing rehabilitation programs were calculated based on a rate of $250 per one-hour session. This covers therapists’ time, administrative costs (e.g., staff, stationary and computer costs), utilities (e.g., lighting and electricity), and building maintenance and cleaning. The cost of providing a high-intensity rehabilitation program is $8,750 based on a mean total of 35 one-hour therapy sessions and the cost of providing usual care is $3,000 based on a mean total of 12 one-hour therapy sessions (Section 5.3.4). The cost difference of $5,750 is significant considering the limited additional benefit demonstrated in patient-centred outcomes for the high-intensity group compared with the usual care group. Cost-effectiveness analysis would be important if widespread implementation of high-intensity therapy following BoNT-A treatment was to be considered.

Allocated resources

Additional physiotherapy time was allocated to study participants at the recruiting hospital because there was a shortage of occupational therapists for a short time during the study period (Table 7.3). Otherwise, the demands of providing high-intensity therapy would not have been met.
External factors influencing therapy delivery

Organisational factors may affect implementation of a therapy program. The recruiting rehabilitation service is likely to be similar to other government-funded tertiary hospital-affiliated ambulatory rehabilitation services throughout Melbourne in terms of model of organisation structure and size, service delivery protocols, funding, therapy setting (centre or home based), disciplines available and waiting times for therapy (which may vary between centres due to periodic fluctuations in patient loads). Service delivery protocols whereby therapy is provided to those living within geographical catchment areas influenced where the high-intensity program was delivered. However, such processes of care ensure services are easily accessible which is important in facilitating completion of the intervention. Other external factors already discussed above, are personal factors such as therapists’ and participants’ attitudes.

Appropriateness of the program logic

The program logic shows that the short-term impacts effecting participants and therapists (e.g., attitudes, self-management) can subsequently influence intermediate and long-term outcomes such as activity, participation and quality of life. While most impacts (Figure 7.2) were addressed, some were not including participants independence with home exercise programs and qualitative data obtained from caregivers regarding their experiences with the rehabilitation programs. During early recruitment participants were asked to complete a home exercise diary. Due to poor compliance prohibiting collection of meaningful data the process was ceased.

7.4.5. Maintenance: what are the long-term effects of the intervention on individuals and settings?

Long-term benefits for participants

Standardised outcome measures were completed up to six months from the time of BoNT-A injection (Study 2, Chapter 5). Participant questionnaires to identify long-term perceived benefits (Appendix 4) were conducted 12 months after
completion of therapy programs, but the benefits did not persist beyond 12 months (Section 7.3.4).

**Feasibility of long-term implementation and potential benefits for organisations**

Incorporation of the high-intensity program into routine practice and policy over time was not within the scope of this thesis. An interview was conducted with the Community Therapy Service manager at the recruiting hospital on the feasibility of routinely implementing a high-intensity rehabilitation program for individuals receiving BoNT-A injections for post-stroke spasticity. Clear barriers to this were funding restrictions, lack of adequate staffing, limited time allocation, frequent staff changes affecting level of expertise and the need to demonstrate evidence for the intervention in terms of costs and benefits. The degree to which treatments were completed (e.g., a priori compliance as presented in Section 7.3.3) may also inform the feasibility and sustainability of the rehabilitation program.

In light of the potential benefit of high-intensity programs on goal achievement in the upper limb following BoNT-A injections (Study 2) programs focusing on intensive upper limb therapy for stroke and other neurological conditions have since been developed at the Royal Melbourne Hospital. Enriched environmental programs using a stimulating environment and robotic devices that facilitate upper limb range of movement exercises, functional tasks and stretching are being implemented in inpatient and ambulatory rehabilitation services while outcomes are evaluated for research purposes and data provided to government departments. Analysis of cost-benefit is required and may be favourable as approaches requiring less hands-on therapist time have potential long-term benefits for organisations. Therapists do however require training to ensure acquisition of an adequate level of expertise.

**7.5. Discussion**

This study highlights the importance of process evaluation in determining whether issues surrounding implementation and delivery of the intervention contributed to the lack of demonstrable benefit rather than genuine ineffectiveness. This is the
first study evaluating implementation of rehabilitation programs following BoNT-A for spasticity in stroke survivors.

7.5.1. Key findings

The process evaluation provides data that shows that the intervention had very good reach, was well-adopted by participants (demonstrated by the high completion rate), was well received by therapists (who expressed positive attitudes towards high-intensity therapy), was implemented at the expected intensity and is potentially generalisable to other contexts. The reach of the screening procedures was high because patients attending a spasticity management clinic rather than a general stroke population were screened for the purposes of Study 2.

Although the benefit of providing high-intensity therapy over usual care was not clearly demonstrated, there may be a benefit for the upper limb because more goals were achieved. The influence of goal-directed therapy on this effect rather than therapy intensity requires further evaluation to determine the important modulators of the black box of rehabilitation. Provision of intensive upper limb therapy, via enriched environments, for neurological conditions has been implemented at the Royal Melbourne Hospital in view of the study finding [251]. Program implementation processes influencing outcomes following lower limb BoNT-A injections also requires further explanation. The lack of benefit of high-intensity therapy for participants who had their lower limb injected may have occurred as therapy was not always directly related to their community mobility goals. Provision of therapy in the local home environment rather than centre based therapy may be more important in achieving community mobility goals. For the lower limb injected group the amount of incidental walking in the community – outside therapy sessions – may play a greater role than the amount of therapist contact time. Activity levels outside formal therapy should be measured in future studies of rehabilitation programs to determine the influence on outcomes.

As underlined by the RE-AIM framework, key factors determining the potential impact of programs and adoption are that they must be appealing to health care providers and realistic to implement in real-life clinical practice. Factors that may influence adoption of a health intervention by staff or a clinical
setting include the amount of resources required, level of expertise available, commitment to intervention programs, evidence for effectiveness and therapists’ beliefs about the intervention. This study identified funding restrictions, lack of adequate staffing, limited time allocation, frequent staff changes affecting level of expertise and the need to demonstrate evidence for the intervention in terms of costs and benefits, as barriers to implementation of the rehabilitation program. For the duration of the study, contextual adaptations and practical strategies, such as appropriately allocating therapists’ time and administrative changes, were successful in overcoming some of these issues because the intervention was successfully delivered at the planned intensity. Additionally, a priori compliance with the intervention was achieved in all participants in the high-intensity group. Implementation barriers need to be addressed in future research to optimise intervention delivery and the rollout of the intervention in other contexts and settings.

The program was adapted so that more than normal group sessions rather than individual sessions were provided in the high-intensity group, and this may have contributed to the apparent ineffectiveness of the intervention. A clearer understanding of the influence of group therapy sessions versus individual sessions on patient-centred outcomes would be useful. Despite the provision of more group sessions, therapists who provided high-intensity rehabilitation expressed beliefs that the programs benefited participants and addressed participant goals to a large extent. Further research is required to determine whether goal-directed therapy has a greater influence on patient-centred outcomes than therapy intensity.

The feasibility of high-intensity therapy becoming part of the routine organisational practices depends on evidence for long-term costs and benefits [21]. From a patient perspective, attending three sessions per week for the duration of the rehabilitation program is challenging and not realistic for all.

Therapists’ beliefs about the intervention may have influenced their commitment to the intervention program and its delivery. Therapists believed that a high-intensity rehabilitation program would be beneficial to patients due to the increased contact time. A positive attitude towards the intervention is important in ensuring programs are implemented as planned and that quality therapy is provided.
7.5.2. Limitations

Although many aspects of program implementation were evaluated in this study, there are other factors that may have influenced effectiveness outcomes that were not addressed. Because the therapy programs were conducted at different sites, an in-depth evaluation of contextual influences on outcomes, such as organisational and cultural differences, would have been useful. Most participants attended community-based rehabilitation programs at tertiary hospitals where service delivery practices are usually similar. However, there may have been differences in staffing levels, resource availability, organisational qualities, and therapist’s experience in managing patients with spasticity, which may have affected program implementation. To identify differences in therapy approaches between centres, analysis of components of rehabilitation programs (Study 3, Chapter 6) comparing high-intensity and usual care would have facilitated this aspect of process evaluation. In considering the broader settings of ambulatory rehabilitation programs, differences between metropolitan and rural services, and between public and private services due to disparate funding sources need to be evaluated. Lack of post-injection follow-up in rural areas has been identified as a problem [43]. Further research encompassing larger multicentre trials to explore differences between centres across Melbourne and Victoria, as well as nationally and internationally, would further inform on variation in service provision in relation to spasticity management.

While qualified occupational therapists and physiotherapists delivered the majority of rehabilitation sessions, regardless of the service attended, the therapists’ experience in managing patients with spasticity and following BoNT-A injections may have been greater in centres such as the recruiting hospital where the spasticity management clinic is based. A survey of Australian therapy practices after upper limb BoNT-A injections reported that almost 28% of therapists worked some or all of the time in a spasticity management clinic; most had worked with 10 or fewer BoNT-A injected patients in their career and 10% or less of their neurology caseload were injected patients [43]. An evaluation of therapists’ level of expertise would indicate whether further training and education in spasticity management is required before program implementation to ensure high quality therapy is delivered.
Although the RE-AIM framework is a comprehensive tool for examining program delivery and effectiveness, its limitations need to be discussed. There is the potential duplication of elements in that some implementation processes may affect more than one of the five domains. For example, therapists’ expertise, beliefs and attitudes may influence effectiveness, adoption and implementation, and the degree to which treatments are completed informs on the adoption, implementation and maintenance (feasibility and sustainability) of programs. Some elements of RE-AIM, such as adoption and maintenance, were not addressed to their full extent because widespread implementation of the intervention across settings was not conducted, but where possible the relevant key questions were addressed.

There is no gold standard process evaluation tool. Instead, one most suited to the specific project needs to be chosen and tailored if necessary because often they have a broad scope. Although the Theoretical Domains Framework [252, 253], which focuses on human behaviour determinants and behavioural change as a key factor influencing implementation, is commonly used, it was not entirely relevant to the purposes of this study. The RE-AIM was considered more applicable and comprehensive because it encompasses process related to recruitment, reach, acceptability and quality of the intervention, barriers and facilitators, and contextual influences.

In critically appraising the process evaluation in this study, the data analysis may not be considered to be trustworthy because the evaluator (MD) was also the principal investigator of the previous studies investigating effectiveness and components of rehabilitation programs after BoNT-A injections (Studies 2 and 3). It is debateable whether the evaluator should be part of the overall project team or whether they should take on the role of a neutral and detached observer [193] to avoid bias. The complexities of how researchers construct and interact with data when conducting qualitative research, and the evaluator’s role in interpreting findings and conclusions, need to be carefully considered in future process and implementation research [193]. However, strengths in the methodology of this study are the use of a formal evaluation framework and well-defined statements of the evaluative research questions and the presentation of clear results, whereas other evaluation studies have simply made a series of evaluative comments in support of the intervention [193, 254].
Some aspects of process evaluation in this study are based on limited numbers and may not be representative of the whole study population. The questionnaires for evaluating therapist and participant experience were conducted 12 months after completion of rehabilitation programs and not all therapists and participants could be contacted. Therefore, almost 60% of all participants and 47% of all therapists participated.

Many important impacts depicted in the program logic were measured, including goal achievement, activity and participation, quality of life, caregiver burden, and translation of skills learnt in everyday life. However, the impact on caregiver experience, participants’ improved confidence in self-management, and knowledge and performance with the home exercise program were not evaluated due to limited resources. Although a thorough cost-effectiveness analysis including calculation of quality-adjusted life years or disability-adjusted life years was not included in this study, this is of importance in future research into program effectiveness and implementation. Inclusion of a measure of quality of life that can be used to calculate these factors would be worthwhile, but unfortunately this was not possible with the WHOQoL-BREF.

A detailed description of rehabilitation programs based on information captured using a standardised stroke rehabilitation taxonomy [55] (Chapter 6) is important in evaluating complex interventions. Therapists found using the therapy documentation forms to be burdensome, and the extent to which the forms were relevant to the study population varied from a moderate to great extent. Further research is required to develop a standardised taxonomy for capturing the multidimensional aspects of ambulatory rehabilitation care for post-stroke spasticity that is relevant to treatments provided and goals of treatment. Assessing the feasibility, relevance and reliability of implementing the tool is required.

7.6. Conclusion

This study has highlighted the importance of process evaluation where the intervention is non-standardised but delivered at different rehabilitation centres. The findings have provided greater explanatory power for the outcomes of ambulatory rehabilitation programs following BoNT-A injections (Study 2, Chapter 5) and identified process factors requiring further research. The influence
of program adaptations such as provision of group rather than individual sessions, contextual or organisational differences between rehabilitation centres, therapists’ experiences with managing patients following BoNT-A injections and the effect of goal-directed therapy on outcomes needs further evaluation. The lack of clear benefit for high-intensity rehabilitation improving patient-centred outcomes (Study 2) may not be due to genuine ineffectiveness. Implementing a high-intensity rehabilitation program in the public hospital setting is challenging due to limited funding and resources and logistical difficulties. Thorough cost-effectiveness analysis would also be critical in informing on the effectiveness and whether implementation of high-intensity rehabilitation programs is warranted.

Chapter 8 discusses the findings of the four studies and draws on the conclusions of this thesis.
Chapter 8. Discussion and conclusions

This chapter discusses the findings of the four studies (Chapters 4 to 7), limitations of the methodology, and implications for clinical practice and future research.

8.1. Overview of the thesis

Mixed methods were used in the four studies to address issues in rehabilitation management following BoNT-A injections for post-stroke spasticity. The overall objective of the thesis was to determine whether multidisciplinary rehabilitation programs following BoNT-A injections for post-stroke spasticity improve patient-centred outcomes. This was undertaken to formulate recommendations to optimise clinical care and for future research in this field.

8.2. Key issues addressed and summary of findings

8.2.1. Evidence for multidisciplinary rehabilitation following BoNT injections for post-stroke spasticity

Key issue 1

Despite expert opinion that comprehensive multidisciplinary rehabilitation programs should be implemented following BoNT injections for post-stroke spasticity, the scientific evidence for this is unclear. To determine the current evidence base for multidisciplinary rehabilitation, the following questions were explored in Study 1 (Chapter 4):

- Does coordinated multidisciplinary rehabilitation achieve better outcomes than the absence of these services in persons with post-stroke spasticity?
- What types of rehabilitation programs are effective, and in which setting?
- Does a greater intensity (time, expertise or both) of rehabilitation lead to better outcomes?
Summary of findings

The systematic review (Study 1, Chapter 4) found low level evidence at best for the effectiveness of outpatient multidisciplinary rehabilitation in improving active function and impairments following BoNT-A injections for upper limb spasticity in adults with chronic stroke. Aside from the paucity of research, this review highlighted the following key deficits in the literature:

- There is heterogeneity in the interventions used (type and intensity), methodological approaches, participant selection criteria and measures of improvement. This and the lack of person-centred outcomes limits comprehensive meta–analyses.
- There is a lack of detailed description of the intervention, which prohibits replication in the clinical setting and effective comparisons of interventions.

None of the trials explored the effect of multidisciplinary rehabilitation on passive function (caring for the affected limb), community participation, goal achievement, caregiver burden and quality of life, which are important outcomes of spasticity management [6, 21, 33, 196, 255], as discussed in Chapters 1 and 2. There was no evidence for benefits of multidisciplinary rehabilitation programs compared with the absence of these services, in different settings, for lower limb spasticity or in children with stroke. Despite some evidence for the effectiveness of multidisciplinary rehabilitation interventions for upper limb spasticity (e.g., CIMT) in adults with chronic stroke, many aspects of multidisciplinary care for people with post-stroke spasticity remain unproven. The optimal types (modalities, therapy approaches and settings) and intensities of therapy for improving activity (active and passive function) in adults and children with post-stroke spasticity, in the short- and longer term, are unclear.

The small number of RCTs with their low methodological quality limited the evidence base for multidisciplinary rehabilitation following BoNT-A injections for post-stroke spasticity. The results of this review do not imply that multidisciplinary rehabilitation after BoNT-A and other intramuscular injections for post-stroke spasticity is ineffective, but rather the results emphasise the need for further research to better define the black box of rehabilitation.
**Comparison with other reviews**

Limited evidence for the effectiveness of the intervention has been found in other reviews. Heterogeneous, poor to moderate quality studies only provide low level evidence for physical activity programs having beneficial effects on spasticity outcomes in people with multiple sclerosis [256], and no demonstrable overall impact of rehabilitation therapies after BoNT-A injection for limb spasticity [35]. These other reviews focused on uni-disciplinary or single treatment modalities, such as electrical stimulation, stretching and manual exercises only, rather than multidisciplinary rehabilitation that reflects the real-life clinical approach. These reviews also found that treatment protocols differed across studies and were poorly described.

Systematic reviews of multidisciplinary rehabilitation interventions in other neurological conditions found strong evidence for intensive inpatient rehabilitation improving levels of activity and participation, and moderate or limited evidence for less intensive outpatient rehabilitation improving levels of activity and participation in multiple sclerosis [214], acquired brain injury [215] and stroke [177, 257].

**8.2.2. Examining the black box of rehabilitation: effect of therapy intensity on patient-centred outcomes**

**Key issue 2**

The optimal types (activities, interventions, modalities, therapy approaches and settings) and intensities of therapies for achieving meaningful patient outcomes following BoNT-A injections for post-stroke spasticity remain unclear. Thus, these elements are known as the black box of rehabilitation because the aspects of rehabilitation that influence outcomes have not been determined. Study 2 (Chapter 5) examines the benefits of high-intensity rehabilitation programs over low-intensity usual care ambulatory rehabilitation programs following BoNT-A injections in adults with upper or lower limb post-stroke spasticity.
Summary of findings

In this study, both groups showed improvement in patient-centred outcomes including goal attainment and satisfaction up to 24 weeks, even after cessation of therapy and the effects of BoNT-A wearing off. However, there were no statistically significant differences between groups. There was evidence of better attainment of upper limb goals for participants in the high-intensity therapy group, but therapy intensity did not modify post-injection outcomes for the lower limb. Further research is required to evaluate this effect in the upper limb and determine which components of therapy optimise outcomes. Evaluation of cost-effectiveness of high-intensity therapy is required as it would be very difficult to justify service enhancement to provide intensive multidisciplinary rehabilitation for all patients following BoNT-A injections particularly for little, or no, clinical benefit.

This study highlights the challenges faced when investigating effectiveness of complex interventions in the real-life clinical setting, as discussed in Section 8.2.5.

Comparison with other studies

This is the first study to compare the entire package of individualised, comprehensive multidisciplinary rehabilitation programs of different intensities (time) following BoNT-A injections for stroke survivors with problematic spasticity.

In this study, older participants showed reduced benefit in terms of goal achievement at 12 weeks. Similarly, a study comparing BoNT-A and standard care versus placebo and standard care demonstrated that younger patients were more likely to demonstrate goal achievement than older patients [258]. Both studies demonstrated that improvements in activity related to goals can be achieved even in chronic (> 1 year) stroke patients [258].

Significantly greater principal active functional goal achievement in patients with upper limb spasticity has been shown for BoNT-A and standard care compared with placebo and standard care, with no difference between treatment
groups in terms of GAS scores for lower limb goals [258]. Different capacities for upper versus lower limb functional achievements after stroke may be related to differing potential for neural and muscle plasticity responsiveness [258]. Spinal reflexes are important in neural control of gait, whereas higher centres control find hand movements [258]. These findings may partially explain the study results where there was a strong trend towards upper limb injected participants in the high-intensity therapy group achieving more goals compared with usual care, with no such observed effect for lower limb treated participants. Sub-group analysis comparing outcomes for active versus passive upper limb goal achievement would be useful in determining which types of patients benefit most, however this was not possible due to the sample size.

The studies identified in the Cochrane review (Study 1, Chapter 4) compared multidisciplinary interventions in stroke survivors with upper limb spasticity based on specific selection criteria (e.g., those with residual upper limb motor activity [117]). In comparison, the heterogeneous study population in Study 2 also included those with non-functional upper limbs, as reflected by treatment goals related to passive function. The three studies included in the review compared different therapy approaches (CIMT versus neurodevelopmental therapy) [117] or multidisciplinary therapy programs with the comparison group receiving an additional intervention (e.g., dynamic elbow splinting [170] or functional electrical stimulation [168]).

8.2.3. Describing the black box of rehabilitation: use of a standardised stroke rehabilitation taxonomy

Key issue 3

While spasticity management guidelines recommend multidisciplinary rehabilitation following BoNT-A injections, there is a lack of information on what the treatment actually encompasses. Studies in this setting rarely describe details of treatment protocols beyond their duration, frequency and generic broad therapy terms, making replication in a clinical setting difficult. In addition, therapy interventions are often investigated in isolation rather than in the milieu of the complex array of rehabilitation interventions provided in everyday clinical
practice. Before the components of rehabilitation management that influence outcomes following BoNT-A injections are able to be determined, a detailed, structured and standardised approach for describing complex rehabilitation interventions needs to be established.

Study 3 (Chapter 6) delves into the black box by using a stroke rehabilitation taxonomy [55, 63] to capture the components (physical and occupational therapy activities and interventions) of ambulatory rehabilitation programs delivered in a real-life clinical setting of patients who have had BoNT-A injection for post-stroke spasticity. The relationships between the therapy provided, injected limb and treatment goals are explored. This is the first study to comprehensively describe therapy in this setting.

Summary of findings

The critical program attributes, including the types of activities and interventions comprising ambulatory rehabilitation programs following BoNT-A injections for post-stroke spasticity varied, to some extent, depending on the limb injected and treatment goals.

The upper limb group received significantly more occupational therapy and the lower limb group received more physiotherapy, which likely reflects the traditional approach for occupational therapy to focus on upper limb function in daily activities and for physiotherapy to focus on gait. The rehabilitation activities that most therapy time was spent in reflected the limb injected in the upper limb group in relation to upper extremity control and in the lower limb group where therapy and goals focused on gait activities. Surprisingly, in all groups, little therapy time was spent addressing community participation and leisure activities, especially considering that participants resided in the community. In the lower limb sub-group, over one-third of goals related to community mobility. In all groups, a large proportion of therapy time was spent remediating performance skills deficits or body structure and function impairments, particularly upper extremity control. This reflected the large proportion of goals related to this activity category in all but the lower limb group.

This study demonstrates that a stroke rehabilitation taxonomy [55] assists in describing therapeutic interventions and activities comprising ambulatory
rehabilitation programs following BoNT-A injections for spasticity in stroke survivors. Furthermore, the relevance of therapeutic activities provided to treatment goals can be analysed.

**Comparison with other studies**

While this is the first study to provide a detailed analysis of the components of multifaceted rehabilitation interventions after BoNT-A injections, similar approaches have been used in the stroke inpatient and outpatient rehabilitation setting [36, 62]. The tendency of clinicians treating spasticity to focus on impairments [166, 178], as discussed in Section 2.6.2, was also reflected in this study because a significant amount of the total therapy time was spent remediating impairments and performance skills.

The ability to determine the extent to which the therapy content provided to the study cohort is consistent with the types of therapy recommended in evidence-based clinical practice guidelines is somewhat limited and emphasises the need for further research in this area. Reasons for this are the lack of details on evidence-based therapy approaches in spasticity management guidelines, as well as study factors including the small study sample size, individualised therapy approaches, range of interventions and activities used, and diversity of presentation of clinical problems in the study population. Stroke guideline recommendations for managing moderate to severe spasticity are to trial BoNT-A in conjunction with goal-directed rehabilitation therapy [22]. In this study little therapy time was spent addressing community participation and leisure activities, particularly in the lower limb sub-group where over one-third of goals related to community mobility. Stroke guidelines state that electrical stimulation and electromyographic biofeedback could be used for spasticity management and highlight that evidence for stretching and splinting is inconclusive (though evidence is more favourable for lower limb rather than the upper limb spasticity [6]). The Stroke guidelines do not provide any additional specific recommendations for therapy approaches. Spasticity management guidelines also lack any detail on recommended therapy interventions as the evidence for the effectiveness of therapeutic intervention is hard to extract from the literature [6, 21]. One reason given is that the interventions are rarely described in detail, but
rather referred to simply as ‘treatment in line with routine practice’ [21]. Based on individual studies, the guidelines suggest use of electrical stimulation, stretching and taping or casting following lower limb BoNT-A injections [6] and electrical stimulation, strength training, CIMT and task-specific training for the upper limb [21]. Electrical stimulation was only used in a small number of study participants. The more commonly used interventions during occupational and physical therapy sessions were stretching and passive range of movement, strengthening exercises and neurodevelopmental therapy. Guidelines recommend strengthening exercises as weakness is one of the major impairments in the upper limb after stroke and a number of studies have found positive effects of increasing strength [21].

8.2.4. Implementing and evaluating rehabilitation programs following BoNT-A for post-stroke spasticity: mixed methods process evaluation

Key issue 4

As well as describing rehabilitation programs in detail to enable determination of the active ingredients, process evaluation is a key step in effectiveness research involving complex interventions. Failure to demonstrate an effect may be due to implementation problems rather than an inherent failure of the intervention. Determining implementation issues and the feasibility of widespread implementation of the intervention is important when translating research into the real-world clinical practice.

Chapter 7 includes an evaluation of the implementation of rehabilitation programs prescribed in Study 2 using the RE-AIM framework. The main objectives of this study are to identify implementation and process issues that may influence effectiveness and outcomes of high-intensity rehabilitation programs over usual care following BoNT-A injections for adults with spasticity.

Summary of findings

This study highlighted the importance of process evaluation in determining the effectiveness of complex interventions, particularly where the intervention is non-standardised and delivered at different rehabilitation centres. The findings have
provided greater explanatory power for the outcomes of ambulatory rehabilitation programs following BoNT-A injections (Study 2, Chapter 5).

The process evaluation provides data that suggests that the intervention was well implemented for the following reasons: the target population was well reached, adoption by participants was very good (demonstrated by the high completion rate), the intervention was well received by the therapists (who expressed positive attitudes towards high-intensity therapy), the intervention was implemented as planned at the expected intensity and is potentially generalisable to other contexts.

Implementing the high-intensity rehabilitation program in the public hospital setting was challenging due to limited funding, limited resources and logistical difficulties. Program adaptations including provision of more group sessions than individual sessions may have contributed to the failure to show a convincing benefit of high-intensity therapy over usual care. Additionally, contextual or organisational influences, previously discussed in Chapter 1, may have differed between the recruiting hospital and other centres, potentially influencing outcomes. The influence of these factors and the provision of goal-directed therapy on outcomes require further evaluation before dismissing the effectiveness of high-intensity rehabilitation programs. Thorough cost—effectiveness analysis would also be important in informing on the effectiveness and whether widespread implementation of these programs is warranted.

**Comparison with other studies**

This is the first process evaluation study for rehabilitation interventions following focal spasticity management. Process evaluation is often used in areas of health promotion [193-195] and chronic disease management programs such as for diabetes [192]. Various process evaluation frameworks and methods have been used in the literature to varying degrees of quality [195].

**8.3. Methodological issues**

The thesis studies were conducted in a real-life clinical setting and highlight the challenges of investigating complex rehabilitation interventions. Nonetheless,
these are the first studies to explore multidisciplinary rehabilitation interventions following BoNT-A injections as a complete package and provide an in-depth description of the therapy components comprising rehabilitation programs and how these relate to treatment goals. In addition to the individual limitations of each study, which are discussed in the text of each chapter, key methodological issues are discussed below.

8.3.1. Study design

While some limitations in study design were potentially preventable, they were practically difficult to avoid particularly given the pragmatic approach to the studies. The multifaceted nature and dependence on local contexts of complex interventions pose methodological challenges and often require adaptations to the standard design of trials, such as RCTs [195].

The existing health care structures and service delivery protocols impede high-quality real-life studies, particularly RCTs, which are not always the most suitable design for investigating effectiveness of complex interventions [56, 60]. Both groups in Study 2 (Chapter 5) received rehabilitation programs for a number of reasons. Firstly, it was not ethically appropriate to have a non-therapy control group because the provision of a rehabilitation program in conjunction with BoNT-A injections is considered best practice [6, 21]. Additionally, over half of the participants were receiving therapy at the time of recruitment, which is not unexpected given that it is the recommended treatment before and after BoNT-A injections [229]. Furthermore, it was not possible to randomly allocate participants to treatments in Study 2 because the high-intensity therapy program could only be provided at the recruiting centre, referral to community-based rehabilitation services is based on geographical catchment areas and the intervention is already in widespread use.

Patient-centred studies that allow participants to receive care in an accessible preferred manner at a number of rehabilitation centres may work against research such as this because the service structures and delivery tend to preference those in less isolated regions because specialist services in Australia tend to be available in large centres [43]. Other potential confounders and sources of bias may be differences between the therapy approaches used, cultural factors
and personal factors (e.g., patient motivation, self-efficacy and compliance, patient-therapist relationship, and therapist experience and expertise). While some variables are immeasurable, mixed methods analyses of those that can be measured are important in future research.

Non-blinding of treating therapists and participants creates an inherent risk of performance bias when investigating rehabilitation interventions. Although participants were not informed of group allocation, it was not determined as to whether this was maintained.

The intervention in Study 2 was not standardised for reasons discussed in Section 3.6.4. Ensuring strict standardisation is inappropriate when investigating individualised rehabilitation programs. Therefore, the approach used reflects real-life clinical practices and ensures that the research is useful and relevant to clinicians. Furthermore, it has been suggested that complex interventions may work better if a specified degree of adaptation to local settings is allowed for in the protocol [60].

8.3.2. Generalisability

Therapy programs were conducted at seven different rehabilitation centres, most of which were tertiary hospital affiliated and government funded. Although these centres represent only a part of Melbourne and recruitment occurred at a single-centre, in Australia treatment for spasticity is largely provided in public hospital spasticity management clinics (72%), with half of the patients receiving injections in multidisciplinary services (50%) similar to those in this research. The study sample was representative of stroke patients with problematic spasticity attending such clinics as the reach of the intended population was very high (Section 7.4.1). The design of a pragmatic trial reflects the heterogeneity of patients in real-life, thus representing the population for whom the treatment is designed and ensuring generalisability of the results [188].

The small sample size needs to be taken into account when interpreting the results. The interpretation of small effects from non-randomised studies requires particular care and should draw on supporting evidence where possible [56]. This evidence might include a consistent pattern of effects across studies, such as a dose-response relationship in which more intensive variants of the interventions
are associated with larger effects, or evidence from other types of study for a causal mechanism that can explain the observed effect [56]. However, in the field of rehabilitation management of spasticity, there are limited or no directly comparable studies to the studies in this thesis, which is the largest study of multidisciplinary rehabilitation interventions following BoNT-A injections.

**8.3.3. Limitations in outcome measurement**

Determining outcomes that are meaningful to patients and their caregivers, particularly attainment of priority goals, are recommended [6, 21, 33]. However, few useful standardised outcome measures following focal spasticity management have been identified other than GAS [33, 34, 196, 199], which was used in Study 2. Because the rehabilitation intervention has an effect across a range of domains (function, satisfaction and caregiver burden) and because goals for treating upper [33] and lower limb [196] spasticity are individualised and varied, a number of outcome measures were used to capture effects [6] (Chapter 3). The standardised outcomes used (e.g., for upper and lower limb function, particularly active function [59]) may not have been sensitive enough for such a heterogeneous group. While measures of participation are recommended, generic health or quality of life measures may fail to capture the effects of focal interventions that affect just one or two items in the scale [33] and measuring participation is difficult, as discussed in Section 3.6.3. These limitations of standardised measures when used to evaluate outcomes of spasticity management, in conjunction with limitations in study design discussed above, may have contributed to the lack of benefit of high-intensity rehabilitation programs over usual care (Study 2, Chapter 5).

Applying outcome measures at appropriate time intervals (such as when maximal change is expected) is important for capturing effects. To not miss improvements in functional goals that take time to develop, the six month follow-up period was chosen because it is beyond the duration of the rehabilitation programs and the expected effect of BoNT-A injection on spasticity reduction [20]. While a study duration of 12 months would have been useful in determining whether effects on goal achievement were maintained over the longer term and thus indicating maintenance at the individual level [194], the study was not
designed as such because of funding limitations and because patients often require re-injection within this time frame (Study 2).

8.3.4. Study differences in participant groupings for data analyses

Although, Studies 2 and 3 are linked the results are not directly comparable because different participant groups and subgroups were used for data analyses as follows:

- Study 2 – high-intensity programs versus low-intensity usual care, with subgroups for those receiving upper or lower limb injections. For the upper and lower limb subgroups data analysed were related to measures of activity (Arm Activity Measure for upper limb and gait speed for lower limb), spasticity (MAS) and limb muscles injected. Participants who had both limbs injected were included in both subgroups.

- Study 3 – participants for whom therapy documentation forms were completed formed the study cohort, and subgroup analysis was performed for those who had the upper limb, lower limb and upper and lower limbs injected.

Analysis of therapy program components for participants receiving high-intensity rehabilitation versus low-intensity usual care were not included in Study 3 for the following reasons:

- Comparison by limb injected rather than therapy intensity was considered clinically relevant to decision-making regarding therapy approaches so is more useful for clinicians.

- Not all participants from Study 2 were included in Study 3 because not all therapists completed the therapy documentation forms. Therefore, data analysis by therapy intensity would not allow direct comparison of study results.

Analysing the data in this way would have been beneficial in demonstrating differences or similarities in the therapy approaches used and clinical practices used at the recruiting rehabilitation centre and other centres.

Classifications for goals also differed between Studies 2 and 3. Categories for classifying goals in Study 2 were based on a study investigating outcome
evaluation with GAS following focal spasticity interventions [33]. Whereas in Study 3, categories used to classify goals needed to be applicable to the rehabilitation activities to be able to draw relationships between the two. The classification used in studies describing occupational therapy stroke rehabilitation programs using the stroke rehabilitation taxonomy [62, 166] was adapted for the purposes of Study 3.

8.3.5. Limitations in determining the direct impact of therapy intensity

Determining the impact of therapy intensity on outcomes is challenging for a number of reasons. Participant’s activity level outside formal therapy sessions is a potential confounder that was not measured in Study 2. This includes, upper limb use during daily activities, walking for the lower limb group and compliance with home exercise programs. Additionally, because both groups received active rehabilitation and a priori compliance was 70%, there may have been insufficient variation in therapy intensity. Nonetheless, the high-intensity group received more therapy (median 3.2 sessions per week for about 11 weeks) than is usual care in Australia where the mean number of post-injection sessions received is 10.2 (median 8, SD 9.57, range 0 to 50) and 6% have no post-injection therapy [43]. A large proportion of study participants were engaged in a therapy program at recruitment and it is possible that the impact of therapy may have already been realised. However, this is similar to practices throughout Australia where most patients receive pre-injection therapy (74%) [43].

The standardised stroke rehabilitation taxonomy used in Study 3 [36, 55] does not allow for recording of rest or inactive time. Therefore, it does not reflect how intensely participants participated in therapy sessions. This data is important in determining therapy effectiveness. While therapists have been found to be inaccurate in their estimations of the time that patients spend engaged in active task practice during therapy sessions [242, 243], objective measures for recording therapy activity time (e.g., accelerometers or counting repetitions) [244, 246], as discussed in Section 6.4.2, were not incorporated into the studies. The main reasons for this were limited funding and risk of overburdening therapists with study demands.
8.4. Clinical practice implications: Recommendations for optimal multidisciplinary rehabilitation management following BoNT-A injections for post-stroke spasticity

8.4.1. Post-injection management

Despite the lack of high-quality evidence for a coordinated, goal-directed multidisciplinary rehabilitation approach to achieving long-term functional improvement after spasticity reduction with BoNT-A injection (Study 1, Chapter 4), the treatment should be provided in clinical practice based on expert opinion [6, 21]. The findings of Study 2 (Chapter 5) also support this recommendation. Both groups (high-intensity and usual care) showed improvement in goal achievement and satisfaction after BoNT-A injections and rehabilitation for up to six months (which is after the effects of BoNT-A on spasticity reduction have worn off) and therapy is likely to have contributed to the functional benefits.

As there is a potential for more intensive therapy following BoNT-A injections for upper limb spasticity to improve patient-centred outcomes, such as goal achievement, further studies evaluating this potential effect have been conducted at the Royal Melbourne Hospital. Provision of more intensive upper limb therapy via enriched environments has been evaluated for neurological patients, including those with spasticity, in the inpatient and ambulatory rehabilitation setting [251]. If such programs are proven to be beneficial for stroke patients with spasticity, detailed cost-effectiveness analyses may be warranted before considering widespread implementation. Establishing cost-effectiveness is critical in justifying service delivery enhancement to provide intensive multidisciplinary therapy given the higher costs related to increased amount of therapist time required.

8.4.2. Outcome evaluation: goal achievement

There is limited detail in current spasticity management guidelines and the literature to guide the provision of multidisciplinary care, including the types of programs that are effective (interventions, activities, intensities, timing and setting) and in which types of patients [6, 21, 35]. Thus, therapy is often delivered
on a trial-and-error basis. However, relevance of therapy to patient goals is important, as demonstrated in Study 3 (Chapter 6) where therapeutic rehabilitation activities reflected treatment goals, particularly for the upper limb. Goals should be set between the patient, their caregiver and the treating team prior to BoNT-A injections. Similarly, following injections, assessment of outcomes that reflect treatment goals [6, 33], particularly related to the ICF domains of activity and participation [12], are recommended to assist with developing patient-centred models of treatment planning [21, 45]. A study of Australian therapy practices that care for patients with spasticity found that just over half of all patients had goals set before they were injected [43]. Study 2 (Chapter 5) demonstrated that a measure of goal attainment such as GAS was useful in measuring the effectiveness of rehabilitation in a group where treatment goals are diverse and other standardised outcome measures are insensitive, similar to other studies of focal treatments of post-stroke spasticity [26, 33, 105]. Combining a measure of goal achievement with a standardised measure for upper limb function (e.g., Arm Activity Measure [161]) or lower limb function (e.g., Rivermead Mobility Index [121]) provides a comprehensive evaluation [6, 19, 21].

8.5. Research implications: Recommendations for future research into multidisciplinary rehabilitation management following BoNT-A injections for post-stroke spasticity

8.5.1. Addressing challenges in investigating complex interventions

This thesis identified challenges in investigating complex rehabilitation interventions in the real-world, which may limit the ability to establish a comprehensive evidence base for multidisciplinary care for spasticity management. Not only is rehabilitation multidimensional and individualised, thus encompassing a matrix of prescribed activities and interventions and levels of complexity (Study 3, Chapter 6), but service delivery and program implementation is influenced by personal factors (of both the therapist and the patient, including their attitudes and beliefs) and the local context (e.g., cultural, social and organisational factors) as demonstrated in Study 4 (Chapter 7). Thus,
evidence-based interventions cannot be expected to work exactly the same way in all contexts and all cultures. The political, geographical, socioeconomic, physical and cultural characteristics of each community are critical in determining what is needed, appropriate and effective. Furthermore, the feasibility of implementing different practices and changing behaviours needs to be considered. Taking these complexities into consideration, approaches to future research in this field that may be useful in contributing to the evidence base and improving clinical practices will be discussed.

Studies investigating the effectiveness of current spasticity management clinic and rehabilitation practices using thorough process evaluation can be of great value in improving implementation of rehabilitation programs following BoNT-A injections. Individual services can then focus on improving service delivery and policies, particularly where implementation issues are identified. Comparison of outcomes of such study approaches across spasticity management services nationally, in conjunction with recommendations to develop local treatment protocols within services [43], may assist in developing consistency of therapy delivery and approaches.

In the rehabilitation setting, pragmatic trials may be more useful than RCTs because it is not likely that all confounders can be identified and measured. A clinical practice improvement study (an observational cohort study that entails the acquisition of prospective and retrospective data while not disrupting the natural milieu of treatment [63]) can uncover best practices more quickly while achieving many of the presumed advantages of RCTs [63]. The purpose of a clinical practice improvement study is to discern the relative contributions of specific rehabilitation interventions and therapies to outcomes while taking into account patient differences, illness severity and other contributing factors [63]. The comprehensive analysis of patient characteristics, process steps and outcome variables [259] is important when investigating complex interventions particularly in a heterogeneous population such as the stroke population.

Further research into rehabilitation interventions following BoNT-A injections for upper limb spasticity needs to be considered in light of the thesis findings. The question of whether increased therapy intensity is important in improving patient-centred outcomes following BoNT-A injections for upper limb
spasticity, or whether goal directed therapy is more important, requires further clarification. There is currently a study underway to investigate the role of intensive upper limb therapy following BoNT-A injections in adults with neurological conditions [231]. However, in other populations, such as children with cerebral palsy, there was no evidence that high-intensity therapy (CIMT) produced a superior effect across a range of outcomes compared with a structured program of bimanual occupational therapy [260].

If future research is to be of value in expanding the evidence base for multidisciplinary rehabilitation programs following BoNT-A injections, greater consistency in research designs is necessary. Only then can comparative analyses of studies and identification of consistent patterns of effects be determined, leading to development of evidence-based spasticity management guidelines and translation of beneficial programs into clinical practice. To achieve this, future studies should focus on the key methodological factors discussed in Sections 8.5.2 to 8.5.4.

### 8.5.2. Detailed descriptions of rehabilitation programs and their contexts

Description of rehabilitation programs and their contexts is accomplished using standard classification systems to describe critical program attributes [175] and specific therapy components [55, 62]. This amount of detail enables identification of the key active ingredients, evidence synthesis, determination of the transferability of the evidence [261], replication of the intervention and appropriate wider implementation across groups and settings [60].

Study 3 (Chapter 6) demonstrated the use of a stroke rehabilitation taxonomy [55] that is useful in providing insight into the black box of rehabilitation by describing the multidimensional nature of therapy, rather than the generic broad terms used in other studies of rehabilitation interventions [6, 35, 41, 117]. Future studies using similar approaches can then determine the relationship between activities, interventions and treatment goals to identify which facets of therapy improve outcomes.
8.5.3. Comprehensive process evaluation nested in effectiveness trials

Research is of no benefit if the programs being studied are not feasible or are difficult to implement in real-life. Process evaluation using mixed methods to assess implementation issues (such as barriers and enablers) and effectiveness (including cost–benefit analyses) assists with translating research into practice. A systematic review of clinical practice guidelines for spasticity management following brain injury identified that critical issues not addressed were: how to implement and integrate recommendations into clinical practice, barriers to implementation and lack of audit criteria to ascertain the uptake of recommendations [262].

Formal frameworks for process evaluation, should be considered (e.g., RE-AIM [189, 190] as discussed in Chapter 3). These methods can provide valuable insight into the reasons why an intervention is ineffective or has unexpected consequences, or how to optimise a successful intervention. Lack of intervention effect may stem from implementation failure rather than genuine ineffectiveness [60]. A thorough process evaluation is needed to assess fidelity and quality of implementation, receipt of intervention, clarify causal mechanisms and identify contextual factors associated with variation in outcomes [60, 263]. Studies investigating rehabilitation programs using the same frameworks would then enable comparisons of interventions and their effectiveness.

8.5.4. Controlling contextual factors influencing implementation of rehabilitation programs

Alternative study designs to clinical practice improvement methodology, where all variables are examined in everyday clinical practice, may be considered. The control of particular contextual factors to assess efficacy including a narrow focus of research question may be achieved in multicentre trials with high-quality research designs. For example, a particular element such as therapy intensity may be examined in a specialist centre so that better standardisation of service delivery can be planned and audited. While this may limit the generalisability of results outside specialist centres, it improves the research quality by reducing confounding and the risk of bias discussed in Section 8.3.1. In evaluations seeking
to identify the active ingredients in a complex intervention, strict standardisation is practically challenging and not necessarily clinically relevant, but controls can be put in place to limit variation in implementation [261].

Attempts should be made to investigate the impact of contextual influences, including personal and organisational factors, on therapy delivery and outcomes. This would shed light on whether a treatment effect is as a result of the intervention protocol, service level or operator level (personal interaction between the therapist and patient plus the therapy they provide) [177]. A combination of qualitative and quantitative methods are recommended to determine how context level factors might modify intervention effectiveness [263].

8.5.5. Recommendations for investigating therapy intensity

When specifically examining the effect of therapy intensity, an objective method to accurately capture the participant’s activity level during and out of therapy time in community-dwelling patients is necessary. This may include simple counting of repetitions of tasks or exercises [244] or using activity monitors, such as arm or leg accelerometers [244, 246]. The contribution of formal therapy time versus home-based activity to patient outcomes can then be determined, which is important in assessing cost effectiveness. In patients receiving lower limb BoNT-A injections, walking regularly during their daily activities may have a greater influence on achieving meaningful goals than time spent in formal therapy.

8.5.6. Recommendations for trials investigating efficacy of BoNT-A

Future trials investigating efficacy of BoNT-A should describe the physical interventions that participants receive in detail, rather than simply stating ‘treatment in line with routine practice’ [21] or ‘standard care’ [26, 258]. Exploring the therapy factors that contribute to outcomes in such studies is warranted. Use of a measure of goal achievement, such as GAS, as a primary outcome would enhance the relevance of BoNT-A studies to real-life clinical practice given that recommendations are for goal-oriented spasticity management [258] and use of outcomes that are meaningful to patients [33]. Stroke patients present with a diverse range of spasticity related problems relating to passive and active function. The effect of BoNT-A on achievement of active versus passive
goals requires further exploration, particularly for the lower limb [258], to assist in determining the types of patients that benefit from focal spasticity treatment.

8.6. Conclusions

This thesis demonstrates a pragmatic approach to exploring potential modulators of the black box of rehabilitation, such as therapy intensity particularly in the upper limb (Study 2, Chapter 5), describing the multifaceted components of rehabilitation programs using a standardised taxonomy and how they relate to treatment goals (Study 3, Chapter 6), and the importance of process evaluation when interpreting the results of effectiveness trials (Study 4, Chapter 7). While the studies in this thesis have contributed to the limited evidence, they highlight an ongoing disparity between recommended clinical practices and the evidence base. Improvement in patient-centred outcomes (such as goal achievement) was demonstrated following BoNT-A injections, regardless of therapy intensity, but there may be a differential effect for the upper limb. The methodology used in the studies and future research recommendations should assist with development of future trials, using uniform approaches, from which evidence can be synthesised to scientifically guide comprehensive rehabilitation management of spasticity in clinical practice.
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Appendices

Appendix 1. Published papers

Multidisciplinary rehabilitation following botulinum toxin and other focal intramuscular treatment for post-stroke spasticity (Review)

Demetrios M, Khan F, Turner-Stokes L, Brand C, McSweeney S

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in The Cochrane Library 2013, Issue 6

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Multidisciplinary rehabilitation following botulinum toxin and other focal intramuscular treatment for post-stroke spasticity

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ABSTRACT

Background
Spasticity may affect stroke survivors by contributing to activity limitations, carer burden, pain and reduced quality of life (QoL). Spasticity management guidelines recommend multidisciplinary (MD) rehabilitation programmes following botulinum toxin (BoNT) treatment for post-stroke spasticity. However, the evidence base for the effectiveness of MD rehabilitation is unclear.

Objectives
To assess the effectiveness of MD rehabilitation, following BoNT and other focal intramuscular treatments such as phenol, in improving activity limitations and other outcomes in adults and children with post-stroke spasticity. To explore what settings, types and intensities of rehabilitation programmes are effective.

Search methods
We searched the Cochrane Stroke Group Trials Register (February 2012), the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library 2012, Issue 12), MEDLINE (1948 to December 2011), EMBASE (1980 to January 2012), CINAHL (1982 to January 2012), AMED (1985 to January 2012), LILACS (1982 to September 2012), PEDro, RehabDATA and OpenCARE (September 2012). In an effort to identify further published, unpublished and ongoing trials we searched trials registries and reference lists, handsearched journals and contacted authors.

Selection criteria
We included randomised controlled trials (RCTs) that compared MD rehabilitation (delivered by two or more disciplines in conjunction with medical input) following BoNT and other focal intramuscular treatments for post-stroke spasticity with placebo, routinely available local services, or lower levels of intervention; or studies that compared MD rehabilitation in different settings, of different types, at different levels of intensity. We excluded RCTs that assessed the effectiveness of an interdisciplinary therapy (for example, physiotherapy only) or a single modality (for example stretching, casting, electrical stimulation or splinting only). The primary outcomes were validated measures of activity level (active and passive function) according to the World Health Organization’s International Classification of
Functioning, Disability and Health. Secondary outcomes included measures of symptoms, impairments, participation, QoL, impact on caregivers and adverse events.

Data collection and analysis
We independently selected the trials, extracted data, and assessed methodological quality using the Grades of Recommendation, Assessment, Development and Evaluation (GRADE). Due to the limited number of included studies, with clinical, methodological and statistical heterogeneity, quantitative meta-analysis was not possible. Therefore, GRADE provided qualitative synthesis of 'best evidence'.

Main results
We included three RCTs involving 91 participants. All three studies scored 'low quality' on the methodological quality assessment, implying high risk of bias. All studies investigated various types and intensities of outpatient rehabilitation programmes following BoNT for upper limb spasticity in adults with chronic stroke. Rehabilitation programmes included: modified constraint-induced movement therapy (mCIMT) compared with a neurodevelopmental therapy programme; task practice therapy with cyclic functional electrical stimulation (FES) compared with task practice therapy only; and occupational, manual therapy with dynamic elbow extension splinting compared with occupational therapy only. There was low quality evidence for mCIMT improving upper limb motor function and spasticity in chronic stroke survivors with residual voluntary upper limb activity, up to six months, and very low quality evidence for dynamic elbow splinting and occupational therapy reducing elbow range of movement at 16 weeks. Task practice therapy with cyclic FES did not improve upper limb function more than task practice therapy alone, only at 12 weeks. No studies addressed interventions in children and those with lower limb spasticity, or after other focal intramuscular treatments for spasticity.

Authors’ conclusions
At best there was 'low level' evidence for the effectiveness of outpatient MD rehabilitation in improving active function and impairments following BoNT for upper limb spasticity in adults with chronic stroke. No trials explored the effect of MD rehabilitation on 'passive function' (caring for the affected limb), caregiver burden, or the individual's priority goals for treatment. The optimal type of modalities, therapy approaches, settings and intensities of therapy for improving activity (active and passive function) in adults and children with post-stroke spasticity, in the short and longer term, are unclear. Further research is required to build evidence in this area.

PLAIN LANGUAGE SUMMARY
Multidisciplinary rehabilitation programmes following treatment of spasticity after stroke

Stroke can cause muscle stiffness, spasms or tightness in the affected arm or leg, with pain and abnormal positioning of the limb. Consequently, there may be difficulties using the arms or legs in everyday activities or in caring for the affected limb. Treatments for spasticity may include botulinum toxin and other injected medications that paralyse the affected muscles. Following such injections, a multidisciplinary (MD) rehabilitation programme (usually delivered by two or more health professionals) is often employed. Interventions may include stretching, splinting, gait training, repetitive practice in using the arm for tasks, and orthotic prescription. Therapies are aimed at reducing spasticity to improve limb use or positioning, or to make it easier to care for the affected limb. The outcomes of such programmes focus on attainment of functional goals that are important to affected people in their everyday life. We included three relevant studies in the review, which investigated different types of MD rehabilitation interventions after botulinum toxin injections into the arms of 91 adults with previous stroke. There was low quality evidence for intensive forced use of the affected arm in improving spasticity, and very low quality evidence for elbow splinting with occupational therapy. We did not identify any studies of MD rehabilitation in children with post-stroke spasticity or after other injected medications. The review findings are limited by the small number of studies that are methodologically flawed. More research is needed into what rehabilitation modalities and treatments are most effective for spasticity management following stroke.
BACKGROUND

Description of the condition

Stroke and epidemiology

Stroke is the second leading cause of mortality and disease burden among adults aged 60 years and over (WHO 2003). The global burden of stroke is expected to rise due to the ageing population. Annually, 15 million people worldwide suffer a stroke. Of these, five million die and another five million are left permanently disabled, placing a burden on families and communities (MacKay 2004).

Spasticity is a common manifestation of neurological insults such as stroke. While the incidence of spasticity is not well known with certainty, it has been estimated to affect 38% of stroke survivors after 12 months (Watkins 2002). Direct costs for stroke survivors with spasticity have been found to be approximately four times those for stroke survivors without spasticity (Lundstrom 2010).

The burden of post-stroke spasticity is high in terms of treatment costs, quality of life (QoL) consequences, caregiver burden and the effects of comorbidities such as falls and fractures (Esquenazi 2011). Thus, the condition not only considerably impacts on the person and their family members but society as a whole due to the increased demand for health care.

Spasticity and the upper motor neurone syndrome

The primary feature of spasticity is hyperreflexia of muscle stretch reflexes (Lear 1990), although this has been debated (Pandyan 2005). Improved understanding of the complex pathophysiology and clinical interpretation of spasticity have led to the broad definition of “a disordered sensorimotor control, resulting from an upper motor neuron (UMN) lesion, presenting as intermittent or sustained involuntary activation of muscles” (Pandyan 2005). This definition suggests that ‘spasticity’ can be used as an umbrella term to describe the positive features of the UMN syndrome. Spasticity typically develops over a few weeks following stroke due to abnormal patterns of supraspinal descending drive (Gracies 2001). It often persists as a chronic neurological condition requiring long-term management. The interaction of spasticity with other features of the UMN syndrome is complex (Barnes 2001). The UMN syndrome is characterized by positive symptoms associated with muscle overactivity (such as spasticity, co-contraction, associated reactions and clonus) and negative symptoms (such as weakness and fatigability). Spasticity results in stiffness and abnormal posturing of the limb due to net imbalance of forces between agonist and antagonist muscles affecting static joint position and dynamic limb movement (Roscan 1990). It may mask the return of effective movement in a paretic limb following stroke and, in some cases, relief of spasticity may facilitate the return of active movement. However, this cannot be guaranteed as underlying weakness will often persist, limiting the functional gains to be made (Ada 2006).

Adaptive features of the UMN syndrome may develop due to untreated spasticity and underlying muscle weakness (Ada 2006), including contractures and rheological changes of muscle, tendons and joints, further exacerbating limb positioning, movement and function. Elongating a spastic muscle may alter the viscoelastic and extensibility properties thereby reducing muscle tone (Gracies 2001). However, the exact mechanisms remain uncertain. Stretching and positioning are used to maintain muscle length and prevent contractures in order to facilitate acquisition of normal postures.

Post-stroke spasticity may be focal (affecting a localised part of a limb) or multifocal (affecting more than one part of a limb or limbs). The overall pattern of spasticity combined with other UMN symptoms and resulting problems may be variable, hence individualised, goal-directed treatment is essential.

Spasticity is not always unwanted, as in some instances patients rely on spasticity to maintain function in an otherwise non-functional limb. Yet, it should be treated when it interferes with activity or the ability to provide care to the stroke survivor, or causes pain or secondary complications. In addition to the broader effects of the UMN syndrome described above, other stroke-related impairments such as neglect, fatigue and cognitive deficits can impact on function in conjunction with spasticity. Therefore, management is complex, requiring comprehensive multidisciplinary (MD) neurorehabilitation programmes.

Impact of spasticity and the World Health Organization International Classification of Functioning, Disability and Health

Spasticity-associated problems can be classified according to the World Health Organization (WHO) International Classification of Functioning, Disability and Health (ICF) (WHO 2001). The ICF is a framework used to describe health and disability. Understanding the impact of disease on a person at different levels facilitates the planning of individualised, goal-directed and functionally oriented rehabilitation programmes. Goals for treatment of post-stroke spasticity may relate to the following issues:

- Impairments (problems with body structures or physiological function) such as restricted joint range of movement, pain and involuntary movements, e.g. associated reactions and spasms.
- Activity limitations impacting on:
  - Active function (the execution of a functional task by the individual) such as reduced mobility, difficulty feeding or dressing limiting independence with self care.
  - Passive function (protection of care to an affected limb) such as difficulty maintaining palmar hygiene or applying a splint or orthotic and increased caregiver burden.

Multidisciplinary rehabilitation following botulinum toxin and other local intramuscular treatment for post-stroke spasticity (Rowell)
Approaches to the management of spasticity

The two main approaches to the management of spasticity include pharmacological and physical interventions (Stevenson 2010). In clinical practice, these are often used in combination, but treatment is often piecemeal or not always planned. One study reported that the majority of people with spasticity received at least one concomitant treatment following botulinum toxin (BoNT) injections, however physiotherapy and occupational therapy were not given as planned in a significant proportion of patients (Turner-Stokes 2010a).

Oral anti-spasmodic agents (for example baclofen) are commonly used for generalised spasticity. However, BoNT or other focal intramuscular treatments such as phenol are increasingly used for focal or multifocal post-stroke spasticity. BoNT is a neurotoxin derived from the bacteria Clostridium botulinum, which binds presynaptically to the acetylcholine receptor at the neuromuscular junction, inhibiting release of acetylcholine. It is effective in reducing spasticity by causing temporary, focal muscle weakness lasting three to four months (De Paiva 1999). Hence, it can provide a window of opportunity to maximise gains to be made during rehabilitation programmes, it can make it easier to stretch and lengthen muscles in order to prevent progression of contractures, and allow strengthening of antagonist muscles which may improve selective movement control. BoNT has been shown to reduce muscle tone (Bhakta 2000; Ellis 2009) and improve passive function, such as for hand hygiene and reducing caregiver burden (Bhakta 2000). However, the effect of active function remains unclear (Maw 2011, Sheean 2001).

Recent guidelines and consensus statements on spasticity management advocate a holistic MD approach to rehabilitation to optimise the likelihood of treatment goals being achieved (Esquerazu 2010; Oliver 2010; Turner-Stokes 2009). This includes physicians trained in spasticity management and integrated allied health services to enable appropriate evaluation, goal setting, outcome measurement, treatment and follow-up. However, recommendations are based on expert opinion rather than formal research evidence.

Trials investigating non-pharmacological interventions for post-stroke spasticity have focused on the use of BoNT injections with or without single treatment modalities, such as casting (Parida 2008), ankle taping (Reiter 1998) or electrical stimulation (Bartisch 2008; Hesse 1990). Trials of BoNT effectiveness often allow concomitant ‘routine’ therapy which is not controlled for and varies amongst centres (McCorky 2009). Additionally, therapy programmes are rarely described in any detail. The optimal timing, type, duration and intensity of therapy remains poorly defined. Similarly, the relationship between the types of rehabilitation therapies provided and patient outcomes is not known. Hence, whilst rehabilitation practices may be routine, they are often based on trial-and-error as they are difficult to characterise and standardise (De Jong 2004).

Description of the intervention

Following BoNT or other focal intramuscular treatment, MD rehabilitation involves the provision of a co-ordinated programme by a specialised team of health professionals delivered by two or more disciplines (nursing, physiotherapy, occupational therapy, orthoptics and others). As described in Sivis 2002, necessary elements of a MD rehabilitation programme are:

- an individualised, patient-centred plan formulated by the patient and rehabilitation team;
- goals derived and prioritised through a MD process, where goals are specific, measurable, achievable, realistic and timely (SMART) (Welle 2010);
- patient participation, required to achieve the goals with improvement in the patient’s personal potential as a result;
- outcomes demonstrating improvement in one or more domains of the ICF.

Unidisciplinary therapy (for example physiotherapy only) or single-treatment modalities (such as casting and functional electrical stimulation) used in isolation do not comply with the definition of MD rehabilitation, therefore we excluded randomised controlled trials (RCTs) or other studies exploring such treatments.

How the intervention might work

Post-stroke spasticity can manifest in multiple ways, with detrimental effects on function, quality of life and caregiver burden (Bhakta 2000; Esquerazu 2001). MD rehabilitation utilises a co-ordinated, goal-directed treatment approach to address these issues, including allied health and medical input. It encompasses multiple therapeutic interventions aimed at improving patient experience at the level of impairment, activity or participation, and enabling patients and caregivers in the ongoing self-management of spasticity. BoNT or other focal intramuscular treatments provide a window of opportunity to facilitate gains to be made during rehabilitation and, in this context, they may be considered to be an adjunct to a MD rehabilitation programme rather than vice versa (Esquerazu 2010).

Why it is important to do this review

The effectiveness of MD rehabilitation in neurological conditions such as multiple sclerosis (Khan 2007), acquired brain injury (Turner-Stokes 2005) and stroke (Langborne 2011) has been proven. However, its effectiveness in managing post-stroke spasticity following BoNT or other focal intramuscular treatment has not been determined.
The general consensus is that optimal treatment of post-stroke spasticity following BoNT requires a comprehensive MD rehabilitation programme (Oller 2010; Sloan 2010). However, these programmes are not always implemented and delivered in practice.

Other Cochrane reviews are focused on the effectiveness of BoNT injections (Lyons 2008) or individual physical interventions (Monaghan 2011) for spasticity management in stroke survivors. To date, no systematic review has evaluated the evidence for the effectiveness of MD rehabilitation following BoNT or other focal intramuscular treatment for post-stroke spasticity. The optimal intensity, type, and setting of rehabilitation programmes and the effects on outcomes are unclear.

**OBJECTIVES**

To assess the effectiveness of MD rehabilitation, following BoNT and other focal intramuscular treatments such as phenol, in improving activity limitations and other outcomes in adults and children with post-stroke spasticity. Specific questions addressed by this review were as follows.

- Does co-ordinated MD rehabilitation achieve better outcomes than the absence of such services in persons with post-stroke spasticity?
- What types of rehabilitation programmes are effective, and in which setting?
- Does a greater intensity (time, expertise, or both) of rehabilitation lead to better outcomes?

**METHODS**

**Criteria for considering studies for this review**

**Types of studies**

We included RCTs that assessed the effectiveness of MD rehabilitation programmes following BoNT or other focal intramuscular treatment for upper limb or lower limb post-stroke spasticity, or both, with either routinely available local services or lower levels of intervention; or studies that compared MD rehabilitation programmes in different settings, of different types or at different intensities.

**Types of participants**

All children (less than 18 years) and adults (18 years or over) with a confirmed diagnosis of stroke who had upper or lower limb spasticity, or both. A diagnosis of stroke fulfils the clinical criteria of the World Health Organization (WHO) of rapidly developed clinical signs of focal (or global) disturbances of cerebral function, lasting more than 24 hours or leading to death, with no other apparent cause than of vascular origin (WHO 1989), with or without confirmation by a computed tomography (CT) scan or magnetic resonance imaging (MRI). A diagnosis of stroke encompassed ischaemic or haemorrhagic stroke (including subarachnoid, intraventricular or intracerebral haemorrhage).

We did not include studies of participants with conditions other than stroke unless stroke-specific data were provided separately or more than 75% of participants had a diagnosis of stroke. Where the proportion of the study population with stroke was < 75%, we would contact study authors for data relating to stroke participants only.

**Types of interventions**

In this review, we defined MD rehabilitation as any co-ordinated therapy programme delivered by two or more disciplines (such as occupational therapy, physiotherapy, exercise physiology, orthotics, other allied health and nursing) in conjunction with medical input (neurologist or rehabilitation medicine physician) and aiming to achieve patient-centred goals related to optimising activity and participation, as defined by the ICF (WHO 2001). BoNT injections were administered using individualised or standardised injection protocols in both the control and intervention groups. Rehabilitation programmes may be delivered in:

- outpatient or day treatment settings, which may be located within private or public hospitals, community rehabilitation centres or specialist rehabilitation centers;
- inpatient rehabilitation settings where care is delivered 24 hours per day, including specialised medical rehabilitation units or hospital wards;

Rehabilitation programmes are individualised, thus the therapy provided can be variable and the actual content of MD care may vary from patient to patient. Therefore, we included any study that stated or implied MD care or rehabilitation provided it satisfied the definition, as stated above, and compared it with a type of control situation.

Control situations were:

- no treatment;
- placebo or sham;
- other interventions, including a lower level or different types of intervention such as "routine available local services" (e.g. medical care or physiotherapy only), "minimal intervention" (such as "information only"), waiting list conditions, or...
intervention given in different settings and at lower intensity of intervention.

We excluded RCTs that assessed the effectiveness of a multidisciplinary therapy (for example physiotherapy only) or a single intervention (for example stretching, casting, electrical stimulation or splinting only).

Types of outcome measures

We expected diverse outcomes given the varied presentations of spasticity-related problems and goals of treatment related to stroke severity.

Primary outcomes

Primary outcomes reflected the level of activity limitation according to the ICF (WHO 2001) and included:
- gait function (e.g. Leeds Arm Spasticity Impact Scale (Bhakta 1996); Disability Assessment Scale (Brahebore 2002); Arm Activity measure (Turner-Stokes 2010b));
- a gait function of the upper limb (e.g. Motor Activity Log (MAL) (Van der Lee 2004); or Action Research Arm Test (ARAT) (Lyk 1981));
- a gait function of the lower limb with such mobility measures including tests of walking speed, balance and gait pattern (e.g. Timed Up And Go (TUAG) (Podsiadlo 1991); 10 m walk test (Green 2002)).

We included the measure of achievement of intended goals for treatment, for example goal attainment scaling (Kiresuk 1968) or other measure of goal achievement. The combination of individualized goals for treatment is increasingly used as an overall measure of outcome in trials of MD rehabilitation.

Secondary outcomes

Secondary outcomes were measures of:
- symptoms and impairments, e.g. pain (measured by verbal scores or visual analogue scales, etc.), spasm frequency, joint range of movement, involuntary movements, measures of spasticity or tone such as the Modified Ashworth Scale (MAS) (Rehabim 1987) or Tabacci scale (Miceli 2005);

- restriction in participation and impact on caregivers. e.g. QoL measures (such as WHOQoL-BREF (Murphy 2000)), reduction of caregiver strain and burden (e.g. Caregiver Strain Index (Robinson 1983)).

We considered adverse events that may have resulted from the intervention. We delineated serious adverse effects as events that were life-threatening or required prolonged hospitalization.

Timing of outcome measures

We divided outcome time points into short term (up to three months) and long term (greater than three months).

Search methods for identification of studies

See the 'Specialized Register' section in the Cochrane Stroke Group module. We searched for trials in all languages.

Electronic searches

The Cochrane Stroke Group Trials Register was last searched by the Managing Editor on 8 February 2012. In addition, we searched the following electronic bibliographic databases:
- Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library 2011, Issue 12) (Appendix 1);
- MEDLINE (1948 to December 2011) (Appendix 2);
- EMBASE (1980 to January 2012) (Appendix 3);
- CINAHL (1982 to January 2012) (Appendix 4);
- AMED (1985 to January 2012) (Appendix 5);
- LILACS (Latin American & Caribbean Health Sciences Literature) at http://search.bvsalud.org regional/index.php (1982 to September 2012) (Appendix 6);
- Physiotherapy Evidence Database (PEDro) at www.pedro.org.au (September 2012) (Appendix 7);
- REHABDATA at www.natic.net research/rehabdata (September 2012) (Appendix 8).

The MEDLINE search strategy was developed with the help of the Cochrane Stroke Group Trials Search Co-ordinator and adapted for the other databases.

We also searched the following ongoing trials registers:
- ClinicalTrials.gov (www.clinicaltrials.gov);
- EU Clinical Trials Register (www.clinicaltrialregister.eu);
- Stroke Trials Registry (www.strokecenter.org/trials);
- Current Controlled Trials (www.currentcontrolled-trials.com);
- WHO International Clinical Trials Registry Platform (http://apps.who.int/trialsearch/);
- Australian New Zealand Clinical Trials Registry (www.anzctr.org.au).

Searching other resources

In an attempt to identify further published, unpublished and ongoing trials we:
- searched the reference lists of all retrieved articles, texts and other reviews on the topic;
- searched journals related to spasticity research and treatment not already searched on behalf of The Cochrane Collaboration.

Handsearching of relevant journals included: Archives of Physical Medicine and Rehabilitation (December 1995 to January 2012)
using the search engine ScienceDirect, and *Journal of Rehabilitation Medicine* (January 2001 to January 2012); used the PubMed related articles feature; used the Science Citation Index Cited Reference Search for forward tracking of important articles; searched Open Grey (formerly SIGLE) (System for Information on Grey Literature in Europe) at www.opengrey.eu; contacted authors, researchers and experts in the field.

**Data collection and analysis**

**Selection of studies**

Two review authors (MD, SM) independently screened all titles and abstracts of records identified from the searches of the electronic databases and excluded obviously irrelevant studies. We obtained the full texts of the remaining articles and assessed them for inclusion and appropriateness based on the previously defined inclusion criteria for eligibility. Once we had obtained all potentially appropriate studies, two review authors (MD, FG) independently evaluated each study for inclusion. Where they could not obtain a consensus about the possible inclusion or exclusion of any individual study, they made a final consensus decision by discussion with a third author (LTS).

We did not mask studies regarding the name(s) of the author(s), institution(s) or publication source at any level of this review.

**Data extraction and management**

Review authors independently extracted the data (MD, LTS, CB) from each study that meet the inclusion criteria. We have individually summarised all studies that met the inclusion criteria in RevMan 5.1 (RevMan 2011) to include the following information:

- publication details;
- study design, study setting, inclusion and exclusion criteria, method of allocation, risk of bias;
- patient population, e.g. age, sex, type of stroke, site of sparsity;
- details of interventions;
- outcome measures;
- withdrawals, length and method of follow-up, and number of participants followed up.

Where sufficient data and methodological details were available, we contacted study authors to obtain further information and clarification (Lai 2009; Sun 2010; Weber 2010).

**Assessment of risk of bias in included studies**

Three authors (MD, LTS, CB) independently assessed the methodological quality of the included studies during data extraction, using the Cochrane 'Risk of bias' tool according to the *Cochrane Handbook for Systematic Reviews of Interventions* Chapter 8.5 (Higgins 2011). We assessed the following domains: random sequence generation and allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), attrition bias, reporting bias, and other sources of bias. We scored each domain as 'low risk of bias', 'unclear risk of bias', or 'high risk of bias'.

We considered studies to be of high methodological quality ('high quality studies') if the risk of bias for domain items was low. We rated studies to be of low methodological quality ('low quality studies') if there was unclear or high risk of bias for one or more domains (Table 1). The review authors resolved any disagreements or lack of consensus through discussion with a fourth review author (FG).

**Measures of treatment effect**

It was not possible to pool data for quantitative analysis due to the small number of included studies, with significant heterogeneity in type and delivery of interventions, outcome measures, study designs (assessment point and duration of follow-up) and participant characteristics. Therefore, we presented a qualitative synthesis of the 'best evidence' based on the GRADE levels of evidence (Table 2), taking into consideration the five factors that impact on quality of evidence (Table 3) according to the *Cochrane Handbook for Systematic Reviews of Interventions* Chapter 12.2 (Higgins 2011). We presented the results of individual studies in Table 4.

**Unit of analysis issues**

We analysed the methodological quality of included RCTs using GRADE, as described in Chapter 12 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

**Dealing with missing data**

We contacted study authors to obtain missing data. Weber 2010 did not report outcomes for the Motor Assessment Scale (MAS). On enquiry, the authors stated that "the journal requested that the MAS not be reported", but they did not provide data for this measure.

None of the included studies had fatal flaws (withdrawals of more than 40% of patients, total or nearly total non-adherence to the protocol, or very poor or non-adjusted comparability in the baseline criteria).

**Assessment of heterogeneity**

We assessed clinical heterogeneity by examining the characteristics of the studies, the similarity between the types of participants, the interventions and the outcomes, as specified in the criteria for included studies. We reported trial strengths and limitations.
We had planned to quantify statistical heterogeneity between studies using the I^2 statistic, where an I^2 greater than 50% indicates substantial inconsistency, as described in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011). However, it was not possible to pool data and so no assessment of heterogeneity was required.

Assessment of reporting biases

We minimised publication bias by sourcing unpublished data where possible. Where data were not reported in full for certain outcomes, we contacted study authors to request the full data set or the reason for not publishing the data (Weber 2010).

Data synthesis

Data synthesis was not possible.

Subgroup analysis and investigation of heterogeneity

Due to the small number of included studies it was not possible to perform a subgroup analysis for:
- type of stroke and location;
- site of spasticity, i.e. upper or lower limb, or both;
- age (children, adults less than 65 years of age versus 65 years of age or older);
- type of rehabilitation programme (e.g. outpatient, home-based);
- intensity of treatment (high intensity, low intensity); and
- time of treatment following stroke (acute, less than six weeks; subacute, six weeks to six months; and chronic, more than six months).

Factors considered in heterogeneity included: setting, type and intensity of MD rehabilitation programmes.

Sensitivity analysis

Due to the small number of included studies it was not possible to perform a sensitivity analysis to determine whether the overall results would be the same if we analysed studies above different methodological cut-off points.

RESULTS

Description of studies

See Characteristics of included studies; Characteristics of excluded studies.

Results of the search

Electronic and manual searches yielded a total of 877 titles and abstracts after removing duplicates. Of these, we selected 35 for closer scrutiny resulting in three studies being included based on the review criteria. We identified two potentially relevant ongoing trials (Graham 2009; Laurin 2011). See Figure 1.
The main reasons for exclusion were:

- RCTs where BoNT versus placebo was compared, with both groups receiving the same therapy programme;
- RCTs where the intervention being compared was not consistent with the definition of MD rehabilitation (see Description of the intervention) e.g. unidisciplinary or single-modality treatment only.

**Included studies**

See Characteristics of included studies.

All three included RCTs investigated MD rehabilitation programmes in the ambulatory setting, in adults with chronic stroke following BoNT for upper limb spasticity (Lai 2009; Sun 2010; Weber 2010). They were single-centre trials, conducted in the USA (Lai 2009; Weber 2010) and Taiwan (Sun 2010), with small sample sizes and underpowered.

**Participants**

There were a total of 91 adults, with 82 included in the analyses. Weber 2010 included people with stroke as well as traumatic brain injury (TBI), with 5/13 of the control group comprising TBI participants (22% of the study population). We included the study as the intervention group consisted only of stroke patients. The five TBI patients in the control group and compared to the intervention group were matched for cognitive deficits and other neurological impairments.

Inclusion criteria for the studies varied (see Characteristics of included studies) and included chronic stroke (greater than six months (Lai 2009; Sun 2010) or one year (Webber 2010) following event) and moderate or severe upper limb spasticity at specified joints (MAS 2 (Lai 2009; Weber 2010) or MAS 3 (Sun 2010)). Two studies included participants with voluntary upper limb motor activity (Sun 2010; Weber 2010), using different criteria for inclusion. Sun 2010 based inclusion on minimal motor criteria (10° active extension at metacarpophalangeal and interphalangeal joints and 20° at the wrist). Weber 2010 used the Chedoke McMaster Assessment of hand impairment (Gowland 1993) and the ability to do at least one of three upper limb tasks. Lai 2009 included participants with range of motion deficits greater than 25% in elbow extension, with no criteria reflecting whether they had functional or non-functional upper limbs.

**Rehabilitation interventions**

All included trials compared outpatient MD rehabilitation programmes in the intervention group with an active control situation, as described in Types of intervention. The types of rehabilitation programmes were diverse, based on various therapies and combinations of physical modalities. Lai 2009 included 56 participants (30 completers) who had occupational, manual therapy combined with dynamic elbow splinting (Elbow Extension Dynamic Splint® (EED)) or occupational therapy alone. Sun 2010 included 32 participants (29 completers) comparing modified constraint-induced movement therapy (modCIMT) (high intensity training of the affected upper limb while restraining the non-affected upper limb) with neurodevelopmental therapy. Weber 2010 included 23 participants (18 completers) and compared task practice therapy, incorporating occupational therapy sessions and a home exercise programme, with cyclic functional electrical stimulation (FES) to facilitate grasp and release versus task practice therapy only.

Therapy protocols for the control and intervention groups differed in all three studies. Variables included: programme duration; amount and frequency of therapist contact; time spent doing a home programme or other activity outside of the programme; and intensity (defined as additional total time (hours)) spent doing the rehabilitation programme (therapy sessions plus home exercises or intervention) when comparing intervention to control group (Perna 2011)). Two studies investigated high versus lower intensity programmes, with intervention groups receiving a total of more than 670 hours (Lai 2009) and 490 hours (Sun 2010) compared with controls. All participants in Lai 2009 received two hours of occupational therapy weekly for 16 weeks. The intervention group additionally had education in using the EED (twice six to eight hours daily during sleep) and fortnightly visits to adjust the device. In Sun 2010 all participants had one hour of occupational therapy and one hour of physiotherapy three times weekly for three months. The modCIMT group had a higher intensity of upper limb training during restraining of the non-affected limb for at least five hours per day. In Weber 2010 the control group received six one-hour sessions and the intervention group received seven one-hour sessions of occupational therapy over 12 weeks. All participants were required to do a one-hour daily task practice home exercise programme, during which the intervention group also wore the cyclic FES device. The frequency of therapy sessions was high (more than two sessions per week) in Sun 2010 and lower (less than or equal to two sessions per week) in Lai 2009 and Weber 2010.

Although the studies provided generic descriptions of the therapy programmes, there was little detail or systematic analysis (conceptualising, measuring, counting) of interventions (De Jong 2004), such as quantification of time spent on specific therapeutic modalities (Lai 2009; Sun 2010). Whilst the home exercise programme (task-specific practice) was clearly described in Weber 2010, interventions and treatments administered during the occupational therapy sessions were not mentioned. See Characteristics of included studies for descriptions of the interventions.
Standardised protocols for upper limb BoNT injections (muscles, doses) were used in two studies (Lai 2009; Sun 2010) and one study used individualised protocols (Weber 2010). Two studies mentioned use of electromyography for needle localisation (Sun 2010; Weber 2010).

**Outcome measures**

A measure of activity limitation, the primary outcome for this review, was used in two studies that is active upper limb function measured by the MAL and ARAT (Sun 2010; Weber 2010). Although both studies used the MAL, the versions and administration varied. The MAL, quality of upper limb use during activities of daily living, was assessed observationally rather than self-reported in Weber 2010. Whereas the MAL was the primary outcome measure in Weber 2010, an impairment measure (MAS) was the primary outcome in Sun 2010. Lai 2009 used impairment-based outcome measures only that is mean per cent change in active range of movement and MAS score at the elbow. Sun 2010 was the only study to assess patient satisfaction. None of the studies considered the impact on caregivers nor used a measure of passive function or goal achievement for example GAS (which have been shown to be more sensitive measures of outcome in this context) (Turner-Stokes 2010c). Different outcome time points were used across the studies: Lai 2009 14 weeks; Sun 2010 one, three and six months; and Weber 2010 six and 12 weeks.

None of the included studies determined the minimal clinically important difference for the primary outcome measure. Power calculations were only provided in Sun 2010. Lai 2009 stated that "The population of patients who completed this study (n = 30) was not adequate to power statistical analysis of variance", Sun 2010 required 16 participants in each group to power the study but only had 14 and 15 participants in the control and intervention groups, respectively. The authors of Weber 2010 stated that "the group sizes in the present study were small (n = 13 and n = 10 in the no-FES and FES groups, respectively). A larger sample size may have been more effective in detecting group differences between the FES and no-FES treatments".

**Excluded studies**

We excluded 28 studies (see Characteristics of excluded studies) for the following reasons:
- the intervention was not consistent with the definition of a MD rehabilitation programme (n = 16);
- the comparator was BoNT versus placebo with both groups receiving the same rehabilitation programmes (n = 12).

**Risk of bias in included studies**

See Characteristics of included studies for risk of bias assessment. Figure 2 shows a risk of bias summary of the review authors’ judgements about each risk of bias item for each included study and Figure 3 shows the risk of bias graph of review authors’ judgements about each risk of bias item presented as percentages across all included studies. All three studies had a high risk of bias and were graded as 'low quality' based on the criteria (Table 1).
Figure 2. Risk of bias summary: review authors’ judgements about each risk of bias item for each included study.

<table>
<thead>
<tr>
<th></th>
<th>Random sequence generation (selection bias)</th>
<th>Allocation concealment (selection bias)</th>
<th>Blinding of participants and personnel (performance bias)</th>
<th>Blinding of outcome assessment (attrition bias)</th>
<th>Selective reporting (reporting bias)</th>
<th>Other bias</th>
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<tbody>
<tr>
<td>Lai 2009</td>
<td>+</td>
<td>-</td>
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<td>Sun 2010</td>
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<td>Weber 2010</td>
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</tr>
</tbody>
</table>
Allocation
As random sequence generation and allocation concealment were often not described, we sought clarification from study authors. Randomization methods were adequate in all studies (LaI 2009; Sun 2010; Weber 2010). However, allocation concealment was not provided by Weber 2010 and LaI 2009 as the treating therapist and physician, respectively, had knowledge of the upcoming assignment.

Blinding
In all three included studies there was a high risk of performance bias (participants and therapists were unblinded) and low risk of detection bias (outcome assessors blinded as clarified by authors). However, outcome assessors were not questioned to assess whether blinding was maintained throughout the follow-up period. In Sun 2010 the therapy sessions were conducted at different times in an attempt to reduce the risk of performance bias. The injecting physician was blinded in Weber 2010 only.

Incomplete outcome data
Attrition rates were moderate to high: 16.7% (LaI 2009), 21.7% (Weber 2010), but only 9.4% in Sun 2010. Reasons for dropouts were: decline in health status (n = 2), personal factors (n = 2), or non-attendance at follow-up (n = 1) (Weber 2010); and inability to attend therapy sessions due to practical reasons (n = 2) and a car accident (n = 1) (Sun 2010). Six participants were excluded in LaI 2009 due to "non-compliance with scheduled therapy sessions", which was not defined, and the timing points of participant withdrawal were unclear. Only Weber 2010 performed intention-to-treat (ITT) analysis and compared baseline differences between completers and dropouts, with no significant differences reported. It is unknown whether dropouts or exclusions would have significantly impacted the outcomes in LaI 2009 and Sun 2010.

Selective reporting
All study outcomes were reported, except the MAS at follow-up in Weber 2010.

Other potential sources of bias
All studies were single-centre, with small sample sizes, and were reported to be underpowered. The sample size calculation was described in Sun 2010 only, with 16 participants required in each group to achieve 90% power to detect differences between the studies (p > 0.1) with standard deviation (SD) ≤ 0.9 and accounting for 5% to 10% dropouts. The authors’ conclusions must be considered in the light of the studies being underpowered and having other high risks of bias. LaI 2009 did not report the baseline data for time since stroke and other stroke characteristics (such as type and location) in Weber.

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2010 the baseline data between the groups were not entirely comparable. The control group was significantly younger (P = 0.03) and had more participants with a diagnosis of TBI (versus 0% in the intervention group) and stratified randomisation by age was not performed. Subgroup analysis for TBI versus stroke was not provided in the control group. The authors rationalised that the differences would not influence findings as there were similar baseline variables, cognitive function and programme adherence for TBI and stroke participants, and age was controlled for in the analysis.

Weber 2010 reported no significant differences between the two groups for any outcome variable at any time point. Hence, the authors proceeded to present collapsed data for the entire cohort to show the benefit of task practice training for improved upper limb function. However, the confounder in this instance was the unknown influence of BoNT versus task practice therapy on outcomes, as there was no BoNT-only group as a comparator.

One study had a long-term follow-up period of six months (three months after completing the rehabilitation programme) (Sun 2010). The other studies had shorter follow-up periods of 12 weeks (at the time of completion of the rehabilitation programme) in Weber 2010 and 14 weeks (two weeks prior to completion of the therapy programme) in Lai 2009, so longer-term impacts could not be ascertained.

The results in Lai 2009 had large standard deviations indicating that the data included a wide range of values (see below).

Effects of Interventions

See Table 5 for the description of the results of the included studies. A meta-analysis was not possible due to the clinical, methodological, and statistical heterogeneity of the included studies. In the three studies, the mean age ranged from 49.1 years (Lai 2009) to 58.7 years (Sun 2010) in the intervention groups and 41.2 years (Weber 2010) to 61.3 years (Sun 2010) in the control groups.

The lower control group mean age in Weber 2010 may have been due to inclusion of TBI participants, however this was unclear. The study populations had chronic stroke, with the mean duration following the cerebral event being 2.9 years in both groups in Sun 2010 and 4.9 and 9.7 years in the control and intervention groups respectively in Weber 2010; this was unreported in Lai 2009. Reporting of stroke characteristics varied (Sun 2010; Weber 2010). Stroke characteristics were unreported in Lai 2009. Baseline ARAT scores for the intervention groups were 32.1 ± 12.7 and 19.5 ± 13.2, and for the control groups they were 29.0 ± 14.1 and 25.8 ± 15.5 in Sun 2010 and Weber 2010 respectively. Results are the mean ± standard deviation (SD).

Lai 2009 reported that occupational therapy in conjunction with dynamic elbow splinting (EED) resulted in a significant improvement in active range of movement elbow extension compared with the control group (occupational therapy only) at 14 weeks (33.5% (29.6%) versus 18.7% (18.7%); mean (SD)). The MAS (elbow flexors) score change was comparable in both groups.

There were no measures of activity level (active or passive upper limb function), goal attainment, or patient or caregiver perspective. The authors concluded that BoNT is effective with some management and occupational therapy in contracture reduction, and there is 'value of dynamic splitting in maintaining gains in range of motion'.

BoNT injection followed by mCIMT was shown to improve spasticity and upper limb motor function in chronic stroke patients with residual voluntary upper limb motor activity, more than BoNT followed by a neurodevelopmental therapy programme, with benefits maintained up to six months (Sun 2010). Both groups had significant improvements in the MAS at four weeks and three months without between-group differences. However, the mCIMT group showed significantly greater improvements in elbow, wrist, and finger spasticity (P < 0.019, P = 0.019, and P < 0.001, respectively) at six months. Compared with the control group, the mCIMT group had greater improvement in the MAL (amount of use (AOU) and quality of movement (QOM)) at three months (1.1 ± 0.5 versus 0.1 ± 0.2; P < 0.001 and 0.9 ± 0.6 versus 0.3 ± 0.2; P < 0.001) and six months (1.2 ± 0.5 versus 0.1 ± 0.2; P < 0.001 and 1.0 ± 0.5 versus 0.1 ± 0.1; P < 0.001), and ARAT at three months (7.3 ± 5.0 versus 3.1 ± 2.6; P = 0.012) and six months (7.9 ± 5.2 versus 1.2 ± 1.7; P < 0.001). Patient satisfaction was high following treatment with BoNT and mCIMT up to three months (95.5% versus 78.6% in the control group) but was not sustained beyond this (66.7% versus 64.3% in the control group at six months).

Following BoNT, cyclic FES in addition to task practice therapy did not improve upper limb motor function and spasticity more than task practice therapy only, up to 12 weeks (Weber 2010). When examining outcomes for the entire cohort, there were significant improvements in upper limb activity: MAL: Observation 0.41 (95% CI 0.24 to 0.58); MAL-Self Report 0.64 (95% CI 0.32 to 0.95); ARAT 6.39 (95% CI 3.35 to 9.41) from baseline to week six. MAL-Self Report 0.65 (95% CI 0.35 to 0.97), and ARAT 6.17 (95% CI 2.31 to 10.03) to week 12. Results are mean difference (95% CI).

No significant adverse events were reported in any of the studies. All three studies were of low methodological quality (high risk of bias). Therefore, using GRADE methodology for best evidence synthesis (Table 2) there was:

- Low quality evidence that high intensity training of the affected limb with mCIMT, compared with a lower intensity neurodevelopmental therapy programme, improved spasticity or tone (MAS) and active upper limb function (ARAT and MAL) and achieved high satisfaction in persons with residual motor function, with benefits maintained up to six months (Sun 2010);
- Very low quality evidence that a higher intensity programme of occupational therapy with additional EED assisted in maintaining active range of movement at the elbow in the short-term, compared with occupational therapy only (Lai 2009);
- no evidence that task practice therapy with cyclic FES was superior to task practice therapy only in improving spasticity or tone (MAS) and upper limb motor function (MAL-Observer, ARAT, and MAL-Self Report) in people with residual motor function, at 12 weeks (Weber 2010).

**DISCUSSION**

**Summary of main results**

This review evaluated the effectiveness of MD rehabilitation following BoNT, or other focal intramuscular treatment, in improving the activity level (primary outcome) and other outcomes (symptoms and impairments, participation restriction, caregiver burden and QoL) in adults and children with post-stroke spasticity.

For chronic stroke survivors treated with BoNT for upper limb spasticity, there is low quality evidence that mCIMT improves upper limb function in the long-term. There is very low quality evidence that occupational therapy with additional dynamic elbow splinting (FED) improves elbow tone and contractions. There is no evidence that task practice therapy with cyclic FES provides additional short-term benefit compared with task practice therapy alone. The quality of the existing evidence is reduced by the methodological weaknesses of the included studies, which were underpowered and had a high risk of bias.

There was no available evidence for benefits of MD rehabilitation programmes compared with the absence of such services in different settings (inpatient, lower limb spasticity, in children with stroke, or after focal intramuscular treatments for spasticity other than BoNT). Although results for intensity of therapy were presented wherever possible, it was difficult to categorise studies based on this criterion only. Subgroup analysis by type of stroke and location, and acute versus chronic stroke was not possible.

There was no evidence for the benefit of MD rehabilitation interventions following BoNT for post-stroke spasticity on passive function, community participation, goal achievement, caregiver burden and QoL.

**Overall completeness and applicability of evidence**

Despite some evidence for MD rehabilitation interventions for upper limb spasticity in adults with chronic stroke, many aspects of MD care for people with post-stroke spasticity remain unproven.

It was not possible to determine the evidence for MD interventions for lower limb spasticity in this review as available studies included single treatment modalities only, such as tapping, casting, or electrical stimulation (Baticic 2008; Hesse 1998; Johnson 2000).

Evidence for multidisciplinary interventions is presented elsewhere (Meehanagh 2011). There were no identified studies that included MD interventions in children or those with an acute stroke. The emerging evidence for the effectiveness of BoNT in stroke is in improving passive function and achieving individual goals (Turner-Stokes 2010). However, none of the included studies addressed these particular outcomes. Two of the studies (Sun 2010; Weber 2010) addressed active function in the minority subset of patients with residual upper limb function, for which this is a realistic goal.

The optimal intensity, duration and frequency of therapy that should be provided are unclear. Although high intensity mCIMT was considered superior to a lower intensity neurodevelopmental therapy programme for those with voluntary upper limb activity (Sun 2010), similar benefits could be achieved with less therapeutic contact time if patients are motivated. While other studies have shown benefits of CIMT in stroke survivors without significant spasticity, the programmes varied in terms of duration and frequency of therapy (Paniela 2011). Further studies are needed to determine optimal protocols for CIMT in stroke survivors with spasticity.

Applying the evidence in clinical practice is challenging. Firstly, evidence for ideal patient selection criteria for spasticity management is not available. Stroke survivors with upper limb spasticity have varied clinical presentations, whereas the study populations were restricted by the strict inclusion criteria for example the degree of residual upper limb motor activity and chronicity of stroke. This may limit the relevance of the evidence to an individual patient and, conversely, the evidence cannot be generalised to the heterogeneous stroke population. Furthermore, it is challenging to replicate the study therapy protocols in real-life due to the variability of available resources, need for specialised equipment for example the elbow extension Dynasplint® device, therapist time and expertise, consistency of therapy programmes (intensity, duration, modalities) and other confounders (therapist-patient interaction).

Performing high quality RCTs when investigating complex interventions such as MD spasticity management is challenging in the real world, for the reasons described below. While high quality RCTs are needed, other study designs, such as the use of clinical practice improvement methodology, may assist in building on the current evidence. Data collected prospectively and retrospectively in the routine clinical setting can be used to identify the relative contributions of specific interventions and therapies (the 'black box') to rehabilitation outcomes whilst accounting for contributing patient and environmental factors (De Jong 2006; Gagnon 2005). This may assist clinicians in translating and generalising study findings to clinical practice. A better understanding of the processes of care in rehabilitation for spasticity management may then improve practice of care and ultimately patient outcomes.

Despite the gaps in the literature we believe that development of integrated MD rehabilitation teams, to provide a long-term, com-
Quality of the evidence

The quality of the evidence was limited as there were only three heterogeneous, single-centre trials of low methodological quality, prohibiting pooling of data for quantitative meta-analysis. The limitations affecting the quality of the evidence in this review included:

- inconsistent terminology and definitions for 'spasticity', given that it is only one element of the UMN syndrome. In practice, rehabilitation interventions target various patterns of muscle overactivity, weakness, and contractures. When investigating 'spasticity', there is ambiguity in what is being treated and measured, causing difficulty in the interpretation and application of evidence. 
- 2011; Malhotra 2009; Sun 2010 and Weber 2010 did not define spasticity, and Lai 2009 used multiple terms such as 'hypertonicity', 'tone', and 'spasticity' with interventions aiming to reduce 'contracture';
- inadequate allocation concealment (Lai 2009; Weber 2010);
- high risk of performance bias due to non-blinding of treating therapists and participants (all studies). Additionally, patients may have revealed information about the intervention to outcome assessors; however, this was not addressed to reduce the risk of detection bias. In rehabilitation trials, blinding of participants and personnel can be particularly challenging;
- small sample sizes and underpowered studies. Recruitment from single-centre trials with strict inclusion and exclusion criteria can be limiting;
- the influence of significant attrition rates (16.7% in Lai 2009 and 21.7% in Weber 2010); non-compliance affecting retention of participants and follow-up, excluding dropouts from analyses and outcome reporting;
- differences in baseline characteristics between groups (Weber 2010) including age and etiology. The authors rationalized that the differences would not influence findings as there were similar baseline variables, cognitive function and programme adherence for TBI and stroke participants, and age was controlled for in the analysis;
- difficulty controlling for personal factors, which influence patient-therapist interaction, compliance, and delivery of therapy thus impacting on outcomes. These include patient motivation and self-efficacy and activity level outside of therapy programmes, which were not assessed in any of the studies;
- selection of inappropriate outcome measures that do not show change following therapy or correlate with meaningful outcomes for patients and their caregivers. Impairment measures, e.g. MAS and range of movement, or other standardised measures such as ARAT do not necessarily translate into improved function or benefits for patients and caregivers, which may be better captured through measures of passive function or individual goal attainment.

Potential biases in the review process

The review authors accept that there may have been a degree of:
- selection bias from the literature search;
- publication bias if trials have not been published due to small study populations and negative results, or effects of treatments have been exaggerated in published trials.

Although Weber 2010 included participants with TBI in the control group, without subanalysis for stroke versus TBI, excluding this study would have resulted in bias in the review as 78% of the cohort had a diagnosis of stroke.

Agreements and disagreements with other studies or reviews

This review found insufficient evidence for the optimal type and intensity of MD rehabilitation programmes following BoNT for upper and lower limb spasticity, consistent with international consensus statements (Ober 2010; Sheean 2010). Thus, recommendations advocating integrated MD rehabilitation programmes following focal spasticity management are based on expert opinion only.

The evidence for CMT after BoNT for post-stroke upper limb spasticity in improving active upper limb function (Sun 2010) is also supported by a cohort study (Levy 2007). This study showed benefits of two weeks of CMT compared with a home exercise programme in patients at more than 90 days following stroke. However, unlike Sun 2010, the benefits diminished by 24 weeks. Other studies have shown that CMT improves arm motor function for stroke survivors with benefits persisting up to one year (Wolf 2000), so longer follow-up is warranted. However, evidence for improvement in active upper limb function after BoNT is variable, being supported by a few studies (Rosseneus 2002; Slawek 2005) but not by others (Elia 2009; Shaw 2011; Sheean 2001).

Authors' Conclusions

Implications for practice

There was limited evidence found in this review, which is matched by a lack of detail in recent spasticity management guidelines.
for recommending optimal multidisciplinary (MD) therapy programmes after BoNT. Hence clinical practices are based on a level of professional judgement and expertise with trial and error to determine which therapies are effective in an individual. Further trials are required to facilitate evidence-based practice.

Implications for research

Robust clinical trials are required to investigate the optimal timing, types (combinations of therapy approaches and modalities) and intensities (frequency, amount and duration of therapy) of MD rehabilitation programmes that improve activity and participation after BoNT and other focal intramuscular treatments for post-stroke spasticity.

Future trials may consider:

- better methodological quality including larger sample sizes and multicentre designs with internationally agreed data sets;

- longer follow-up (beyond six months) to determine the benefits of an intervention, as there may be a time lag between improvement in function and change in spasticity (Franch 2004), and whether the effects are maintained;

- development of appropriate outcome measures or consensus on a bank of measures that assess the ‘activity (passive and active function) and participation and ‘environmental factors’ domains of the ICF which translate into real-world functional abilities rather than focusing on impairments only. Other areas include addressing personal factors in the ICF that influence outcomes of rehabilitation interventions, and using appropriate patient-centred outcomes with standardised measures to provide a more holistic picture;

- evaluation of the perspectives of patients and caregivers, and cost-effectiveness of rehabilitation programmes;

- investigating optimal and effective mCIMT protocols;

- investigating the contribution of individual components of rehabilitation programmes to outcomes, individually and combined, in order to explore the ‘black box’ of rehabilitation.

ACKNOWLEDGEMENTS

We thank Professor Peter Langmore, Hazel Fraser and Brenda Thomas, and the Editorial Board of the Cochrane Stroke Group for their support and assistance, and Catherine Vontier and Dr Basker Amatya for their assistance with literature searches.

REFERENCES

References to studies included in this review

Lai 2009 [published and unpublished data]


Sun 2010 [published and unpublished data]


Wober 2010 [published and unpublished data]


References to studies excluded from this review

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Borg 2011 [published data only]


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Cheldas K, Barcich A, Jostefsky P, Rahling M, Alexander D, Good D, et al. Dose-dependent response to intramuscular botulinum toxin type A for upper-limb...

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Dauar E, Marco E, Caravantes C, Daza D, Chiaranda SC, Escalada F. Effects of botulinum toxin type A injections on clonic flexor spasticity of the upper limb in stroke. Randomized, clinical trial. Rehabilitation (Germany) 2011;45(3):194-201.

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Hesse 1998 [published data only]

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Karadag-Seryl 2010 [published data only]

Kurt 2006 [published data only]

Lagalla 1997 [published data only]

Marcos 2007 [published data only]

Mawson 2007 [published data only]

McCoy 2009 [published data only]

Meuth 2007 [published data only]

Nieber 2011 [published data only]

Piatus 2002 [published data only]

Raike 1998 [published data only]

Shaw 2011 [published data only]

Sheikh 2006 *(published data only)*
Sheikh M, Olyaei GR, Abdollahi R, Hoseini HA. Assessment of the effects of neurodevelopmental treatment (NDT) and botulinum toxin injection on spastic hemiplegic patients. *Journal of Iran University of Medical Sciences* 2006;13(5):156.

Sinto 2001 *(published data only)*

van Wijk 2006 *(published and unpublished data)*

Werner 2011 *(published data only)*

Wool 2007 *(published data only)*

References to ongoing studies

Graham 2009 *(published data only)*

Larrain 2011 *(published data only)*

Additional references

Aza 2006

Baldick 2011

Barros 2001

Bhakta 1996

Bhakta 2000

Bomanson 1987

Brassard 2002

De Jong 2004

De Pauw 1999

Ella 2009

Esquenazi 2001

Esquenazi 2010
Eskandani 2011  

Francis 2004  

Gassaway 2005  

Gowland 1993  

Gracies 2001  

Green 2002  

Higgins 2011  

Khan 2007  

Küesch 1960  

Lance 1950  

Langhorne 2001  

Lewy 2007  

Lundström 2010  

Lyle 1981  

Lyons 2008  

Mackay 2004  

Malhotra 2009  

Mehrholz 2005  

Morgan 2011  

Murphy 2000  

Oliver 2010  

Pandya 2005  

Peurala 2011

Podelcic 2011

RevMan 2011

Robinson 1983

Roncallo 2002

Shenaq 1998

Shenaq 2001

Shenaq 2010

Slawek 2005

Stevenson 2010

Stevenson 2002

Tennant 2007

Turner-Stokes 2005

Turner-Stokes 2009

Turner-Stokes 2010a

Turner-Stokes 2010b

Turner-Stokes 2010c

Vos van der Lee 2004

Wade 2010

Waxman 2002

WHO 1989

WHO 2001
WHO 2003

Wolf 2006
* Indicates the major publication for the study
## CHARACTERISTICS OF STUDIES

### Characteristics of included studies [ordered by study ID]

**Lai 2009**

<table>
<thead>
<tr>
<th>Methods</th>
<th>Single-blind pilot RCT</th>
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<tbody>
<tr>
<td><strong>Participants</strong></td>
<td>36 adults (18 to 75 years) ≥ 6 months after stroke with spasticity (MAS ≥ 2) of elbow flexors and range of movement deficit of ≥ 24% in elbow extension. 30 completed the study (6 excluded due to non-compliance). Intervention: N = 15; age = 49.1 (4) years; % female = 53.3%. Control: N = 15; age = 55.6 (5) years; % female = 33.3%. *Mean (SD).</td>
</tr>
<tr>
<td><strong>Interventions</strong></td>
<td>All groups: BoNT (standard injections into biceps, brachialis and brachioradialis), occupational, manual therapy (2 x 1-hour sessions weekly for 16 weeks) for moist heat, patient education and re-evaluation of symptoms, joint mobilisation, passive and active ROM, proprio-neural facilitation, and therapeutic exercise. Intervention group: adjunctive dynamic elbow splinting with EED worn for 6 to 6 hours during sleep and education in use of EED with change in tension prescribed twice a month.</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td>Impairments: mean % change in active range of movement elbow extension and MAS elbow flexors. Time points: before and 14 weeks after injection.</td>
</tr>
<tr>
<td><strong>Notes</strong></td>
<td>No outcomes of activity limitations (active or passive upper limb function) used. Physicians monitored adherence to wearing time of EED on a monthly basis.</td>
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<tr>
<td><strong>Risk of bias</strong></td>
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<tr>
<td>Bias</td>
<td>Authors' judgement</td>
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<td>Random sequence generation (selection bias)</td>
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<td>Blinding of outcome assessment (detection bias) All outcomes</td>
<td>Low risk</td>
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<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>High risk</td>
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<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
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<tr>
<td>Other bias</td>
<td>High risk</td>
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</tbody>
</table>

Sun 2010

Methods | Single-blinded RCT |

Participants | 32 adults (18 to 80 years) ≥ 1 year after stroke with severe spasticity (MAS ≥ 3) in elbows, wrist or finger flexors and ≥10° active interphalangeal and metacarpal phalangeal extension and 20° active wrist extension (minimal motor criteria). 29 completed the study (3 dropouts). Intervention: N = 15; age = 56.7 (9.9)* years; % female = 20%; time since stroke = 2.9 (1.5) years; Infarction = 80%. Control: N = 14; age = 61.5 (9.4)* years; % female: 21.4%; time since stroke = 2.9 (1.3) years; infarction = 78.6%. *Mean (SD). |

Interventions | All groups: BoNT (1000 units Dysport®), standard injections into elbow, wrist and finger flexors). Physiotherapy and occupational therapy (2 hours, 3 times per week for 3 months) starting the day following injections. Intervention group: modified CIMT with non-affected UL restrained for ≥ 5 hours per day. Therapy included massed practice, shaping (individualized task selection), graduated tasks difficulty and complexity, positive verbal feedback and physical assistance with movements; behavioural contract (activities to be done with restrain on and situations in which to remove it), and daily treatment diary. Participants encouraged to use the affected upper limb during home activities. Control group: NDT focusing on normalizing tone and movement patterns, proximal upper limb control, restoration of stance, gait, dexterity and stamina training exercises. 40% of therapy time focused on upper limb exercises. |
| Outcomes | Primary outcome: Impairment: MAS  
Secondary outcomes: activity limitation: MAL; amount of use (ADU) and quality of movement (QOM) (questionnaire for patient self-report), ARAT  
Other: patient's global satisfaction with treatment (7-point categorical scale from completely satisfied to completely dissatisfied) and adverse events  
Time points: before injection, 1, 3 and 6 months  
Exceptions: MAL not assessed at 1 month; patient satisfaction recorded at 3 and 6 months, and baseline ARAT performed twice, 4 weeks apart with averaged score used |
|---|---|
| Notes | Baseline data comparable  
Therapy adherence rates, assessed with daily exercise diaries, were high (93% and 87% for intervention and control groups respectively) |

### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
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<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Central web-based randomisation; block randomisation in groups of 4</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Sealed opaque envelopes</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias) All outcomes</td>
<td>High risk</td>
<td>Unblinded participants and therapists. Therapy sessions conducted at different times to avoid contact between participants. Unclear whether injectors were blinded</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias) All outcomes</td>
<td>Low risk</td>
<td>Blinded outcome assessor. MAL and patient global satisfaction associated with high risk of bias as participants unblinded</td>
</tr>
</tbody>
</table>
| Incomplete outcome data (attrition bias) All outcomes | High risk | Low attrition rate 9.4% (3/32). Reasons for dropouts given: 1 in intervention group relocated, 2 in control group due to transportation and traffic accident  
No ITT analysis or comparison of baseline characteristics between withdrawals and compliers |
| Selective reporting (reporting bias) | Low risk | All outcomes reported |
| Other bias | High risk | Single centre  
Small sample size and underpowered (16 participants required in each group to achieve 90% power to detect differences between the groups of MAS ≥ 1 with SD ≤ 0.9 and accounting for 5% to 10% dropouts) |
<table>
<thead>
<tr>
<th>Methods</th>
<th>Single-blind pilot RCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>23 adults with ≥ 6 months unilateral spastic hemiparesis (MAS ≥ 2 for wrist or finger flexors) due to stroke or TBI and moderate-severe hand impairment based on Chedoke-McMaster Assessment ≥ 2 with ability to do at least 1 of the following stage-3 tasks: active wrist extension greater than half range; active finger/wrist flexion greater than half range; or actively touch thumb to index finger when the hand was placed in supination with thumb fully extended. Exclusion criteria: no voluntary motion or severe fixed joint contracture of the affected arm. 18 completed the study. Intervention: N = 8, age = 54.0 (10.3)* years, % female = 70%; time since cerebral event = 9.7 (8.6)* years; cortical insult = 100%. Control: N = 10, age = 41.2 (14.2)* years, % female = 62%; time since cerebral event = 4.3 (2.5)* years; cortical insult = 92.3%. TBI participants: 39% of control group, 0% of intervention. Mean (SD).</td>
</tr>
<tr>
<td>Interventions</td>
<td>All groups: BoNT (using individualised injections). Task practice therapy: 6 x 1-hour visits with the occupational therapist; 1-hour home-based daily task practice (4-5 individualised functional tasks) for 12 weeks using a standardised protocol without constraining the unimpaired arm. Intervention group H200 FES device (Bioness0) with forearm-wrist-hand orthosis, worn during daily task practice activities, to activate flexor/extensor muscles producing grasp/release at an individualised intensity. 1 additional hour of occupational therapy to fit and train in use of FES device. Subsequent visits to check functioning and use of FES device and make adjustments.</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Primary outcome: activity limitation: How Well Scale of MAL—Observation (MAL-O) for observational assessment of upper limb function during activities of daily living. Investigator standardised administration and scoring of each MAL item through observation and trained the blinded assessor to inter-rater reliability (intra-class correlation coefficient 0.97) with the occupational therapist researcher (ERS). Secondary outcomes: activity limitation: ARAT, MAL—Self Report (MAL-SR). Time points: baseline (2 weeks prior) and 6 and 12 weeks after injection.</td>
</tr>
<tr>
<td>Notes</td>
<td>All TBI participants randomised to control group (5/13). Control group were significantly younger (P value = 0.03) which may be related to TBI participants. Adherence to the task practice programme, assessed through home diary records and additional electronic log in the intervention group, was high in both groups.</td>
</tr>
</tbody>
</table>

### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Random sequence of numbers; block randomization in groups of 4</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>High risk</td>
<td>Author’s response: &quot;true list of participants’ group assignment was kept by the treating therapist and used to determine whether or not to use the Boccia device.&quot;</td>
</tr>
<tr>
<td>----------------------------------------</td>
<td>-----------</td>
<td>------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>High risk</td>
<td>Unblinded participants and therapists. Blinded injecting physician</td>
</tr>
<tr>
<td>All outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Low risk</td>
<td>Blinded outcome assessor for primary outcome (MAL-O) and ARAT MAL-SR associated with high risk of bias as participants unblinded</td>
</tr>
<tr>
<td>All outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>High attrition rate (21.7%). Provided reasons for dropouts (n = 5): 3 in control group (discontinued intervention), 2 in intervention group (discontinued intervention and lost to follow-up) ITT analysis (n = 23) No significant baseline differences between dropouts and completers</td>
</tr>
<tr>
<td>All outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Unclear risk</td>
<td>MAS reported at baseline but not at follow-up. All other outcomes reported</td>
</tr>
<tr>
<td>Other bias</td>
<td>High risk</td>
<td>Single-centre study Convenience sample Small sample size and underpowered Groups unbalanced: all TBI participants randomised to control group (5/13) which was significantly younger (P value = 0.03). Age controlled for in analyses No subgroup analysis for TBI versus stroke participants in control group Authors’ conclusions related to results for entire cohort as there were no significant outcome differences between control and intervention groups</td>
</tr>
</tbody>
</table>

ARAT: Action Research Arm Test
BoNT: botulinum toxin
CI/MT: constraint-induced movement therapy
EED: Elbow Extension Dynastat®
FES: functional electrical stimulation
ITT: intention-to-treat
MAL: Motor Activity Log
MAS: Modified Ashworth Scale
NDT: neurodevelopmental treatment
RCT: randomized controlled trial
ROM: range of motion
SD: standard deviation
TBI: traumatic brain injury
UL: upper limb

**Characteristics of excluded studies (ordered by study ID)**

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baczek 2008</td>
<td>Intervention not MD (electrical stimulation, stretching or taping)</td>
</tr>
<tr>
<td>Bayram 2006</td>
<td>Intervention not MD (short-term electrical stimulation)</td>
</tr>
<tr>
<td>Hoog 2011</td>
<td>Comparator BoNT versus placebo, rehabilitation programme (standard care) in both groups</td>
</tr>
<tr>
<td>Calsa 2011</td>
<td>Intervention not MD (casting, stretching or taping)</td>
</tr>
<tr>
<td>Children 2004</td>
<td>Comparator 3 doses of BoNT, splinting and physical therapy in both groups</td>
</tr>
<tr>
<td>Clark 2011</td>
<td>Comparator BoNT A versus placebo, upper limb rehabilitation programme in both groups</td>
</tr>
<tr>
<td>Clarke 2003</td>
<td>Intervention not MD (functional electrical stimulation)</td>
</tr>
<tr>
<td>Cui 2006</td>
<td>Comparator BoNT A + rehabilitation therapy versus rehabilitation therapy</td>
</tr>
<tr>
<td>Duarte 2011</td>
<td>Intervention not MD (electrical stimulation)</td>
</tr>
<tr>
<td>Farina 2008</td>
<td>Intervention not MD (casting)</td>
</tr>
<tr>
<td>Gao 2006</td>
<td>Comparator BoNT A versus placebo, rehabilitation programme in both groups</td>
</tr>
<tr>
<td>Hess 1995</td>
<td>Intervention not MD (short-term electrical stimulation)</td>
</tr>
<tr>
<td>Hess 1998</td>
<td>Intervention not MD (physiotherapy only with short-term electrical stimulation)</td>
</tr>
<tr>
<td>Johnson 2004</td>
<td>Intervention not MD (physiotherapy only with electrical stimulation)</td>
</tr>
<tr>
<td>Karadjay-Saygi 2010</td>
<td>Intervention not MD (kinesiotaping versus sham taping)</td>
</tr>
<tr>
<td>Kran 2006</td>
<td>Intervention not MD (physiotherapy only and resting splint/orthotic)</td>
</tr>
<tr>
<td>Lagella 1997</td>
<td>Intervention not MD (forearm splint)</td>
</tr>
<tr>
<td>Marco 2007</td>
<td>Comparator BoNT versus placebo, inpatient rehabilitation programme and transcutaneous electrical nerve stimulation in both groups</td>
</tr>
<tr>
<td>Mawson 2007</td>
<td>Intervention not MD (BoNT + physiotherapy versus BoNT + stretching advice versus placebo + physiotherapy)</td>
</tr>
<tr>
<td>McGrorey 2009</td>
<td>Comparator BoNT versus placebo, physiotherapy and occupational therapy as per 'routine practice' in both groups</td>
</tr>
</tbody>
</table>
(Continued)

<table>
<thead>
<tr>
<th>Meythaler 2009</th>
<th>Comparator BoNT versus placebo, occupational therapy programme both groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pieber 2011</td>
<td>Intervention not MD (FES only), participants were children with mixed neurological diagnoses</td>
</tr>
<tr>
<td>Ponsa 2002</td>
<td>Intervention not MD (physiotherapy only with short term electrical stimulation)</td>
</tr>
<tr>
<td>Reicer 1998</td>
<td>Intervention not MD (ankle taping)</td>
</tr>
<tr>
<td>Shaw 2011</td>
<td>Comparator BoNT versus placebo, upper limb therapy programme in both groups</td>
</tr>
<tr>
<td>Sheikh 2006</td>
<td>Comparator BoNT versus placebo, NDT programme in both groups</td>
</tr>
<tr>
<td>Sato 2001</td>
<td>Intervention not MD (acupuncture)</td>
</tr>
<tr>
<td>von Wijck 2006</td>
<td>Intervention not MD (task specific therapy programme was physiotherapy only)</td>
</tr>
<tr>
<td>Werner 2011</td>
<td>Comparator BoNT versus placebo, inpatient rehabilitation programme in both groups</td>
</tr>
<tr>
<td>Wolf 2007</td>
<td>Comparator BoNT versus placebo, rehabilitation programme (modalities, repetitive task practice, strengthening and functional activities) in both groups</td>
</tr>
</tbody>
</table>

BoNT: botulinum toxin
FES: functional electrical stimulation
MD: multidisciplinary
NDT: neurodevelopmental treatment

Characteristics of ongoing studies [ordered by study ID]

Graham 2009

<table>
<thead>
<tr>
<th>Trial name or title</th>
<th>Efficacy and safety study of botulinum neurotoxin A with rehabilitation versus botulinum neurotoxin A alone in treatment of post-stroke spasticity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methods</td>
<td>RCT</td>
</tr>
</tbody>
</table>
| Participants        | Adults ≥18 years  
Stroke (ischaemic or haemorrhagic) ≥ 6 months prior  
Upper limb focal spasticity at elbow, wrist, fingers and thumb. MAS ≥ 3 at wrist and/or fingers  
Functional impairment secondary to spasticity e.g. difficulty with hygiene, dressing, posture or pain |
| Interventions       | BoNT with rehabilitation therapy for the duration of the study (for up to 2 injections of BoNT A) versus BoNT only |

Multidisciplinary rehabilitation following botulinum toxin and other focal intramuscular treatment for post-stroke spasticity (Review)  
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### Graham 2009 (Continued)

| Outcomes | Primary outcome measure: Fugl-Meyer upper extremity score  
Secondary outcome measures: length of time to meet re-injection criteria, number of participants that do not meet re-injection criteria prior to completion of the study |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Starting date</td>
<td>January 2009</td>
</tr>
<tr>
<td>Contact Information</td>
<td>Principal Investigator: Glenn D Graham, New Mexico VA Health Care System, Albuquerque, New Mexico, USA</td>
</tr>
<tr>
<td>Notes</td>
<td>Status: Recruiting</td>
</tr>
</tbody>
</table>

### Laniin 2011

<table>
<thead>
<tr>
<th>Trial name or title</th>
<th>The effectiveness of best practice therapy after Botulinum Toxin A injections for adults diagnosed with neurological impairment and onset of spasticity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methods</td>
<td>RCT</td>
</tr>
</tbody>
</table>
| Participants | Adults ≥18 years  
Neurological injury (including stroke and brain injury) ≥ 1 month prior  
Spasticity in at least 1 limb |
| Interventions | Group A: best practice therapy provided by an occupational or physical therapist including evidence-based protocols for casting, electrical stimulation, task-specific movement training and home practice. 14 sessions (1 hour per session) of best practice therapy is provided over 8 weeks (2 weeks of casting (1 session per week)), followed by 2 weeks of 3 x weekly therapy, then 2 weeks of 2 x weekly therapy, and finishing with 2 weeks of 1 x weekly therapy  
Group B: best practice therapy plus botulinum toxin injections  
Group C: botulinum toxin injection only (i.e. without best practice therapy) |
| Outcomes | Primary outcome measure: Goal Attainment Scaling T-score change score  
Secondary outcome measures: Box and Block Test change score (hand dexterity), 6 metre walk test change score, Tardieu Scale |
| Starting date | September 2010 |
| Contact Information | Natasha Laniin, Alfred Health Clinical School Level 4 The Alfred Centre 99 Commercial Road Prahran Victoria 3181, Australia. Email: n.laniin@latrobe.edu.au |
| Notes | Status: recruitment completed |

---

BoNT: botulinum toxin  
MAS: Modified Ashworth Scale  
RCT: randomised controlled trial
DATA AND ANALYSES

This review has no analyses.

ADDITIONAL TABLES

Table 1. Levels of quality of individual studies

<table>
<thead>
<tr>
<th>Judgement of risk of bias</th>
<th>Methodological quality – 'high-quality study'</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk of bias of all domains low</td>
<td>High</td>
</tr>
<tr>
<td>Unclear or high risk of bias for one or more domains</td>
<td>Low</td>
</tr>
<tr>
<td>High risk of bias for most domains</td>
<td>Very low methodological quality – 'very low-quality study'</td>
</tr>
</tbody>
</table>

Table 2. Levels of quality of a body of evidence in the GRADE approach

<table>
<thead>
<tr>
<th>Underlying methodology</th>
<th>Quality rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomised trials or double-upgraded observational studies</td>
<td>High</td>
</tr>
<tr>
<td>Downgraded randomised trials or upgraded observational studies</td>
<td>Moderate</td>
</tr>
<tr>
<td>Double-downgraded randomised trials or observational studies</td>
<td>Low</td>
</tr>
<tr>
<td>Triple-downgraded randomised trials or downgraded observational studies or case series/case reports</td>
<td>Very low</td>
</tr>
</tbody>
</table>

Table 3. Factors that may decrease the quality level of a body of evidence

1. Limitations in the design and implementation of available studies suggesting high likelihood of bias
2. Indirectness of evidence (indirect population, intervention, control, outcomes)
3. Unexplained heterogeneity or inconsistency of results (including problems with subgroup analyses)
4. Imprecision of results (wide confidence intervals)
5. High probability of publication bias
<table>
<thead>
<tr>
<th>Study</th>
<th>Description of results of included studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lal 2009</td>
<td></td>
</tr>
<tr>
<td><strong>Participants</strong></td>
<td>N = 36 (N = 30 in analysis)</td>
</tr>
<tr>
<td><strong>Summary of Results</strong></td>
<td>Greater improvement in active range of movement elbow extension at 14 weeks in intervention compared with control group. MAS scores for elbow flexors showed comparable changes of 9.3% and 8.6% in intervention and control groups respectively. Statistical analysis trends and mean changes in outcomes were assessed using Excel tables.</td>
</tr>
<tr>
<td><strong>Results in favour of the intervention</strong></td>
<td>Active range of movement mean % change: 33.5 (29.6) versus 18.7 (48.7) in control group. <em>Mean (SD)</em></td>
</tr>
<tr>
<td><strong>Authors’ conclusions</strong></td>
<td>This study confirmed the efficacy of BoNT in tone management and occupational therapy in contracture reduction, and showed the value of dynamic splinting in maintaining gains in range of motion.</td>
</tr>
<tr>
<td>Sun 2010</td>
<td></td>
</tr>
<tr>
<td><strong>Participants</strong></td>
<td>N = 32 (N = 29 in analysis)</td>
</tr>
<tr>
<td><strong>Summary of Results</strong></td>
<td>MAS improved in both groups at 4 weeks and 3 months post injection, with no between-group differences. Median MAS score change was -2 in all cases, except at the elbow in the control group at 3 months where it was -1.5. At 6 months, there was a significant reduction in MAS at elbow (P value = 0.004), wrist (P value = 0.003), hand (P value = 0.001), and fingers (P value &lt; 0.001) in the intervention group (median MAS score change of -1). Benefit persisted only in the wrist flexors in the control group (P value = 0.014).</td>
</tr>
<tr>
<td><strong>Results in favour of the intervention</strong></td>
<td>Intervention group had statistically significant improvements compared with the control group: at 6 months in MAS at elbow (P value = 0.019), wrist (P value = 0.019), and fingers (P value &lt; 0.001); and 3 and 6 months on the ARAT (P value = 0.012 and P value &lt; 0.001) and MAL (AOU (P value &lt; 0.001 and P value &lt; 0.001), QOM (P value = 0.007 and P value &lt; 0.001)). Both groups improved on the ARAT at 4 weeks, with no between-group differences. Patient satisfaction was high in the intervention group at 3 and 6 months and declined in both groups at 6 months.</td>
</tr>
<tr>
<td><strong>Statistical analysis</strong></td>
<td>Mann-Whitney U tests. Chi^2 tests or Fisher exact tests for baseline comparisons. Wilcoxon signed rank tests for within-group change from baseline. Mann-Whitney U test for between-group comparisons. P value &lt; 0.05 were statistically significant.</td>
</tr>
</tbody>
</table>

Multidisciplinary rehabilitation following botulinum toxin and other focal intramuscular treatment for post-stroke spasticity (Review) 2013 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.
Table 4. Description of results of included studies  (Continued)

<table>
<thead>
<tr>
<th>Authors' conclusions</th>
<th>Combined BoNT and mCIMT produced significantly greater improvements in spasticity and upper-extremity motor function than BoNT and conventional rehabilitation in chronic stroke patients with upper extremity spasticity, with benefits lasting up to 6 months. The combined therapy resulted in high patient satisfaction with no serious adverse events.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weber 2010</td>
<td></td>
</tr>
<tr>
<td>Participants</td>
<td>N = 23 (all included in analysis)</td>
</tr>
<tr>
<td>Summary of Results</td>
<td>No significant differences between intervention and control groups for any outcome variable over time. Positive but insignificant trends toward improvement for MAL-O, MAL-SR and ARAT for both groups from baseline to week 6, and MAL-SR for intervention group from 6 to 12 weeks. Control group had an insignificant trend toward deterioration in MAL-SR from 6 to 12 weeks. The entire cohort had significant improvements in MAL-O (0.41 (0.24 to 0.58)), MAL-SR (0.64 (0.32 to 0.95)) and ARAT (6.39 (3.38 to 9.4)) from baseline to week 6. Improvements in MAL-SR (0.65 (0.33 to 0.97)) and ARAT (6.17 (2.31 to 10.03)) were sustained to week 12. Results were mean difference (95% CI)</td>
</tr>
<tr>
<td>Results in favour of the intervention</td>
<td>Nil</td>
</tr>
<tr>
<td>Author's conclusions</td>
<td>BoNT and task practice therapy combined are effective in improving upper limb motor function and reducing spasticity in patients with chronic spastic hemiparesis. However, the cyclic FES protocol used in this study did not increase the gains achieved</td>
</tr>
</tbody>
</table>

AOU: amount of use
ARAT: Action Research Arm Test
BoNT: botulinum toxin
FES: functional electrical stimulation
MAL: Motor Activity Log
MAL-O: Motor Activity Log Observation
MAL-SR: Motor Activity Log Self Report
MAS: Modified Ashworth Scale
mCIMT: modified constraint-induced movement therapy
QOM: quality of movement
SD: standard deviation
APPENDICES

Appendix 1. Cochrane Central Register of Controlled Trials (CENTRAL)

1. MeSH descriptor Cerebrovascular Disorders explode all trees
2. stroke or poststroke or post-stroke or cerebrovascular or brain vascular or cerebral vascular or cva or apoplexy or SAH
3. brain* or cerebr* or cerebell* or intracranal* or intracerebral
4. ischaemia* or ischaemic* or infarct* or thrombo* or emboli* or occlus*
5. (#3 AND #4)
6. brain* or cerebr* or cerebell* or intracerebral or intracranial or subarachnoid
7. haemorrhage* or hemorrhage* or haematoma* or hematoma* or bleed*
8. (#6 AND #7)
9. hemiplegia* or hemipar* or paroxy or parox
10. MeSH descriptor Hemiplegic, this term only
11. MeSH descriptor Paralysis explode all trees
12. (#1 OR #2 OR #5 OR #8 OR #9 OR #11)
13. MeSH descriptor Muscle Spasticity, this term only
14. MeSH descriptor Muscle Hypertonia, this term only
15. MeSH descriptor Muscle Rigidity, this term only
16. MeSH descriptor Muscle Tonia, this term only
17. MeSH descriptor Spasm, this term only
18. MeSH descriptor Dystonia, this term only
19. MeSH descriptor Paraparesis, Spastic, this term only
20. spastic* or high tone
21. muscle*
22. spasm or spams or rigid* or tone or tonic or hypertonia* or hypermyoton* or dystonia* or contracture*
23. (#21 AND #22)
24. (#13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #23)
25. MeSH descriptor Botulinum Toxins explode all trees
26. MeSH descriptor Pneumos explode all trees
27. MeSH descriptor Ethanol, this term only
28. MeSH descriptor Injections, Intramuscular, this term only
29. MeSH descriptor Nerve Block, this term only
30. botulinum* or botulin or botulins or BoNT* or BTX* or dysport or zioxin or myobloc or neurobloc or oculinum or onabotulinum* or abobotulinum* or incobotulinum* or rimabotulinum*
31. phosp or phos or phos or alcohol or nerve block* or motor point block*
32. intramuscular
33. injection* or treatment* or medication* or neurology
34. (#32 AND #33)
35. (#25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #34)
36. (#12 AND (#21 AND #35))

Appendix 2. MEDLINE (Ovid)

1. cerebrovascular disorders/ or exp basal ganglia cerebrovascular disease/ or exp brain ischemic/ or exp carotid artery disease/ or exp intracranial arterial disease/ or exp intracranial embolism and thrombosis/ or exp intracranial hemorrhages/ or stroke/ or exp brain infarction/ or vertebral artery dissection/
2. stroke or poststroke or post-stroke or cerebrovascular or brain vascular or cerebral vascular or cva or apoplexy or SAH.
3. (ischaemia* or ischaemic* or infarct* or thrombo* or emboli* or occlus*)
4. (hemiplegia* or hemipar* or paroxy or parox)
5. hemiplegia/
6. paraparesis/

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7. 1 or 2 or 3 or 4 or 5 or 6
8. muscle spasticity/ or muscle hypertonia/ or muscle rigidity/ or muscle tonus/
9. spasm/ or dystonia/ or paresis/ or spastic/
10. (spastic$ or high tone$).tw.
11. (muscle3 adj5 (spasm or spasms or rigid$ or tone or tonus or hypertonus$ or dystonia$ or contracture$)).tw.
12. 8 or 9 or 10 or 11
13. exp botulinum toxins/ or exp phenol$ or exp ethanol$ or exp injections, intramuscular/ or nerve block/
14. (botulinum$ or botulin or botulon or BoNTS or BTXS or dysport or toxinin or toxun or toxumin or neurobloc or oculinum or onabotulinum$ or abobotulinum$ or incobotulinum$ or rimabotulinum$).tw.
15. (phenol or ethanol or alcohol or nerve block$ or motor point block$).tw.
16. (intramuscular adj3 (injection$ or treatment$ or medication$ or neurolysis$)).tw.
17. 13 or 14 or 15 or 16
18. 7 and 12 and 17
19. cerebral palsy/ or cerebral palsy.tw.
20. 18 not 19
21. Randomized Controlled Trials as Topic/
22. random allocation/
23. Controlled Clinical Trials as Topic/
24. control group/
25. clinical trials as topic/
26. double-blind method/
27. single-blind method/
28. Placebo/
29. placebo effect/
30. Multicenter Studies as Topic/
31. Therapies, Investigational/
32. Research Design/
33. Program Evaluation/
34. evaluation studies as topic/
35. randomized controlled trial.pt.
36. controlled clinical trial.pt.
37. clinical trial.pt.
38. multicenter study.pt.
40. randomi$.tw.
41. (controlled adj5 (trial$ or stud$)).tw.
42. (clinical$ adj5 trial$).tw.
43. ((control or treatment or experiment$ or intervention$) adj5 (group$ or subject$ or patient$)).tw.
44. (quasi-random$ or quasi-random$ or pseudo-random$ or pseudo random$).tw.
45. ((multicenter or multicentre or therapeutic) adj5 (trial$ or stud$)).tw.
46. ((control or experiment$ or conservative) adj5 (treatment or therapy or procedure or manage$)).tw.
47. ((single$ or double$ or triple$ or triple$) adj5 (blind$ or mask$)).tw.
48. versus.tw.
49. placebo.s.tw.
50. sham.tw.
51. (assign$ or alternate or allocate$).tw.
52. control.tw.
53. or 21-52
54. 20 and 53
55. exp animals/ or not humans.sh.
56. 54 not 55

Multidisciplinary rehabilitation following botulinum toxin and other focal intramuscular treatment for post-stroke spasticity (Review) 35
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Appendix 3. EMBASE (Ovid)

1. cerebrovascular disease/ or basal ganglia hemorrhage/ or cerebral artery disease/ or cerebrovascular accident/ or stroke/ or exp carotid artery disease/ or exp brain hemorrhage/ or exp brain infarction/ or exp brain ischemia/ or exp intracranial aneurysm/ or exp occlusive cerebrovascular disease/ 
2. stroke unit/ or stroke patient/ 
3. (stroke or poststroke or post-stroke or cerebrovascular or brain vascular or cerebral vascular or cva or apoplexy or SAH),tw. 
4. ((brain$ or cerebr$ or cerebell$ or intracran$ or intracerebral) adj5 (isch$ or infarct$ or thrombo$ or embol$ or occlus$)),tw. 
5. ((brain$ or cerebr$ or cerebell$ or intracranial or intracerebral or subarachnoid) adj5 (haemorrhage$ or hemorrhage$ or haematomas$ or hematoma$ or bleed$)),tw. 
6. hemiplegia/ or paresis/ 
7. (hemiplegia$ or hemiparesis$ or paresis$ or paresis),tw. 
8. 1 or 2 or 3 or 4 or 5 or 6 or 7 
9. muscle hyper trophy/ or muscle rigidity/ or spastic paresis/ or spasticity/ 
10. muscle spasm/ or muscle tone/ or dystonia/ or paraplegia/ 
11. (spastic$ or high tone),tw. 
12. (muscle$ adj5 (spasm or spasms or rigid$ or tone or tonus or hypertonia$ or hypermyoton$ or dyton$)),tw. 
13. 9 or 10 or 11 or 12 
14. botulinum toxin/ or botulinum toxin a/ or botulinum toxin b/ or botulinum toxin e/ or botulinum toxin f/ 
15. phenol/ or alcohol/ or intramuscular drug administration/ or exp nerve block/ 
16. (botulinum$ or botulin$ or botox or BoNT$ or BTX$ or dysport or toxim$ or myobloc$ or neucobloc$ or oculinum$ or onabotulinum$ or abobotulinum$ or incobotulinum$ or rimabotulinum$),tw. 
17. (phenol or ethanol or alcohol or nerve block$ or motor point block$),tw. 
18. (intramuscular adj5 (injection$ or treatment$ or medication$ or neurolysis$)),tw. 
19. 14 or 15 or 16 or 17 or 18 
20. 8 and 13 and 19 
21. cerebral palsy/ or cerebral palsy,tw. 
22. 20 not 21 
23. Randomized Controlled Trial/ 
24. Randomization/ 
25. Controlled Study/ 
26. control group/ 
27. clinical trial/ 
28. Double Blind Procedure/ 
29. Single Blind Procedure/ or triple blind procedure/ 
30. placebo/ 
31. Multicenter Study/ 
32. experimental design/ or experimental study/ or quasi experimental study/ 
33. experimental therapy/ 
34. evaluation/ or"evaluation and follow up"/ or evaluation research/ or clinical evaluation/ 
35. "types of study"/ 
36. Comparative Study/ 
37. random$,tw. 
38. (controlled adj5 (trial$ or study$)),tw. 
39. (clinical$ adj5 trial$),tw. 
40. (control or treatment or experiment$ or intervention) adj5 (group$ or subject$ or patient$),tw. 
41. (quasi-random$ or quasi random$ or pseudo-random$ or pseudo random$),tw. 
42. (multicenter or multicentre or therapeutic) adj5 (trial$ or study$),tw. 
43. (control or experiment$ or conservative) adj5 (treatment or therapy or procedure or manage$),tw. 
44. ((sing$, double$ or triple$ or triple$ or treble$ adj5 (blind$, or mask$)),tw. 
45. version,tw. 
46. placebo,tw. 
47. sham,tw.
Appendix 4. CINAHL (EBSCO)

S37. S33 not S36
S36. S34 or S35
S35. TI cerebral palsy OR AB cerebellar palsy
S34. (MH “Cerebral Palsy")
S33. S22 and S32
S32. S25 or S24 or S25 or S20 or S27 or S28 or S29 or S30 or S31
S31. AB intramuscular AND AB ( injection" or treatment" or mediation" or neuromuscular injection")
S30. TI intramuscular AND TI ( injection" or treatment" or medication" or neurolysis)
S29. TI ( phenol or ethanol or alcohol or nerve block" or motor point block") OR AB ( phenol or ethanol or alcohol or nerve block" or motor point block")
S28. TI ( botulinum" or botulin or botulin or BoNT" or BTX" or dysport or toxin or myobloc or neurobloc or occlumin or onabotulinum" or abobotulinum" or incobotulinum" or rimabotulinum") OR AB ( botulinum" or botulin or botulin or BoNT" or BTX" or dysport or toxin or myobloc or neurobloc or occlumin or onabotulinum" or abobotulinum" or incobotulinum" or rimabotulinum")
S27. (MH “Nerve Block”)
S26. (MH “Injection, Intramuscular”)
S25. (MH “Ethanol”)
S24. (MH “Phenol")
S23. (MH “Botulinum Toxins”)
S22. S12 and S21
S21. S13 or S14 or S15 or S16 or S17 or S20
S20. S18 and S19
S19. TI ( spasm or spasms or rigid" or tone or tautness or hypertonus" or hyperreflexia" or dyston") or AB ( spasm or spasms or rigid" or tone or tautness or hypertonus" or hyperreflexia" or dyston")
S18. TI muscle" or AB muscle"
S17. TI ( spastic" or high tone" or AB ( spastic" or high tone")
S16. (MH “gait disorders, neurologic”)
S15. (MH “dystonia”)
S14. (MH “spasm”)
S13. (MH “Muscle Spasticity”) OR (MH “Muscle Hypertonia”) OR (MH “Muscle Tone”)
S12. S1 or S2 or S5 or S8 or S9 or S10 or S11
S11. (MH “brain injuries”)
S10. TI ( hemiplegia or hemiparetic or paresis or paralytic") OR AB ( hemiplegia or hemiparetic or paresis or paralytic")
S9. (MH “Hemiplegia”)
S8. S6 and S7
S7. (TI (haemorrhage" or hemorrhage" or haematoma" or hematoma" or bleed") or AB (haemorrhage" or hemorrhage" or haematoma" or hematoma" or bleed")
S6. TI ( brain" or cerebellum" or intracerebral or infratentorial or subarachnoid") OR AB ( brain" or cerebellum" or intracerebral or infratentorial or subarachnoid")
S5. S3 and S4
S4. TI ( ischemia" or ischemic" or infarct" or thrombus" or embolism" or occlusion") OR AB ( ischemia" or ischemic" or infarct" or thrombus" or embolism" or occlusion")
S3. TI ( brain" or cerebellum" or intracranial or infratentorial") OR AB ( brain" or cerebellum" or intracranial or infratentorial")
Appendix 5. AMED (Ovid)

1. cerebrovascular disorders or cerebral hemorrhage or cerebral infarction or cerebral ischemia or cerebrovascular accident or stroke/
2. (stroke or poststroke or post-stroke or cerebrovascular or brain vasc* or cerebral vasc or cva or apoplexy or SAH) or AB (stroke or poststroke or post-stroke or cerebrovascular or brain vasc* or cerebral vasc or cva or apoplexy or SAH)
3. (tbi or cerebr or cerebell or intracran or intracerebral adj5 (ischemia or infarct or thromb or emboli or occlus)).tw.
4. (tbi or cerebr or cerebell or intracran or intracerebral or subarchn adj5 (haemorrhage or hemorrhage or haematomy or brain)).tw.
5. (hemiplegia or hemiparet or paraly or paretic).tw.
6. (spastic or dystonia or spastic or spasm or rigidi or tone or tone or hypertoni or hyperkineti or dystoni or contractur).tw.
7. (1 or 2 or 3 or 4 or 5 or 6)
8. exp muscle spasticity or muscle hypertonia or muscle tonus
9. (spastic or dystonia or spastic or spasm or rigidi or tone or tone or hypertoni or hyperkineti or dystoni or contractur).tw.
10. (tbi or cerebr or cerebell or intracran or intracerebral adj5 (ischemia or infarct or thromb or emboli or occlus)).tw.
11. (tbi or cerebr or cerebell or intracran or intracerebral or subarchn adj5 (haemorrhage or hemorrhage or haematomy or brain)).tw.
12. (1 or 2 or 3 or 4 or 5 or 6)
13. (botulinum toxin or phenol or alcohol ethyl or nerve block)
14. (botulinum toxin or botulinum toxin or onabotulinum or abobotulinum or incobotulinum or rimobotulinum).tw.
15. (phenol or ethanol or alcohol or nerve block or motor point block).tw.
16. (intramuscular adj3 (injection or treatment or medication or neurolysis)).tw.
17. (1 or 2 or 3 or 4 or 5 or 6)
18. (1 or 2 or 3 or 4 or 5 or 6)

Appendix 6. LILACS

(MH: "cerebrovascular disorders" or MH: "basal ganglia cerebrovascular disease" or MH: "brain ischemia" or MH: "cerebral artery diseases" or MH: "intracranial arterial disease" or MH: "intracranial embolism and thrombosis" or MH: "intracranial hemorrhages" or MH: "stroke" or MH: "cerebral infarction" or MH: "cerebral artery disease" or TW: "stroke" or TW: "poststroke" or TW: "post-stroke" or TW: cerebrovascular or TW: "cerebral vasc" or TW: "cerebr vasc" or TW: "cerebr" or TW: "cerebell" or TW: "intracranial" or TW: "intracerebral" or TW: "subarchn" or MH: "hemiplegia" or MH: "paraly" or TW: "hemiplegia" or TW: "hemi" or TW: "paraly")

AND

(MH: "muscle spasticity" or MH: "muscle hypertonia" or MH: "muscle rigidity" or MH: "muscle tonus" or MH: "spasm" or MH: "dystonia" or MH: "paresthesia" or MH: "spastic" or MH: "rigid" or MH: "tone" or MH: "tonus" or MH: "hyperkineti" or MH: "hyperkinesia")

AND

(MH: "botulinum toxin" or MH: "phenol" or MH: "ethanol" or MH: "injections intramuscular" or MH: "nerve block" or TW: "botulinum toxin" or TW: "botulinum toxin" or TW: "onabotulinum toxin" or TW: "abobotulinum toxin" or TW: "incobotulinum toxin" or TW: "rimobotulinum toxin")

AND

(MH: "multidisciplinary rehabilitation following botulinum toxin injection and other focal intramuscular treatment for post-stroke spasticity (Review)")

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Appendix 7. PEDro

Search completed in advanced search using the abstract and title field using the following terms:

- spasticity ethanol
- spasticity phenol
- spasticity rimabotulinum
- spasticity incobotulinum
- spasticity abobotulinum
- spasticity onabotulinum
- spasticity oculturnum
- spasticity neurobloc
- spasticity myobloc
- spasticity xeomin
- spasticity dysport
- spasticity BTX
- spasticity BoNT
- spasticity botulinum
- spasticity botulinum*

Appendix 8. REHABDATA

Botulinum* botulin botulin BoNT* BTX* dysport xeomin myobloc neurobloc oculturnum onabotulinum* abobotulinum* incobotulinum* rimabotulinum* phenol ethanol

“nerve block”, “motor point block”, “intramuscular injection”

Contributions of Authors

Marina Demerelod (MD), Lynne-Turner Stokes (LTS) and Fary Khan (FK) were involved in writing the protocol and review, incorporating comments from the reviewers. Caroline Brand (CB) and Shane McSweeney (SM) were involved at the review stage.

Declarations of Interest

The authors are therapists or clinicians in the field of Physical and Medical Rehabilitation with a clinical interest in management of spasticity.

Lynne-Turner Stokes has received honoraria from Ipsen Ltd and from Allergan on a number of occasions over the last few years for lecturing and running training courses and workshops - particularly with respect to the use of goal attainment scaling in spasticity. She has been involved with the development of clinical guidelines and consensus statements regarding spasticity management that were sponsored variously by Ipsen Ltd and Allergan. She has received consultancy fees for advising on research projects and for data analysis, and has held research grants from Ipsen Ltd to conduct studies relating to spasticity management. She has also published papers and presented abstracts at conferences reporting trials and other studies relating to the use of botulinum toxin for spasticity. Some of her work in this area may have been eligible for inclusion in the review.
SOURCES OF SUPPORT

Internal sources
- Department of Rehabilitation Medicine, Royal Melbourne Hospital, Australia.

External sources
- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW
We did not include studies involving participants with conditions other than stroke unless stroke-specific data were provided separately or more than 75% of participants had a diagnosis of stroke. Where the proportion of the study population with stroke was < 75% we contacted study authors for data on stroke participants only.

Due to the lack of clinical homogeneity, the variability of methods and available data between the included studies, quantitative meta-analysis was not possible. Thus, it was not possible to use a fixed-effect model and the $I^2$ statistic for heterogeneity to assess outcome data for compatibility with the assumption of a uniform risk ratio (P value < 0.10), perform visual inspection of forest plots, or conduct statistical analysis as described in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011).

Subgroup analysis for the following subgroups was not possible:
- type of stroke and location;
- site of spasticity, i.e. upper or lower limb, or both;
- age (children, adults less than 65 years of age versus 65 years of age or older);
- type of rehabilitation programme (e.g. outpatient, home-based);
- intensity of treatment (high intensity, low intensity); and
- time of treatment following stroke (acute, less than six weeks; subacute, six weeks to six months; and chronic, more than six months).

INDEX TERMS

Medical Subject Headings (MeSH)
*Patient Care Teams; Botulinum Toxins [*therapeutic use]; Muscle Spasticity [drug therapy; etiology; *rehabilitation]; Neuromuscular Agents [*therapeutic use]; Randomized Controlled Trials as Topic; Stroke [*complications; drug therapy]

MeSH check words
- Adult; Humans; Middle Aged
MORE THAN A BLACK BOX OF REHABILITATION: CHARACTERIZING THERAPY PROGRAMMES FOLLOWING BOTULINUM TOXIN INJECTIONS FOR SPASTICITY IN ADULTS WITH STROKE

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INTRODUCTION

Stroke-related disability is globally increasing with the ageing population (1). Spasticity is a chronic impairment contributing to this and requires long-term management. Spasticity has been reported in over 40% of stroke survivors (2), with disabling or severe spasticity affecting 4% (1) to 39% (6). Prevalence rates are even higher in those attending outpatient rehabilitation facilities, with severe or symptomatic spasticity in 30–36% (3). It can interfere with activity or provision of care, or cause pain or secondary complications (6, 7).

Botulinum toxin type A (BoNT-A) is widely used for focal muscle overactivity following stroke to manage these limitations. This is usually part of an integrated multidisciplinary rehabilitation programme (8, 9) targeting individualized patient and caregiver goals (10). However, rehabilitation in this setting assumes a “black box.” Whilst guidelines recommend multidisciplinary management following BoNT-A (6, 11), the details of therapy content, and optimal therapy types (activities, interventions, therapy approaches), settings and intensities are unclear and highly variable (12). Studies rarely describe details of rehabilitation programmes beyond duration, frequency and generic broad therapy terms (13–15), making replication in a clinical setting difficult. In addition, therapy interventions are often investigated in isolation rather than in the milieu of the complex array of rehabilitation interventions provided in everyday clinical practice during rehabilitation programmes (12).

Excessive work has been done in opening and examining the “black box” of stroke rehabilitation programmes (16) during occupational therapy (OT) (17–19) and physiotherapy (PT) (19, 20). However, no such studies have investigated the therapy components provided following BoNT-A for post-stroke spasticity, although rehabilitation is often routinely provided. These complex rehabilitation interventions are difficult to standardize and define, and measuring what actually works in rehabilitation is a challenge. Standardized approaches to documenting therapy interventions are a step towards bridging...
this gap. A general model for describing critical attributes of disease management programmes for chronic conditions has been developed, allowing for comparisons across interventions.

2.1.1.4. A more detailed level, use of a taxonomy to characterize the complex array of therapy activities and interventions systematically provides a means of capturing what actually happens in stroke rehabilitation programmes. (16, 22) and determining how therapy prescription relates to patients' goals. Patient factors and specific therapy activities associated with better outcomes can then be identified (24), improving patient selection, service delivery and effectiveness. Stroke rehabilitation in inpatient (17, 18, 20, 23) and day hospital settings (19) has been defined in such a way. This is yet to be described specifically for multidisciplinary rehabilitation programmes following BoNT-A, for post-stroke spasticity.

Using a standardized taxonomy (16, 21, 24), this study describes the therapeutic activities and interventions utilized within multidisciplinary ambulatory rehabilitation programmes for stroke survivors receiving BoNT-A for upper and/or lower limb spasticity. Furthermore, how rehabilitation content differs, as categorized by the limb injected or the goals selected, is investigated; thus, exploring the "black box" of rehabilitation.

METHODS

Study design and participants

Adult stroke survivors (stroke ≥3 months poststroke) treated with BoNT-A for problematic upper and/or lower limb spasticity were recruited from a multidisciplinary, tertiary referral, spasticity management service in Victoria, Australia. Ethics approval was obtained from the relevant ethics committees. This study was part of a larger trial, comparing high intensity and lower intensity (usual care) ambulatory rehabilitation programmes following BoNT-A, as described elsewhere (24). All participants received individualized BoNT-A injections in the affected limb(s), as determined by clinical factors, spasticity pattern and treatment goals (6, 11). Up to 2 individualized SMART (specific, measurable, achievable, realistic, and timable) goals for each treated limb (maximum 8 goals if both limbs were treated) were negotiated between participants, caregivers and therapist(s) using the goal attainment scaling (GAS) protocol (26). Baseline data included demographic and clinical characteristics, such as stroke etiology and localization.

Following BoNT-A injections, participants were referred to ambulatory rehabilitation services determined by geographical catchment areas (24). Details of treatment goals were provided to the treating therapist. Therapy programmes were individualized and goal-directed following testing reassessment, where interventions and therapy approaches were determined.

Standardized therapy documentation forms. Treatment therapists used a stroke rehabilitation intervention classification system (comprising 2 forms: physical and occupational therapy) (17, 20, 22, 23) to document rehabilitation activities and interventions used by therapists during each PT and OT session for the programme duration. System occupational and physical therapy activities of variable complexity comprise the key structure of the classification system, in addition to 31 interventions classified by target body systems (Chapters D). To construct the documentation grid, therapists recorded the duration of each therapeutic activity in 5-min intervals and codes for the interventions (maximum of 5) used to facilitate performance of these activities. A category for "other" interventions was utilized if needed. Additional information recorded included: the therapist's discipline and level of experience, i.e. therapist, assistant or student, session duration, and time spent in formal assessment, co-orientation with other disciplines or in a group. Therapists were provided with written and verbal instructions in completing the forms, the relevant reference (22) and definitions of terms obtained from De Jager et al. (22). Therapists could use either form depending on relevance.

To categorize rehabilitation activities and goals, the classification system used in studies describing OT stroke rehabilitation (17, 23) was modified for the purposes of this study. The 4 activity categories used in this study were: (1) performance skill or body structure or function impairments (17, 23; e.g. pre-functional activities, community upper extremity control, grasp/relax, pre-gait, sitting balance or trunk control); (2) gait; (3) personal care tasks or home management; and (4) community participation (community mobility, community integration) or leisure (Table D).

Concordance between the total number of sessions for which therapy documentation forms were completed and the total number of OT and PT sessions attended according to the hospital computerized health management system was determined. Participant's experiences with the rehabilitation programme were assessed using questionnaires. Participants were asked to rate the degree to which the programme addressed and contributed to goal achievement, translation of skills learnt in everyday life and overall satisfaction.

Outcome measurement

Information provided in the therapy documentation forms was used to determine the following:

- Programme and session data: median programme duration (weeks), number and intensity of therapy sessions in total and per discipline (OT and PT), therapy time (min) in total, and per discipline, session duration (min), and percentage of concurrent and group sessions.

- Intervention comfort percentage of therapy time spent in each occupational and physical therapy rehabilitation activity and activity category, percentages of participants spending time in each activity and percentage of total sessions during which interventions were used to facilitate the 3 occupational and physical therapy activities that most time was spent in.

- Therastric: discipline, level of expertise.

Participant goals were categorized as described above and the percentage of total goals relating to each category, and upper or lower limb, was determined.

Data analysis

Data was entered into Microsoft Excel database and exported into Stata12 (StatCorp, TX, USA) for analysis. Descriptive statistics were presented as means and standard deviation (SD) for continuous normally distributed data, median and interquartile ranges (IQR) for skewed data. Spearman's rank correlation (r) was used to determine statistical significance. Sub-analyses were carried out for groups based on limb's injected, i.e. upper and lower limb (U/L/L, upper limb (UL) and lower limb (LL)).

Programme duration (weeks) was calculated by dividing the number of days from first and last session, inclusive, by 7. Therapy intensity was defined as the number of sessions divided by programme duration (sessions per week). The total amount of therapy time for each activity (addition of time spent in the activity by each participant) and activity category was converted to a percentage of total therapy time across all participants and subgroups.

Clinical trial registration number. Melbourne Health RNSC 1016.165

RESULTS

Of the 59 participants recruited to the larger study (21), between January 2011 to June 2012, therapy documentation forms were

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Table 1. Rehabilitation activities and interventions comprising physical and occupational therapy: standardized documentation forms

<table>
<thead>
<tr>
<th>Physical activities</th>
<th>Pre-functional activity</th>
<th>Pre-functional activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bed mobility*</td>
<td>Gut*</td>
<td>Gut*</td>
</tr>
<tr>
<td>Sitting*</td>
<td>Advanced gut*</td>
<td>Advanced gut*</td>
</tr>
<tr>
<td>Sitting*</td>
<td>Community mobility*</td>
<td>Community mobility*</td>
</tr>
</tbody>
</table>

**Categories and examples of Physical interventions**

- Motor training, paresis awareness, motor learning, RN, NDT, involved upper extremity addressed, CMT.
- Sensory-stimulating, motor training, sensorimotor training, PROM/STROM, manual therapy, motor control.
- Cerebellum training, sensorimotor conditioning exercises.
- Cognitive perceptual/sensory, cognitive, perceptual, visual and auditory training.

**OT activities**

- Pre-functional activity*.
- Upper extremity control.
- Upper extremity control.
- Upper extremity control.
- Upper extremity control.
- Upper extremity control.
- Upper extremity control.
- Upper extremity control.

**Categories and examples of OT interventions**

- Neurological: Balance training, paresis awareness, motor learning, RN, NDT, CMT.
- Adaptive equipment: One-handed skills, sensory conservation, environmental adaptation, adaptive equipment.
- Musculoskeletal: Strengthening, motor training, manual therapy, PROM/STROM, edema control.
- Cerebellum training, sensorimotor conditioning exercises.
- Cognitive perceptual/sensory, cognitive, perceptual, visual and auditory training.

Adapted from De Jong, J. et al., 2004 (22).

Activities related to "performance skill or body structure and function," "judgement," "personal care skills tasks and management," and "community participation.""Leisure.

Definitions (22, 23).

- Pre-functional activities: activities related to or provided in preparation for functional activities; upper extremity control: "training facilitation of normal movement, strength, range of motion, and alignment in the upper extremity. Initiating and completing care of the upper extremity for functional activities: intervention(s) not related to functional activity: interventions may span on patient's behalf, but not in direct contact with patient, e.g. time spent selecting and ordering a splint.

**OT: occupational therapy; PhysT: physical therapy; RN: proprioceptive neuromuscular facilitation; NDT: neurodevelopmental therapy; CMT: constraint-induced movement therapy; PROM: passive range of movement.**

completed for 47 participants (median age 60.7 years and 2.9 years post-stroke) (Table II) documenting 183 OT sessions and 50 PT sessions (total 921 sessions). The only significant baseline differences was a shorter median time since stroke (1.0 vs 1.7 years) in the LL group compared with other groups (p = 0.004) (Table II). Whilst this group received more PT sessions in total (p = 0.019), there was no significant difference in programme duration and total number of therapy sessions (Table III).

Concordance between the number of sessions for which therapists' completed therapy documentation forms and those actually attended by a sample of 22 participants was 68.8%.

**Programme and section characteristics**

Table III shows programme and section characteristics using data from the therapy documentation forms. The UL group received significantly more OT and the LL group more PT per participant compared with other groups (Table III).

**Intervention content**

Fig. 1 shows the proportion of total therapy time all participants and subgroups spent in the various physical and occupational therapy activities. For all participants most time was spent in "upper extremity control," followed by physical therapy activities including "interventions not related to functional activity." Gut* and "pre-functional activity." Following "upper extremity control," the next most common OT activities were "intervention not related to functional activity" and "pre-functional activity." In the UL and ULL groups most time was spent in "upper extremity control" activities (Fig. 1), whilst 88.5% and 43.5% of goals related to the UL, respectively, and the remainder to gait.

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Table II. Baseline characteristics of all participants and sub-groups based on limbs injected with botulinum toxin type A

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All (n=17)</th>
<th>UL (n=19)</th>
<th>LL (n=12)</th>
<th>ULLL (n=15)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic factors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex: male, n (%)</td>
<td>14 (70.5)</td>
<td>15 (78.9)</td>
<td>11 (78.6)</td>
<td>9 (60.0)</td>
</tr>
<tr>
<td>Age, years, median (IQR)</td>
<td>60.7 (47.5–69.3)</td>
<td>61.0 (45.6–68.3)</td>
<td>59.0 (50.7–65.2)</td>
<td>59.2 (54.9–69.5)</td>
</tr>
<tr>
<td>Time since stroke, years, median (IQR)</td>
<td>2.0 (1.1–4.0)</td>
<td>2.5 (1.0–7.2)</td>
<td>1.0 (0.3–1.7)</td>
<td>3.0 (1.4–5.4)</td>
</tr>
<tr>
<td><strong>Clinical characteristics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke severity, n (%)</td>
<td>14 (70.5)</td>
<td>10 (52.6)</td>
<td>12 (80.0)</td>
<td>13 (86.7)</td>
</tr>
<tr>
<td>Hemorrhage-related</td>
<td>12 (65.7)</td>
<td>9 (47.4)</td>
<td>10 (76.9)</td>
<td>9 (60.0)</td>
</tr>
<tr>
<td>Cerebral infarction</td>
<td>38 (100)</td>
<td>16 (48.6)</td>
<td>10 (33.3)</td>
<td>13 (86.7)</td>
</tr>
<tr>
<td>Baseline side affected, n (%)</td>
<td>20 (10)</td>
<td>10 (33.3)</td>
<td>10 (33.3)</td>
<td>10 (66.7)</td>
</tr>
<tr>
<td>Living arrangements, n (%)</td>
<td>41 (23.5)</td>
<td>16 (53.3)</td>
<td>12 (33.3)</td>
<td>12 (80.0)</td>
</tr>
<tr>
<td>Ambulatory</td>
<td>2 (1.2)</td>
<td>1 (3.3)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Other</td>
<td>12 (6.5)</td>
<td>2 (6.8)</td>
<td>1 (3.3)</td>
<td>1 (6.7)</td>
</tr>
</tbody>
</table>

*p-value >0.05: IQR: interquartile range; UL: upper limb; LL: lower limb; ULLL: upper and lower limb.

Table IV shows the percentage of total therapy time and goals related to the activity categories for all participants and sub-groups. Most time was spent in performance skill or body structure and function activities, with more than one-third of goals for all groups except LL relating to this activity category. There was a higher percentage of total therapy time and goals related to self-care activities in those who had the LL injected. Minimal time was spent in community participation and leisure activities (Fig. 1 and Table IV). A small proportion of goals, except in the LL group (mostly related to community mobility), related to this activity category. While little time was spent in personal care activities and home management, a large proportion of goals in all but the LL group were associated with these tasks (Table IV).

Table V shows the percentage of participants participating in occupational and physical therapy activities for the group and sub-groups. More than 30% of all participants participated in “upper extremity control” activities, as the UL was injected more often.

Tables VI and VII show the percentage of total sessions during which interventions were used to facilitate 5 occupational and physical therapy activities, respectively, in which most time was spent.

Overall, 87.3% of participants and/or their caregiver's received some educational intervention during at least one occasion (range 1–21) relating to any of the rehabilitation activities.

**Delivery personnel**

Of all participants: 93.6% received PT and 61.7% received OT. The majority of participants in the ULLL and UL group received OT (n=11/15 (73.3%) and n=16/19 (64.2%), respectively).

Table III. Programme and session characteristics per participant

<table>
<thead>
<tr>
<th></th>
<th>AB (n=17)</th>
<th>ULLL (n=15)</th>
<th>UL (n=19)</th>
<th>LL (n=12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Program duration, weeks, median (IQR)</td>
<td>10.0 (8.0–12.7)</td>
<td>10.0 (8.0–12.7)</td>
<td>9.0 (7.0–10.0)</td>
<td>12.7 (10.0–14.1)</td>
</tr>
<tr>
<td>Total sessions, median (IQR)</td>
<td>17.0 (10.0–28.0)</td>
<td>17.0 (10.0–28.0)</td>
<td>18.0 (10.0–30.0)</td>
<td>17.0 (13.0–26.0)</td>
</tr>
<tr>
<td>Total number of sessions by discipline, median (IQR)</td>
<td>3.0 (0.0–10.0)</td>
<td>4.0 (0.0–10.0)</td>
<td>5.0 (0.0–10.0)</td>
<td>7.0 (5.0–11.0)</td>
</tr>
<tr>
<td>OT</td>
<td>12 (7.5–18.0)</td>
<td>12.0 (7.5–18.0)</td>
<td>12.0 (7.5–18.0)</td>
<td>17.0 (13.0–25.0)</td>
</tr>
<tr>
<td>Sess/mem, mean, median (IQR)</td>
<td>1.5 (1.0–2.2)</td>
<td>1.4 (1.0–2.2)</td>
<td>1.1 (0.5–1.7)</td>
<td>1.0 (0.5–1.7)</td>
</tr>
<tr>
<td>OT</td>
<td>0.4 (0.1–1.3)</td>
<td>0.3 (0.1–1.3)</td>
<td>1.4 (0.7–1.7)</td>
<td>1.1 (0.5–1.7)</td>
</tr>
<tr>
<td>PT</td>
<td>1.2 (0.5–1.7)</td>
<td>1.1 (0.5–1.7)</td>
<td>1.0 (0.5–1.7)</td>
<td>1.0 (0.5–1.7)</td>
</tr>
<tr>
<td>Total therapy time, min, median (IQR)</td>
<td>2.5 (0.0–9.0)</td>
<td>2.5 (0.0–9.0)</td>
<td>7.5 (0.0–17.0)</td>
<td>7.5 (0.0–17.0)</td>
</tr>
<tr>
<td>OT+PT</td>
<td>11.8 (6.0–15.0)</td>
<td>17.5 (9.0–15.0)</td>
<td>9.0 (7.5–15.0)</td>
<td>8.0 (7.5–15.0)</td>
</tr>
<tr>
<td>Duration of sessions, min, mean (SD)</td>
<td>50.0 (9.5)</td>
<td>50.0 (9.5)</td>
<td>50.0 (9.5)</td>
<td>50.0 (9.5)</td>
</tr>
</tbody>
</table>

*p-value <0.05

2: Two participants who had lower limb BoNT-A injections had OT.

OT: occupational therapy; PT: physiotherapy; IQR: interquartile range; UL: upper limb; LL: lower limb; ULLL: upper and lower limb; SD: standard deviation.

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spectively) compared with the LL group (n = 3/13 (23.1%), p = 0.002). All participants who had LL DNTA injections had PT. Over 25% of all participants were also seen by other disciplines including orthotists, podiatrists, exercise physiologists, social workers and dietitians.

Qualified occupational therapists and physiotherapists delivered the majority of rehabilitation sessions. Allied health assistants provided a small number of sessions (ranging from 1 to 12 sessions) in OT (n = 2474 participants) and PT (n = 11,547 participants). Group sessions accounted for just over 20% (n = 186925) of all sessions, involving 17 participants. Co-treatment with 2 disciplines (OT and PT) occurred in almost 9% (n = 82922) of sessions, all of which were group sessions, and involved over 20% (n = 10147) of participants.

Environment/therapy setting

The majority of participants (n = 46/47) attended government-funded, community-based rehabilitation services, whilst just a private therapist. Rehabilitation programs were centre-based, except for 3 patients who received home-based therapy. All sessions were face-to-face contact.

Participants experience

Of the participants who completed questionnaires (n = 35/47), most reported that the program assisted them (71.4%) and helped contribute to their goals (74.3%) to a great deal or extreme amount. Over 70% reported being able to use skills learnt during the program in everyday life.

Table IV. Percentage of total therapy time and goals related to each of the activity categories for all participants and subgroups

<table>
<thead>
<tr>
<th>Activity and goal categories</th>
<th>All (n = 47)</th>
<th>U.L.L. (n = 15)</th>
<th>U.L. (n = 19)</th>
<th>L.L. (n = 13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Performance skill body structure &amp; function</td>
<td>36.6</td>
<td>34.5</td>
<td>45.9</td>
<td>38.7</td>
</tr>
<tr>
<td>Goal</td>
<td>18.6</td>
<td>23.8</td>
<td>22.2</td>
<td>46.8</td>
</tr>
<tr>
<td>Personal care tasks and home management</td>
<td>51</td>
<td>10.6</td>
<td>16.6</td>
<td>7.0</td>
</tr>
<tr>
<td>Community participation issues</td>
<td>2.4</td>
<td>12.2</td>
<td>6.4</td>
<td>1.8</td>
</tr>
</tbody>
</table>

Percentages of total therapy time spent in "intervention not related to functional activity" and formal assessment not included.

U.L., upper limb; L.L., lower limb; U.L.L.L., upper and lower limb.
Table V. Proportion of participants participating in occupational and physical therapy activities

<table>
<thead>
<tr>
<th>Activity</th>
<th>All (n=47)</th>
<th>UL (n=15)</th>
<th>LL (n=13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>OT activities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-functional activity</td>
<td>16 (34.0)</td>
<td>2 (13.3)</td>
<td>11 (52.4)*</td>
</tr>
<tr>
<td>Bedding</td>
<td>1 (2.1)</td>
<td>0 (0.0)</td>
<td>1 (2.1)</td>
</tr>
<tr>
<td>Dressing</td>
<td>5 (10.6)</td>
<td>1 (6.7)</td>
<td>3 (13.0)</td>
</tr>
<tr>
<td>Grooming</td>
<td>3 (4.9)</td>
<td>0 (0.0)</td>
<td>2 (10.0)</td>
</tr>
<tr>
<td>Toiletting</td>
<td>3 (4.3)</td>
<td>2 (13.3)</td>
<td>1 (5.3)</td>
</tr>
<tr>
<td>Feeding/eating</td>
<td>7 (14.9)</td>
<td>0 (0.0)</td>
<td>6 (31.0)*</td>
</tr>
<tr>
<td>Transfers</td>
<td>7 (14.9)</td>
<td>1 (6.7)</td>
<td>4 (21.1)</td>
</tr>
<tr>
<td>Bed mobility</td>
<td>4 (8.5)</td>
<td>0 (0.0)</td>
<td>3 (13.0)</td>
</tr>
<tr>
<td>Functional mobility</td>
<td>11 (23.4)</td>
<td>1 (6.7)</td>
<td>7 (34.8)</td>
</tr>
<tr>
<td>Home management</td>
<td>5 (10.6)</td>
<td>2 (13.3)</td>
<td>3 (13.0)</td>
</tr>
<tr>
<td>Community integration</td>
<td>1 (2.1)</td>
<td>1 (6.7)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Leisure activities</td>
<td>1 (2.1)</td>
<td>1 (6.7)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Upper extremity control</td>
<td>25 (53.2)</td>
<td>8 (53.3)</td>
<td>16 (34.8)*</td>
</tr>
<tr>
<td>Wheelchair management</td>
<td>23 (49.0)</td>
<td>6 (40.0)</td>
<td>17 (78.3)</td>
</tr>
<tr>
<td>Sitting balance trunk control</td>
<td>12 (25.5)</td>
<td>4 (26.7)</td>
<td>7 (34.8)</td>
</tr>
<tr>
<td>Intervention not related to functional activity</td>
<td>17 (35.9)</td>
<td>7 (46.7)</td>
<td>9 (47.4)</td>
</tr>
</tbody>
</table>

PhysT activities

Pre-functional activity       | 34 (72.3)   | 10 (66.7)   | 13 (58.4)   | 13 (54.3) |
| Bed mobility                  | 22 (46.8)   | 9 (40.0)    | 8 (42.1)    | 6 (51.5)  |
| Sitting                       | 22 (46.8)   | 5 (33.3)    | 9 (54.4)    | 7 (53.8)  |
| Transfers                     | 22 (46.8)   | 9 (52.1)    | 9 (54.4)    | 7 (53.8)  |
| Side-to-side                  | 32 (68.1)   | 12 (80.0)   | 10 (52.6)   | 10 (76.9) |
| Wheelchair mobility           | 8 (17.0)    | 1 (6.7)     | 3 (15.0)    | 0 (0.0)   |
| Pre-pat                        | 27 (57.4)   | 12 (80.0)   | 11 (51.2)   | 12 (92.3) |
| Pat                          | 39 (83.0)   | 14 (93.3)   | 12 (52.6)*  | 12 (92.3) |
| Advanced pat                  | 20 (42.6)   | 0 (0.0)     | 4 (21.1)    | 10 (76.9)* |
| Community mobility            | 11 (23.4)   | 3 (20.0)    | 1 (5.3)     | 7 (53.8)* |
| Intervention not related to functional activity | 33 (70.2) | 12 (80.0) | 10 (52.6) | 11 (84.6) |

Formal assessment             | 25 (53.2)   | 9 (60.0)    | 10 (52.6)   | 7 (53.8)  |

*p<0.05.

OT: occupational therapy; PhysT: physical therapy; UL: upper limb; LL: lower limb; UL,LL: upper and lower limb.

Table VI. Occupational therapy interventions used to facilitate the most common activities: percentage of total sessions.*

<table>
<thead>
<tr>
<th>OT activities</th>
<th>Pre-functional activity %</th>
<th>Upper extremity control %</th>
<th>Not related to functional activity %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuromuscular</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Balance training</td>
<td>0.1</td>
<td>0.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Postural reposition</td>
<td>0.4</td>
<td>1.2</td>
<td>1.0</td>
</tr>
<tr>
<td>Motor learning</td>
<td>1.5</td>
<td>2.3</td>
<td>0.0</td>
</tr>
<tr>
<td>NDT: Bobath</td>
<td>1.7</td>
<td>4.2</td>
<td>0.0</td>
</tr>
<tr>
<td>Adaptive compensatory</td>
<td>1.0</td>
<td>0.5</td>
<td>0.0</td>
</tr>
<tr>
<td>Manual/motor control</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stimulation</td>
<td>2.2</td>
<td>5.1</td>
<td>1.4</td>
</tr>
<tr>
<td>Mobilization, manual</td>
<td>2.1</td>
<td>3.6</td>
<td>1.1</td>
</tr>
<tr>
<td>PICOI: assessing</td>
<td>4.9</td>
<td>8.8</td>
<td>0.9</td>
</tr>
<tr>
<td>Educational</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient</td>
<td>1.2</td>
<td>3.5</td>
<td>1.8</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exercise prescription</td>
<td>2.3</td>
<td>5.8</td>
<td>0.8</td>
</tr>
</tbody>
</table>

Data are % of total therapy sessions. Only interventions for which ≥1% of total use were included. Total sessions: OT and PT sessions.

OT: occupational therapy; PT: physical therapy; NDT: neurodevelopmental therapy; PICOI: passive range of movement.

Discussion

Therapeutic activities and interventions (physical and occupational therapy) comprising individualized ambulatory rehabilitation programmes following BeoTA for spasticity in stroke survivors were exposed using a standardised taxonomy (23). As far as we are aware this is the first study to explore current rehabilitation practices for post-stroke spasticity in such detail. The 45 chronic (>1 year) stroke survivors had a similar median age to those in other studies (18, 23). Whilst the LL group had a significantly shorter median time since stroke at baseline, they did not receive more therapy compared with other groups. Long-term motor improvement has been shown in those with chronic stroke following rehabilitation (27). In order to determined effectiveness, the therapeutic components of rehabilitation programmes need to be identified. Programme characteristics varied depending on the limb injected. The UL group received significantly more OT and the LL group more PT. These results may reflect the tendency in...
As the majority of sessions were centre- rather than home- based, this factor in conjunction with resource limitations may have restricted the therapists' focus on community activities. Nonetheless, translation of skills learnt in rehabilitation to the home and community environment is important in improving activity level and participation. Further studies are needed to explore how rehabilitation activities relate to goal categories (10) in this group, as diverting resources to relevant therapeutic activities may improve outcomes such as goal achievement.

A large proportion of therapy time in all groups was spent in remediating performance skills, either body structure and function impairments, particularly upper extremity control, with “passive range of motion,” being the intervention most frequently used to facilitate such activities, similar to other studies of OT in stroke rehabilitation (18, 23). More than 1/ 3 of goals in all but the LL group related to performance skills or body structure and function impairments. The importance of addressing performance skill deficits and motor preparation may be due to the window of opportunity after BotNT-A to normalize motor patterns, which have previously been inhibited by spasticity, before translation into functional activities, particularly as optimal reduction in spasticity occurs before the maximum change in function (28). Research into how therapeutic activities vary over the course of rehabilitation programmes following BotNT-A and their relationship to long-term functional outcomes is warranted.

The therapy documentation forms used in this study (16, 22, 35) combine documentation of therapeutic activities and corresponding interventions allowing the multidimensional nature and complexity of therapy to be described, whereas other tools record activities only (19). Further studies to assess the relevance of the current taxonomy to describing similar rehabilitation programmes would be beneficial. The forms, however, have inherent limitations. Firstly, they do not allow for recording of rest or inactive time, so do not reflect how intensively participants participated in therapy. This is important in determining therapy effectiveness, as greater intensity of therapy has been suggested to result in increased recovery of motor function to a varying degree (29–31) and greater UL goal achievement following BotNT-A (24) after stroke. Stroke impairments have been found to spend approximately one-third of therapy time in rest or inactivity (32), so it is also important to capture this time in ambulatory settings. In addition, the forms rely on therapists estimating activity time rather than an objective measure of accuracy. Therapists have been found to be inaccurate in their estimation of the time patients spend engaged in active task practice during therapy sessions (33, 34), overestimating active time by 28% and underestimating rest time by 56% (33). Objective measures for recording therapy activity time include simple counting of repetitions of tasks or exercises (35) or using activity monitors, such as accelerometers (36, 37), which also capture activity level out of therapy time in community-dwelling patients. This would be useful in determining the contribution of formal therapy time to home-based activity to patient outcomes.

Although the therapists who completed the therapy documentation forms received instructions and written definitions.
ACKNOWLEDGEMENTS

We are grateful to all participants and therapists who completed the therapy documentation form. We thank Louisa Ng for her help in the study design. There were no conflicts of interest with respect to this study. We would like to thank Professor Mary Gordon for valuable advice and Mary Gordon for comments during the editing phase.

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OUTCOMES OF AMBULATORY REHABILITATION PROGRAMMES FOLLOWING BOTULINUM TOXIN FOR SPASTICITY IN ADULTS WITH STROKE

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Objective: To examine the benefits of high intensity ambulatory rehabilitation programmes over usual care following botulinum toxin A (BoNT-A) for post-stroke spasticity in Australian adults.

Methods: Prospective single centre, controlled clinical trial.

Participants: Fifty-nine adults, median 61 years old and 2.5 years following stroke.

Primary outcomes: Functional improvement in the 6-month to 1-year intervention period was measured using the Functional Independence Measure (FIM), a validated measure of physical function.

Secondary outcomes: Quality of life measures included the Short Form 36 (SF-36), a validated measure of health-related quality of life.

Conclusions: Both BoNT-A and usual care participants showed significant improvements in ambulatory function and quality of life. BoNT-A participants showed greater improvements in ambulatory function and quality of life compared to usual care participants. This suggests that BoNT-A may be a safe and effective treatment for post-stroke spasticity and should be considered for patients with moderate to severe spasticity who are not eligible for other treatments.

Key words: botulinum toxin; muscle spasticity; stroke; rehabilitation.


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INTRODUCTION

Stroke is a leading cause of disability worldwide, with spasticity affecting up to 43% (1) of stroke survivors. The burden of post-stroke spasticity is high in terms of treatment costs, quality of life (QoL) consequences, caregiver burden and other health-related outcomes (2).

Post-stroke spasticity contributes to a diversity of patient-centred problems (3). These may relate to ‘impairments’ (problems with body structures or physiological function) such as restricted joint range of movement, pain and involuntary movements, ‘activity limitation’ (active and passive function) and ‘restriction of participation’ which limit societal involvement such as engagement in work, family roles and leisure activities. Spasticity can impact on ‘active’ function (the execution of a functional task by the individual) by restricting mobility and upper limb use during daily activities, and ‘passive’ function (caring for and an affected limb), such as maintaining position or applying a splint. As spasticity affects individual stroke survivors differently, treatment goals are variable. Hence, the use of functional outcome measures, such as the Functional Independence Measure (FIM), that identify outcomes of importance to the individual and caregivers are recommended (3–6).

The effectiveness of botulinum toxin A (BoNT-A) in reducing spasticity following stroke has been well established in both upper (8–9) and lower limbs (10, 11). However, spasticity management utilises a multimodal rehabilitation approach to achieve long-term functional improvement after spasticity reduction (12). In this capacity, BoNT-A is considered an adjunctive intervention, with transient effects (13), that provides a window of opportunity to maximise gains during a rehabilitation program. An appropriate rehabilitation management program should ideally be in place prior to BoNT-A treatment, and should continue thereafter (14). Whilst spasticity management guidelines advocate a multidisciplinary approach (15, 16), recommendations are based on expert opinion rather than scientific evidence. The guidelines lack details on optimal therapy programmes and patient selection.

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Rehabilitation programme after benzodiazepine toxin injections: for post-stroke spasticity

Physical therapy used in rehabilitation following Benz-A injections may include electrical stimulation (17), stretching (18), casting (19), constraint-induced movement therapy (CIMT) (20, 21) and task-specific practice (22). A meta-analysis found limited and low-quality evidence for the effectiveness of multidisciplinary rehabilitation intervention following Benz-A for post-stroke spasticity (23). The few included trials had methodological limitations including small sample sizes and use of outcome measures that do not necessarily translate into improved function or benefit for patients and caregivers. Studies of physical interventions following Benz-A have tended to focus on single treatment modalities or use-disciplinary therapy, rather than the complex array of interventions delivered in real-life rehabilitation settings. The optimal types (modalities, therapy approaches, settings) and intensities of therapy for achieving meaningful patient outcomes following Benz-A remain unclear; these elements are described in the ‘black box’ of rehabilitation (24).

Traditionally, stroke patients are told their recovery stabilizes within 6–12 months (25). These patients may be due to patient physiological or psychological adaptations to their rehabilitation routines, rather than reduced capacity for motor recovery (26). Adjusting the rehabilitation approach (modifying intensity or modalities) and challenge of new motor exercises allows positive neuromuscular adaptations to occur (26). Additionally, there is often a time lag between peak spasticity reduction following Benz-A and maximal functional gain (27). These factors emphasize the need for comprehensive rehabilitation and longer follow-up periods to ensure that the benefits of treatment are not missed and to determine whether effects are maintained after treatment cessation.

This study examined the effectiveness of a high-intensity rehabilitation multidisciplinary rehabilitation program versus low-intensity usual care as measured by goal achievement and other outcomes up to 24 weeks. In Australian adult stroke survivors receiving Benz-A injections for upper and/or lower limb spasticity.

METHODS

Participants and setting

The study was conducted at a multidisciplinary tertiary referral spasticity management service. Following ethics committee approval, consecutive adult patients treated with Benz-A for upper and/or lower limb post-stroke spasticity and eligible for rehabilitation were invited to participate in the study. Inclusion criteria were age ≥18 years, stroke diagnosis within 12 months, upper and/or lower limb spasticity (MAS ≥2) interfering with function or causing a clinical problem and no contraindications to Benz-A injections. Patients were excluded if they had treatments with Benz-A within 6 months, intracerebral haemorrhage or subarachnoid haemorrhage or surgery to the affected limb; concurrent neurological conditions; pregnancy, or were unable to participate in therapy due to cognitive or language impairment, psychiatric or medical illness.

Procedures

Group allocation. This trial was designed to reflect ‘real-life’ clinical practice in an ambulatory rehabilitation service in Australia. In this context, therapy is delivered based on accessibility to services, testing group assessment, and service delivery protocols determined by geographical constraints. Thus, allocation to rehabilitation programs was based on participants’ areas of residence. Those residing within a 12-km radius of the investigating hospital received high-intensity therapy, while subjects outside of this geographical constraint underwent usual care being based on therapists’ and the patient’s local community or hospital rehabilitation service. Participants were not informed of allocation within the trial.

Assessments. Structured assessments were completed in the hospital clinic. Baseline data included demographic data collection, assessment history, medical record, clinical examination of neurological impairments and prior Benz-A administrations. Up to 2 individuals, SMART physician(s), neurologist, therapist and nurse (17). Using the G-A5 process (28), a ‘composite’ measurement of expected outcomes was determined for each goal at 12 weeks following Benz-A injection. Participants were referred to ambulatory rehabilitation services based on geographical, clinical need and extent of treatment goals previously provided. A blinded assessment comprised standardised outcome measures and details of treatment goals previously provided. A blinded assessment comprised standardised outcome measures and details of treatment goals previously provided.

Treatment schedule

Benz-A injection: All participants received individualized Benz-A injections in the affected limb/s, as determined by clinical factors, spasticity pattern, spasticity presence and treatment goals (15, 16). Injection settings were administered by one of 2 rehabilitation physicians using neuromuscular stimulation.

Rehabilitation programme. High-intensity multidisciplinary rehabilitation program comprised of 3 or more 1-h sessions per week for approximately 16 weeks. This protocol was more intensive than treatments previously provided for spasticity management in local tertiary hospital community-based rehabilitation (CBR) services. Usual care was a lower-intensity rehabilitation program (3–5 h sessions per week). Therapy settings included out-patient hospital CBR services or outpatient community care, depending on service accessibility and availability per patient’s specific service delivery. Treatment attendance was attended in >70% of scheduled therapy sessions.

All participants received goal-directed, individualized rehabilitation programmes, consistent with ‘real-life’ rehabilitation practice in Australia. Therapy was based on neurodevelopmental techniques, interventions targeting relevant impairments were primarily motor learning, strength training, postural awareness, balance training, aerobic conditioning exercises, range of movement, stretching, adaptive compensatory strategies (environmental adaptation, one-handed tasks), task-specific practice and sensory training. The main activities focused on muscle and upper extremity control in relation to activities of daily living (dressing, feeding, cleaning, etc). Others included transfer practice, sitting balance, trunk control, multifunctionality. Participants received inclusion in a Korean and yoga programme. Therapists documented details of therapy sessions (discipline, date, duration, activities and interventions) using standardised forms (29).

Outcome measurement

Investigator-observed and participant (or caregiver) reported outcome measures were completed at 0 (baseline), 6, 12 (primary outcome time point), and 24 weeks.

Primary outcome measures

The proportion of participants who at 12 weeks achieved at least 50% of their total goals, as measured by G-A5 process, and change in G-A5 scores (30), using methods described elsewhere (4, 5). Goals were identified using the goal-setting procedure and weighted by importance...
and difficulty (each graded on a 0–3 scale) of achieving the goal. Baseline goal scores were 1–3 or 4 if participants could not have been at a worse level). Goal attainment score was calculated using a 5-point scale (0–2, where a GA score of 0 indicates an unmet goal). The blinded assessor assigned the level of individual goal attainment according to the severity of the impairment (0–3) or follow-up. The composite goal attainment score (0–3 score) is the average weighted score of each participant's goals, was calculated (22) as a standardized variable normally distributed around a mean of 0 and with a standard deviation (SD) of 10 points (23).

Secondary outcome measures

The Modified Ashworth Scale (MAS) (24) assessed muscle tone during passive range of movement of the joints, associated with impaired muscle groups in the treated limbs; a 0–4 scale increase in muscle tone was assessed with the MAS. Change in mean MAS score for treated limbs, and upper and lower limbs separately, were obtained.

The Arm activity measure (ArAm) (20) assessed the grip function (7-activities section A) and active (13-activities section B) arm function for participants with unilateral upper limb motor impairment. Participants or their caregivers rated the difficulty in performing each function, based on activity over the preceding 7 days, using a 5-point ordinal scale (0 = no difficulty; 1 = mild; 2 = moderate; 3 = severe; 4 = unable to do). The 10-cm scale with 90 (21) measured comfortable joint speed (in-s), with scores and visual aid aid for participants who had lower limb injections. The mean of two trials was used.

Global assessment scale (GAS) rated participants’ subjective improvement or worsening of symptoms and satisfaction following treatment (+1=very much improved; 0= no change; -1=very much worsened). A good treatment was defined as a change of 0.5 or more on the GAS scale. The scales used for the study were the UMS and the GAS.

Power calculation and statistical analysis

A change in GAS score of at least 10 points is associated with clinically important change (4). Sample size was estimated assuming a difference in GAS score change of 10 (SD 15) points between high intensity and usual care groups. Allowing for a 15% dropout rate, 27 participants were required in each group to detect the difference with 80% power. Data was entered into MS Access database and exported into Stata12 (Stata Corp, TX, USA) for analysis. Descriptive statistics were presented as means and SD for continuous normally distributed data, medians and interquartile range (IQR) for skewed or ordinal data and n (%) for categorical data.

Data analysis was performed using intention-to-treat principles with Last Observation Carried Forward for missing data. Continuous normally distributed variables were analyzed using Student t-test and skewed or ordinal data were analyzed using Wilcoxon rank-sum test. Change scores were calculated as follow-up minus baseline score. Categorical variables were analyzed using Chi or Fisher’s exact test. Multivariate logistic regression was used to determine variables associated with participants achieving at least 50% of their goals and generalized linear model was used to determine variables associated with the change in GAS scores. Variables of interest included in the models were: treatment allocation, age, gender, stroke localization (cortical versus subcortical), and time since stroke (<1 year versus >1 year). p-values < 0.05 indicated statistical significance for all tests.

RESULTS

Fifty-one of 75 stroke survivors recruited from January 2011 to June 2012 were recruited to the study, with 28 allocated to high intensity rehabilitation programme and 23 to usual care (Fig. 1). There were no losses to follow-up or adverse events.

![Image](image-url)

Fig. 1. Study flow chart.
Rehabilitation programs after botulinum toxin injections for post-stroke spasticity

Table 1. Baseline characteristics of high intensity and usual care groups

<table>
<thead>
<tr>
<th></th>
<th>High intensity (n=21)</th>
<th>Usual care (n=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic factors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex, n (%)</td>
<td>19 (90.5)</td>
<td>20 (95.2)</td>
</tr>
<tr>
<td>Age, years, mean (SD)</td>
<td>60.6 (40.6–69.1)</td>
<td>61.4 (46.4–69.6)</td>
</tr>
<tr>
<td>Range</td>
<td>30.5–83.1</td>
<td>37.4–78.5</td>
</tr>
<tr>
<td>Secondary stroke, years, mean (SD)</td>
<td>2.3 (1.1–5.5)</td>
<td>2.5 (1.2–7.0)</td>
</tr>
<tr>
<td>Range</td>
<td>0.4–15.3</td>
<td>0.3–320</td>
</tr>
<tr>
<td>Education, n (%)</td>
<td>1 (4.8)</td>
<td>1 (4.8)</td>
</tr>
<tr>
<td>Primary</td>
<td>1 (4.8)</td>
<td>1 (4.8)</td>
</tr>
<tr>
<td>Secondary</td>
<td>19 (89.5)</td>
<td>19 (89.5)</td>
</tr>
<tr>
<td>Tertiary</td>
<td>1 (4.8)</td>
<td>1 (4.8)</td>
</tr>
<tr>
<td>Living arrangement, n (%)</td>
<td>9 (32.1)</td>
<td>10 (39.1)</td>
</tr>
<tr>
<td>With family/friend</td>
<td>3 (10.3)</td>
<td>2 (9.5)</td>
</tr>
<tr>
<td>Alone</td>
<td>1 (3.7)</td>
<td>1 (4.8)</td>
</tr>
<tr>
<td>Other</td>
<td>13 (52.4)</td>
<td>15 (66.7)</td>
</tr>
<tr>
<td>Caregiver, n (%)</td>
<td>10 (75.0)</td>
<td>21 (81.0)</td>
</tr>
<tr>
<td><strong>Clinical characteristics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke etiology, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic</td>
<td>20 (95.2)</td>
<td>18 (85.7)</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>1 (4.8)</td>
<td>3 (14.3)</td>
</tr>
<tr>
<td>Stroke localization, n (%)</td>
<td>20 (95.2)</td>
<td>16 (76.2)</td>
</tr>
<tr>
<td>Cerebral</td>
<td>18 (85.7)</td>
<td>16 (76.2)</td>
</tr>
<tr>
<td>Subcortical</td>
<td>2 (9.5)</td>
<td>2 (9.5)</td>
</tr>
<tr>
<td>Left cerebral lesion, n (%)</td>
<td>18 (85.7)</td>
<td>18 (85.7)</td>
</tr>
<tr>
<td>Dominant side affected, n (%)</td>
<td>10 (47.6)</td>
<td>10 (47.6)</td>
</tr>
<tr>
<td><strong>Dependent variables</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GAS T-score, median (IQR)</td>
<td>31.3 (20.9–42.1)</td>
<td>36.4 (31.0–57.2)</td>
</tr>
<tr>
<td>MAS thumb, median (IQR)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All (UL + LL) (n=59)</td>
<td>2.1 (2.0–2.7)</td>
<td>2.2 (2.0–2.7)</td>
</tr>
<tr>
<td>LL (n=20)</td>
<td>2.0 (2.0–2.0)</td>
<td>2.1 (2.0–2.0)</td>
</tr>
<tr>
<td>UL (n=20)</td>
<td>2.2 (2.0–2.0)</td>
<td>2.3 (2.0–3.0)</td>
</tr>
<tr>
<td>Ankle, median (n=20)</td>
<td>9 (8–11)</td>
<td>10.5 (9–16)</td>
</tr>
<tr>
<td>Section B</td>
<td>46 (42–62)</td>
<td>40.5 (42–64)</td>
</tr>
<tr>
<td>Cost report, n (%)</td>
<td>1 (4.8)</td>
<td>1 (4.8)</td>
</tr>
<tr>
<td>Prior treatments</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Therapy program actuating and continued, n (%)</td>
<td>18 (85.7)</td>
<td>17 (80.9)</td>
</tr>
<tr>
<td>BoNT-A = 6 months prior to recruitment, n (%)</td>
<td>16 (76.2)</td>
<td>15 (71.4)</td>
</tr>
<tr>
<td>Criteria, median (IQR)</td>
<td>1.3 (1–2)</td>
<td>2.5 (1–4)</td>
</tr>
</tbody>
</table>

*p<0.05

Grouped (n=21) for participants receiving LL injections. One participant unable to complete 10-cm walk test.

GAS: Goal Attainment Scaling; MAS: Modified Ashworth Scale; IQR: interquartile range; SD: standard deviation.

Rehabilitation programs after botulinum toxin injections for post-stroke spasticity

Four participants received upper limb (UL) injections (21 in high intensity and 19 in usual care groups) and 37 received lower limb (LL) injections (16 in high intensity and 21 in usual care groups).

Nine participants in each group had both limbs injected. There were no significant differences in the proportion of participants who had UL and LL injections in each group (p = 0.40 and 0.26, respectively).

Fifty-four participants were injected with Dyndorp (open label, Slough, UK) and 5 with Botox (Allergan Inc., Irvine, USA). Mean doses of BoNT-A (Dyndorp) were 766 (SD 249) in the high intensity and 675 (SD 119) in the usual care groups (p = 0.18). There were no significant differences between UL and LL dose, between groups (p = 0.19 and 0.24, respectively).

Elbow flexors and long finger flexors were most commonly injected in the UL, and gastrocnemius and/or soleus were injected in over 90% of those receiving LL injections (Table II).

Rehabilitation programs

Therapy commenced within 14 days of BoNT-A injections for the majority of participants. Participants in the high intensity group attended a mean of 3.2 ± 1.2 therapy sessions per week (SD 0.6, range 2–6) and the usual care group an average of 1.2 (SD 0.4, range 0–2) sessions per week. Mean duration of therapy programs in the high intensity group was 11 weeks (SD 3.3, range 7–19,4) for the high intensity group and 10 weeks (SD 3.9, range 1–20) for the usual care group. All participants attended hospital CBR services for therapy programs, except for 3 in the usual care group who attended community health centers (n = 2) and a private therapist (n = 1). Rehabilitation programs included physiotherapy (96.4% of high intensity and 97.1% of usual care participants), occupational therapy (64.3% and 48.4%, respectively) or at least 2 disciplines (64.3% and 48.4%, respectively). A priori compliance was achieved in all but one participant (usual care group) who declined to participate in therapy after one session.

Goals

There were 93 goals set in the high intensity and 96 in the usual care groups (mean 3 goals per participant, range 1–8), with the majority of goals related to the ICF domains of activity participation rather than symptoms/improvements (Table III).

Primary outcomes

The majority of participants in high intensity and usual care groups achieved at least 50% of their goals at 12 weeks (75.0% and 77.4%, respectively; p = 0.689) and 24 weeks (78.6% and 51.3%, respectively; p = 0.170). GAS T-scores improved significantly (p < 0.001) at all time points in both groups. When considering all goals, median change in GAS T-score from baseline to 24 weeks approached statistical significance.
Table II. Number of participants injected in the various upper and lower limb muscle groups

<table>
<thead>
<tr>
<th>Muscle group</th>
<th>High intensity (n=26)</th>
<th>Usual care (n=31)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shoulder muscles, pectoralis, latissimus dorsi, rhomboids, deltoids</td>
<td>8 (30.8)</td>
<td>5 (16.1)</td>
</tr>
<tr>
<td>Elbow flexors, biceps, brachialis, biceps medialis</td>
<td>12 (57.1)</td>
<td>11 (35.4)</td>
</tr>
<tr>
<td>Triceps: biceps, triceps minor, triceps major</td>
<td>8 (38.1)</td>
<td>3 (10)</td>
</tr>
<tr>
<td>Wrist flexors: flexor carpi ulnaris, flexor carpi radialis</td>
<td>14 (65.7)</td>
<td>4 (13)</td>
</tr>
<tr>
<td>Finger flexors: flexor digitorum superficialis, flexor digitorum profundus</td>
<td>15 (71.4)</td>
<td>13 (42)</td>
</tr>
<tr>
<td>Thumbs: thenar muscles, adductor pollicis, flexor pollicis brevis, opponens pollicis</td>
<td>11 (50.0)</td>
<td>8 (25.8)</td>
</tr>
<tr>
<td>Lower limb injections: quadriceps, vastus intermedius, rectus femoris</td>
<td>3 (18.4)</td>
<td>3 (22.5)</td>
</tr>
<tr>
<td>Hamstring: gastrocnemius medialis, gastrocnemius lateralis, soleus</td>
<td>15 (65.6)</td>
<td>10 (65.5)</td>
</tr>
<tr>
<td>Extensor: rectus femoris, iliotibialis, iliacus superior</td>
<td>5 (37.5)</td>
<td>4 (19.0)</td>
</tr>
<tr>
<td>Iliopsoas: iliopsoas, rectus femoris, sartorius</td>
<td>2 (11)</td>
<td>2 (12)</td>
</tr>
</tbody>
</table>

n is the number of participants injected in ≥1 of the muscles in the muscle group and calculated as a % of those injected in the upper or lower limb for high intensity vs usual care groups. Total n>100% as participants had injections in multiple locations.

Favouring the high intensity vs usual care group (20.1 (IQR 10.4–25.5) vs 12.3 (IQR 5.9–18.7), respectively, p=0.071) (Table IV). However, analysing goal attainment by upper and lower limb GAG revealed a strong statistical trend towards participants with UL injections achieving more goals at 24 weeks in the high intensity compared to the usual care group (median 3 (IQR 1–3) versus 1 (IQR 1–2), p=0.052), with no observed difference for those who had LL injections.

Secondary outcomes

The high intensity group showed greater reduction in mean UL MAS score compared with the usual care group at 6 (p=0.005) and 12 (p=0.017) weeks, and overall mean MAS score at 12 weeks (p=0.025) (Table IV). The usual care group had a greater reduction in LL MAS score at 24 weeks (p=0.004). Overall, MAS scores trended towards baseline at 12 and 24 weeks. Participant satisfaction with treatment, measured using the global assessment scale, improved throughout the study in both groups (Table IV). There were no significant differences in change scores for secondary measures of activity participation (Arndt, gait speed, Global Assessment Scale, SES) at any time point. There were no differences in secondary outcomes for participants receiving UL or LL injections in either group.

Factors contributing to effect size

Gender, time since stroke and stroke localization (cental vs sub-central) did not correlate with goal achievement outcomes. Older patients had less change in GAG score at 12 weeks (8–0.37, 95% confidence interval (CI): -0.45 to -0.28, p=0.005) and 24 weeks (8–0.36, 95% CI: -0.45 to -0.24, p=0.009). Participants who achieved at least 50% of their goals at 6 weeks were more likely to do so at 12 weeks (crude OR = 3.7, 95% CI 1.1–12.6, p=0.041, adjusted OR = 4.95 CI: 1.1–19.6, p=0.040) and 24 weeks (crude OR = 5.6, 95% CI: 1.7–18.6, p=0.005, adjusted OR = 8.4 (95% CI: 1.7–32.9, p=0.005). At 6 weeks, the chance of achieving at least 50% of goals was 3.5 times higher with 1 point decrease in MAS score (95% CI: 1.2–8.9, p=0.035). However, this correlation was not found at other time points.

DISCUSSION

In this pragmatic controlled trial, a high intensity ambulatory rehabilitation program (mean 3.2 ± 1.8 sessions per week for approximately 10 weeks) following BoNT-A injections for post-stroke upper and or lower limb spasticity was compared against a lower intensity, usual care program (mean 1.3 ± 1.0 weekly sessions). Both groups improved significantly in terms of goal achievement and participant satisfaction up to 24 weeks. There was a strong trend towards UL-injected participants in...
Table IV: Summary of outcomes of high intensity rehabilitation programmes and usual care: changes from baseline at 6, 12 and 24 weeks

<table>
<thead>
<tr>
<th>Treatment</th>
<th>6 weeks</th>
<th>12 weeks</th>
<th>24 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>High intensity (n=29)</td>
<td>Usual care (n=29)</td>
<td>High intensity (n=29)</td>
</tr>
<tr>
<td><strong>Primary outcomes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Participants achieving ≥50% of goals, n (%)</td>
<td>19 (69.0)</td>
<td>20 (69.0)</td>
<td>21 (72.4)</td>
</tr>
<tr>
<td>G.A.S. mean (SD)</td>
<td>15.9 (7.7 to 12.9)</td>
<td>12.4 (6.4 to 9.1)</td>
<td>13.4 (11.5 to 25.6)</td>
</tr>
<tr>
<td><strong>Secondary outcomes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M.A.S. mean (SD)</td>
<td>-1.0 (0.6)</td>
<td>-0.7 (0.6)</td>
<td>-0.6 (0.8)</td>
</tr>
<tr>
<td>U.L. (mm)</td>
<td>-0.6 (0.4)</td>
<td>-0.6 (0.4)</td>
<td>-0.5 (0.5)</td>
</tr>
<tr>
<td>A.S. (mm)</td>
<td>-0.1 (0.1)</td>
<td>-0.1 (0.1)</td>
<td>-0.1 (0.1)</td>
</tr>
<tr>
<td>U.C. (mm)</td>
<td>-0.9 (0.9)</td>
<td>-0.9 (0.9)</td>
<td>-0.9 (0.9)</td>
</tr>
</tbody>
</table>

The high intensity therapy group achieving more goals at 24 weeks compared with usual care. This effect was not observed for U.L. goals. Demographic and clinical characteristics of study participants were similar to those of other studies including age (6, 8, 9), time following stroke (11), and proportion of male participants (7%) compared with 58–63% (6, 7, 9, 10). Although the usual care group had more cortical strokes, there were no differences in cortical and grey matter deficits on assessment and reduction analysis. There was no effect of sex on outcomes. Lower baseline G.A.S. scores in the high intensity group suggest patients’ ability to achieve their goals at a lower level. However, gender, time since stroke and stroke localisation (cortical versus sub-cortical) did not correlate with goal achievement outcomes, older patients showed reduced benefit at 12 weeks.

Benefits relating to goal achievement were maintained up to 24 weeks post-therapy, even after cessation of therapy and despite the effects of BoNT-A on spasticity seen off. Other studies have demonstrated a similar delay between spasticity reduction and improved upper limb function (5, 12), suggesting that motor relearning continues after muscle tone is returning to baseline, and supporting the use of BoNT-A to be used with active rehabilitation (12). Most trials of physical interventions or single treatment cycles of BoNT-A for spasticity rarely extend beyond 4 months (23, 34). The longer follow-up in this study ensured that the effects of therapy and their maintenance after completion of the intervention could be identified. At 6 weeks, spasticity reduction was related to a greater chance of achieving at least 50% of goals, however, this relationship did not continue after 6 weeks. Hence, the prolonged benefits of combined BoNT-A and therapy are more likely to result from other factors such as ongoing neuroplasticity, particularly as the study cohort were a median of 2.5 years post-stroke. This finding supports other literature on chronic (>1 year) stroke, showing long-term motor improvement after participation in novel rehabilitation protocols or therapy modalities were observed due to neuroplastic and adaptive changes (25).

This study showed a statistical trend suggesting a benefit of goal-directed higher intensity therapy over usual care following BoNT-A injections to the upper limb. Comparison of the study findings with other studies is limited due to the lack of literature investigating the influence of therapy intensity on outcomes after BoNT-A injections for post-stroke spasticity. Instead, studies have tended to compare single treatment modalities such as stretching, joint or electrical stimulation (17, 18) or qualitatively different therapy approaches such as CIBIT and neurodevelopmental therapy (20). While the optimal type and amount of therapy has not been determined, rehabilitation programmes have been suggested to play an important role in improving outcomes following BoNT-A treatment (20, 25, 26). A feasibility study showed that neurological patients receiving therapy (serial casting and movement training) with or without BoNT-A, vs BoNT-A alone, had greater improvement in G.A.S. scores (25). A limited impact of higher intensity rehabilitation programmes (impaired and non-impaired) on functional outcomes after stroke has been found in other studies (37–39), partially supporting the findings of this study. As both study groups received individualized, scheduled rehabilitation programmes (neurodevelopmental; therapy) in similar settings, the current...
study suggests that while therapy is important, more intensive therapy in stroke may have a differential capacity to modulate patient outcomes following upper and lower limb BoNT-A injections. However, the "black box" of therapy requires further investigation as systematic management guidelines lack details on optimal therapy approaches (15, 16). In particular, it may be that provision of goal-directed therapy is more important than the amount of therapy, although further exploration is required.

Limitations of research design have the potential to contribute to the findings of this study. Both groups received active rehabilitation following BoNT-A injections; there may have been insufficient variation in intensity of therapy. However, the high-intensity group received almost 3 times as many therapy sessions compared with the usual care group. In comparison, other studies have reported an intensity differential of only 1.2–2 times the control intervention (17, 18). At the provision of a rehabilitation program in conjunction with BoNT-A injections is considered best practice (15, 16), it was not ethically possible to have a non-therapy control group. More than 50% of participants were receiving therapy at the time of recruitment, which may have influenced the results as some of the benefits of rehabilitation may have already been realized. Furthermore, participants may have been undertaking "informal therapy", particularly for the lower limb, in the form of walking that may have been much greater in extent than the difference between formal therapy. The different locations of therapy provision between the groups may have been a confounding, as therapy approaches may have differed between sites.

Other factors external to therapy intensity may have impacted on the outcomes of this study. At the participant level, these include their activity levels outside of therapy, personal factors such as motivation and self-efficacy, and participation in study measurements (18) including formal goal-setting procedures. At the therapist level, potential confounders include those factors that influence the patient-therapist interaction, compliance, and delivery of therapy.

This trial, conducted in the "real-life" clinical setting, highlights the challenges of conducting complex rehabilitation interventions. A randomized controlled trial design was not possible due to the nature of service delivery, limitations in resources, and those reasons outlined above. While the outcome assessor was blinded, it was not possible to blind therapists. Participants were not informed of study design related to intensity of therapy; however, it is unclear whether this was maintained throughout the study period. Demonstrating functional benefits following focal spasticity management can be difficult to standardize outcomes for treatment and control groups. Control groups may have included varied interventions, making comparisons between the two groups difficult.

ACKNOWLEDGEMENTS

We are grateful to all participants and therapists who provided therapy. We thank the Rehabilitation Medicine Department staff, including Dr. Grace Abbott, Louise Ng, Shona Lui, Phoebe Yap, and Dr. Raj Mohan and Dr. Brigid Vaziri for performing outcome assessments, and Lynne Turner-Stokes for providing valuable advice. This study was partially funded by the Australian Faculty of Rehabilitation Medicine, Ipswich Open Research Fellowship. The funder had no influence on the interpretation of data and the final conclusions drawn.

Conflict of interest

Manuela Domenico is on the Advisory Board for Ipsen and has received research sponsorship to attend meetings. Julie Turner-Stokes has received research sponsorship to attend meetings and/or consultancy fees from Allergan and Ipsen. Julie Turner-Stokes has received honoraria from Ipsen. No author has a personal financial interest in BoNT-A or in any of the methods used in this research.

REFERENCES

Sandoz D. A. Reabilitat13 ion programmat: after benzodiazepine t13m injections: for post-stroke spasticity.

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## Appendix 2. Goal attainment scaling assessment form

Goal Attainment Scaling Lower limb
Baseline date: 02/01/2011

<table>
<thead>
<tr>
<th>Goal Attainment Level</th>
<th>Score</th>
<th>GOAL 1</th>
<th>GOAL 2</th>
<th>GOAL 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Best anticipated outcome</td>
<td>+2</td>
<td>Walking 15 mins before needing a rest</td>
<td>Walking 100% indoors, not using manual w/c</td>
<td>When I stand up my right heel touches the floor and all my weight is on the right side</td>
</tr>
<tr>
<td>More than expected outcome</td>
<td>+1</td>
<td>Walking 10 mins before needing a rest</td>
<td>Walking 75% indoors, using manual w/c 75%</td>
<td>When I stand up my right heel touches the floor and I have even weight on both legs</td>
</tr>
<tr>
<td>Expected outcome</td>
<td>0</td>
<td>Walking 6 mins before needing a rest</td>
<td>Walking 50% indoors, using manual w/c 50%</td>
<td>When I stand up my right heel touches the floor and isn’t shaking</td>
</tr>
<tr>
<td>Less than expected outcome</td>
<td>-1</td>
<td>Walking 4 mins before needing a rest</td>
<td>Using manual w/c indoors most of the time</td>
<td>When I stand up my right heel touches the floor and is shaking a little</td>
</tr>
<tr>
<td>Unfavourable outcome</td>
<td>-2</td>
<td>Walking &lt;4 mins before needing a rest</td>
<td>Using manual w/c indoors all of the time</td>
<td>When I stand up my right heel is off the round a lot and shaking</td>
</tr>
<tr>
<td>Level at Intake</td>
<td>-1</td>
<td>-1</td>
<td>-1</td>
<td></td>
</tr>
<tr>
<td>Follow Up: 6 weeks</td>
<td>+1</td>
<td>+1</td>
<td>-1</td>
<td></td>
</tr>
<tr>
<td>12 weeks</td>
<td>+1</td>
<td>+1</td>
<td>+1</td>
<td></td>
</tr>
<tr>
<td>24 weeks</td>
<td>+2</td>
<td>0</td>
<td>+2</td>
<td></td>
</tr>
<tr>
<td>Importance</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td></td>
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<tr>
<td>Difficulty</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>
**Goal Attainment Scaling Upper limb**

**Baseline date: 25/02/2011**

<table>
<thead>
<tr>
<th>Goal Attainment Level</th>
<th>Score</th>
<th>GOAL 1</th>
<th>GOAL 2</th>
<th>GOAL 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Best anticipated outcome</td>
<td>+2</td>
<td>Moving/stretching my right hand is not hard work</td>
<td>Cleaning my right hand is 1-2/10 hard work</td>
<td></td>
</tr>
<tr>
<td>More than expected outcome</td>
<td>+1</td>
<td>Moving/stretching my right hand is 1-2/10 hard work</td>
<td>Cleaning my right hand is 3-4/10 hard work</td>
<td></td>
</tr>
<tr>
<td>Expected outcome</td>
<td>0</td>
<td>Moving/stretching my right hand is 3/10 hard work</td>
<td>Cleaning my right hand is 5/10 hard work</td>
<td></td>
</tr>
<tr>
<td>Less than expected outcome</td>
<td>-1</td>
<td>Moving/stretching my right hand is 5/10 hard work</td>
<td>Cleaning my right hand is 8/10 hard work</td>
<td></td>
</tr>
<tr>
<td>Unfavourable outcome</td>
<td>-2</td>
<td>Moving/stretching my right hand is &gt;5/10 hard work</td>
<td>Cleaning my right hand is 9-10/10 hard work</td>
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<table>
<thead>
<tr>
<th>Level at Intake</th>
<th>Follow Up: 6 weeks</th>
<th>12 weeks</th>
<th>24 weeks</th>
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<table>
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<tr>
<th>Importance</th>
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<tr>
<td>2</td>
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</table>
Appendix 3. Standardised therapy documentation forms

Rehabilitation Specificity Study
The Royal Melbourne Hospital

(for all enquiries please contact Dr Marina Demetriou or Julie Lute on 03 8317 2000)

<table>
<thead>
<tr>
<th>Occupational Therapy Rehabilitation Activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient ID</td>
</tr>
<tr>
<td>Therapist</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>INTERVENTION CODES</th>
<th>Duration of Activity</th>
<th>Interventions</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Pre Functional Activity</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Resting</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Eating</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Grooming</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Toileting</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Feeding / Eating</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Transfers</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bed Mobility</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Functional Mobility</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Home Management</td>
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</tr>
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<td>Community Integration</td>
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</tr>
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<td></td>
<td>Leisure Performance</td>
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</tr>
<tr>
<td></td>
<td>Upper extremity</td>
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<tr>
<td></td>
<td>Control</td>
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<td>Wheelchair</td>
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</tr>
<tr>
<td></td>
<td>Management</td>
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</tr>
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<td></td>
<td>Sitting Balance</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Trunk Control</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Intervention not Related to Functional Activity</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Intervention #2 not Related to Functional Activity</td>
<td></td>
</tr>
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</table>

Co-Treat:  
No. of minutes:  
Disciplines:  

Patient Assessment:  
Formal Assessment (initial, re-assessment, discharge)  
HMS Evaluation:  
Initial Evaluation:  
Therapy Time:  
OFF:  
OT Assistant:  
OT Aids / Tech:  
OT Student:  
Group Occupational Therapy Time:  
OT Group / Deviation:  

Enter the number of each that participated in the Group Session:

Enter the number of each that participated in the Group Session:

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## Physical Therapy Rehabilitation Activities

<table>
<thead>
<tr>
<th>Patient ID</th>
<th>Date of Therapy Session</th>
<th>Therapist</th>
<th>Time Session Begins</th>
</tr>
</thead>
</table>

### Intervention Codes

#### Neurovascular Interventions:
- Balance Training
- Posture Awareness
- Motor Training
- Fall
- SIT
- Gait with Body Weight Support
- Informed, Appropriate Addressed
- Occupational Related Movement Therapy

#### Pharmacological Interventions:
- Strength Therapy
- Motivation
- Motion / Swaying
- Manual Therapy
- Motor Control

#### Contra-Interventions:
- Exercise
- Hand / Foot Exercises
- Cerebral Palsy / Sensory Interventions
- Gait Training
- Percussive Training
- Wheelchair Training
- Sensory Training

#### Education Interventions:
- Patient
- Family / Caregiver
- Staff

#### Equipment Interventions (including seating and splints):
- Prosthetics / Orthotics
- Application
- Evaluation

#### Gaiting

#### Mobility Interventions:
- Distal Stimulation
- Rollbacks
- Ultrasonic
- Posture Therapy

#### Assistive Devices:
- 10. Walker / Cane
- 11. Crutches
- 12. Chair
- 13. Wheelchair
- 14. Braces
- 15. Splints
- 16. Orthotic
- 17. Custom

#### Co-Treat

#### No. of minutes

#### Patient Assessment
- Formal Assessment (Initial, re-evaluation, discharge)
- Home Evaluation
- Work Site Evaluation:

#### Physical Therapy Time

#### Group Physical Therapy Time

#### Number of each that participated in the Group PT:

### Duration of Activity

#### Task
- Pre-Functional Activity
- Bed Mobility
- Sitting
- Transfers
- Sit-to-Stand
- Wheelchair Mobility
- Pre-gait
- Gait
- Advanced Gait
- Community Mobility

#### Intervention Not Related to Functional Activity

#### Intervention #2 Not Related to Functional Activity

#### Co-Treat

#### No. of minutes

#### Disciplines

#### Physical Therapy Time

#### NP

#### PT Group / Devrel:

#### Enter the number of each that participated in the Group PT:

### Notes:

### 284
OCCUPATIONAL THERAPY
DEFINITION OF TERMS

Activities

Pre-functional activity: An activity that will be related to a functional activity at a later time (preparation activity).

Bathing: Obtaining and using supplies; soaping, rinsing, and drying body parts; maintaining bathing position; and transferring to and from bathing positions.

Dressing: Selecting clothing and accessories appropriate to time of day, weather, and occasion; obtaining clothing from storage area; dressing and undressing in a sequential fashion; fastening and adjusting clothing and shoes; and applying and removing personal devices, prostheses, or orthoses.

Grooming: Obtaining and using supplies; removing body hair (use of razors, tweezers, lotions, etc.); applying and removing cosmetics; washing, drying, combing, styling, and brushing hair; caring for nails (hands and feet); caring for skin, ears, and eyes; and applying deodorant.

Toileting: Obtaining and using supplies; clothing management; maintaining toileting position; transferring to and from toileting position; cleaning body; and caring for menstrual and continence needs (including catheters, colostomies, and suppository management).

Feeding/Eating: Setting up food; selecting and using appropriate utensils and tableware; bringing food or drink to mouth; cleaning face, hands, and clothing; sucking, masticating, coughing, and swallowing, and management of alternative methods of nourishment.

Transfers: Process of relocating a body from one object or surface to another (e.g., in/out of bed, w/c to and from bed). Bathing and toileting transfers are addressed in the bathing and toileting activities above.

Bed mobility: Process of moving while in bed. Including rolling, supine to and from sit, sit to supine, scooting up and down, sideways and bridging.

Functional mobility: Moving from one position or place to another, such as in-bed mobility or wheelchair mobility. Performing functional ambulation and transporting objects with and without transporting objects during functional tasks.

Home management: Obtain, maintain, and/or practice using personal and/or household possessions and environment. May include clothing care, cleaning, meal preparation and cleanup, shopping, money management, household maintenance. It may also include levels of supervision for safe performance of specific activities.
Community integration: Moving self in the community and using public or private transportation, such as driving, or accessing busses, taxi cabs, or other public transportation. Functional mobility in community, interaction with environment including physical, social, and cognitive goal directed behavior.

Leisure performance: Planning and participating in play or leisure activities. Maintaining a balance of play or leisure activities with work and productive activities, and activities of daily living. Obtaining, utilizing, and maintaining equipment and supplies.

Upper extremity control: Training/facilitation of normal movement, strength, range of motion, and alignment in the upper extremity. Initiating and completing care of the upper extremity for functional activities.

Wheelchair management: Ability to manage wheelchair including set and remove brakes, remove/ move footrests in preparation for transfer, and all other parts on a variety of surfaces. Mobilize wheelchair in environment safely.

Sitting balance/trunk control: Facilitation of patient’s ability to sit unsupported, ability to move outside of patient’s center of gravity while seated and while maintaining control of body. Training/facilitation of normal movement, strength, range of motion, and alignment of trunk. Initiating and completing care of the trunk for functional activities.

Intervention(s) not related to functional activity (two rows): Interventions/time spent on patient’s behalf but not in direct contact with patient. For example, time spent selecting and ordering a splint.

Neuromuscular Interventions

1. Balance training: The ability to maintain the body in equilibrium with gravity both statically and dynamically.

2. Postural awareness: Awareness that the alignment and positioning of the body in relation to gravity, center of mass and base of support.

3. Motor learning: A set of processes associated with practice or experience leading to relatively permanent changes in the capability for producing skilled action.


5. NDT/Bobath: Inhibition of abnormal patterns of movement to accomplish before normal selective isolated movement can be achieved. Big emphasis on postural equal weight bearing.
6. **Brunstrom**: Treatment technique that utilizes synergies & reflexes to encourage movement as part of the sequence of the return of motor function. Proprioceptive and exteroceptive (i.e. external stimuli) are used to assist in eliciting synergies.

7. **Constrained induced movement therapy**: The immobilization of the unaffected extremity during the therapy session with intense repetitive exercise, used within a functional application.

**Adaptive and Compensatory Interventions**

8. One-handed skills: demonstration/instruction in use of 1 hand to perform daily living tasks. Could include adaptive equipment instructions.

9. Energy conservation: Instruction in skills to pace individuals with low endurance to manage fatigue better through rest breaks, requesting assistance, adaptive equipment.

10. Environmental adaptation: modification of the surroundings and or use of adaptive equipment (furniture placement, removing potential obstacles, etc.) to increase safety and functional ability.

11. Adaptive equipment: selection, recommendation, training, and practice with adaptive equipment such as reacher, dressing stick, elastic shoelaces, rocker knife, and adaptive cutting board.

**Musculoskeletal Interventions**

12. **Strengthening**: Strength-building exercises in which the occupational therapist does one of the following: applies resistance through the range of active movement (active); assists the patient/client through active movement (assistive); or a static or dynamic muscular contraction is resisted by an outside force applied manually or mechanically (resistive).

13. **Mobilization / Manual therapy**: A broad group of skilled hand movements including but not limited to mobilization and manipulation used by the therapist to mobilize or manipulate soft tissues and joints. The purpose of these movements is to modulate pain, increase range of motion, and/or reduce or eliminate soft tissue swelling, inflammation, or restriction. This includes relaxation, improving contractile and noncontractile tissue extensibility, and improving pulmonary function. A passive therapeutic movement at the end of the available range of motion at variable amplitudes and speed.

14. **PROM/Stretching**: Passive range of motion (PROM) is a form of bodily movement that is carried through by the therapist, assistant, aide, or patient that does not include the assistance or resistance of the affected body part. Stretching is a sustained, long duration lengthening of soft tissue such as muscle or tendon applied to increase range of motion at least 12-15 seconds. Stretching may be applied by therapist, assistant, or aide or by the patient independently.
15. Edema control: Use of retrograde massage, compression garments, elevation, ice drips, and patient/family education in techniques and management.

Cardiopulmonary Interventions:

16. Breathing: Coordinating inhalation and exhalation with movement during exercise, IADL.

17. Aerobic/Conditioning exercises: performance of therapeutic exercise and activities to increase endurance

Cognitive/Perceptual/Sensory Interventions

18. Cognitive training: Impulse control, attention, orientation, memory, problem solving, sequencing, social skills, safety, insight, and goal setting.

19. Perceptual training: interventions used to address apraxia, neglect, awareness in space, figure ground, care of sensory impaired body parts.

20. Visual training: Interventions to increase attention to visual field deficits, diplopia, scanning, and visual coordination.


Equipment Interventions

22. Prescription / Selection: identifying items that meet the patient’s need and financial resources. Writing justification for these items and obtaining doctor’s approval.

23. Application: Placing edema control garments, and/or splints on the patient’s body.

24. Fabrication: Obtaining necessary supplies and forming supplies into equipment, e.g., splints.

25. Ordering: Seeking insurance authorizations, calling/faxing equipment prescriptions and orders.

Modality Interventions


27. Biofeedback: A training technique that enables an individual to gain some element of voluntary control over muscular or autonomic nervous system functions using a device that produces auditory or visual stimuli.

Education/Training Interventions

29. Patient: Individual patient or group of patients. Verbal or written education/training takes place or hands-on practice occurs. Topics may include managing care needs, therapeutic treatments, disease prevention, etc. Education activity lasts longer than 10 minutes.

30. Family / Caregiver: Verbal or written education/training takes place or hands-on practice occurs with individual family member or personal caregiver or group of family members or caregivers. Does not include facility staff. Topics may include instruction on managing care needs, therapeutic treatments, disease prevention, etc. Education activity lasts longer than 10 minutes.

31. Staff: Verbal or written education/training takes place or hands-on practice occurs with individual facility staff member or group of staff members. Topics may include instruction on managing care needs, therapeutic treatments, disease prevention, etc. Education activity lasts longer than 10 minutes.

Co-treat

Therapists from two or more disciplines working together to form a treatment plan for the patient or to perform multiple treatment plans during a patient session. Multiple therapists may also provide additional skilled assistance for handling patient and performing tasks.

Patient Assessment

Formal Assessment (initial, reevaluation, discharge), comprised of an *Examination and/or an *Evaluation. This examination/evaluation is performed upon admission to the rehab facility, when there is a significant change in patient status, and upon discharge from the rehab facility.

*Examination: The process of obtaining a history, performing relevant systems reviews, and selecting and administering specific tests and measures.

*Evaluation: A dynamic process in which the physical therapist makes clinical judgments based on data gathered during the examination.

Home evaluation: Assessment of patient’s home to determine accessibility and to make recommendations to maximize patient’s functioning in the home.

Work site evaluation: Assessment of patient’s work site to determine accessibility and environmental demands and to make recommendations to maximize patient’s functioning at work.

Group Occupational Therapy Time:

Group: Ratio of ≥1 OT staff member to ≥3 patients for a therapy session.

Dovetail: Therapy session that involves 1 OT staff member and 2 patients.
PHYSICAL THERAPY
DEFINITION OF TERMS

* Definitions derived from the Guide to Physical Therapist Practice.

Activities

Pre-functional activities: activities that will be related to a functional activity at a later time (preparation activities).

Bed mobility: The process of moving while in bed. Includes rolling, supine to sit, sit to supine, scooting up, down, and sideways, and bridging.

Sitting: The major weight-bearing surface is the buttocks. May include: long, supported, unsupported, static, or dynamic sitting. Does not include lying down or standing.

*Transfers: The process of relocating a body from one object or surface to another (e.g. getting into or out of bed, moving from a wheelchair to a bed)

Sit-to-Stand: The process of moving from a sitting to a standing position. This also includes working on forward weight shift and any component of the sit to stand motion, such as squatting.

Wheelchair mobility: The process of moving a wheelchair on a level surface. This can be done with any combination of limbs. It can also include driving a power wheelchair. Advanced wheelchair skills, e.g., stairs, curbs, uneven surfaces, are part of the definition of Community Mobility below. Wheelchair mobility also includes parts management/maintenance.

Pre-gait: Standing activity which includes development of upright control against gravity, the ability to shift weight in different directions and weight acceptance onto the involved limb in preparation for locomotion.

Gait: Training of skills needed for ambulation over level surfaces and stairs; includes controlled weight shifts, single-limb stance, advancing the lower limb, balance recovery, training with assistive devices and training the ability to approach the sitting surface, turn and backup to the sitting surface.

Advanced Gait: Training of higher-level locomotor skills; includes increasing speed, quick direction changes, walking over different surface textures and grades, negotiating around and over obstacles, backwards walking, tandem walking, crossovers, jumping, hopping, skipping, jogging, and adding tasks during ambulation such as ball handling or carrying objects, etc.

Community Mobility: Training of ambulatory or wheelchair mobility skills needed to manage situations encountered in the community; includes locomotion on uneven grades, negotiating physical barriers (doors, thresholds, curbs, etc.), use of elevators, escalators, public transportation, and the problem/judgment inherent to these tasks.
Intervention not related to functional activity: An intervention that is performed by the physical therapist that is not related to a functional activity. Intervention/time spent on patient's behalf but not in direct contact with patient. For example, time spent selecting and ordering a wheelchair.

Neuromuscular Interventions

1. **Balance training**: The ability to maintain the body in equilibrium with gravity both statically and dynamically.

2. **Postural awareness**: Awareness that the alignment and positioning of the body in relation to gravity, center of mass and base of support.

3. **Motor learning**: A set of processes associated with practice or experience leading to relatively permanent changes in the capability for producing skilled action.

4. **PNF (Proprioceptive Neuromuscular Facilitation)**: Simultaneously applied sensory stimulation techniques repeated with active movement to achieve a desired motor response.

   Sensory stimulation techniques applied to specific movement patterns of the limb or trunk.

   Manual resistance applies to isometric or isotonic contractions within specific movement patterns to achieve inhibitory or excitatory responses to agonists or antagonists.

5. **NDT (Neurodevelopmental Technique)**: Treatment using handling skills to help the individual make modifications in his movement, normalize muscle tone, and inhibit abnormal movement. Patterns and facilitation for normal movement.

   Treatment philosophy developed by Berta Bobath. Emphasis is on facilitating normal movement patterns of the trunk and limbs, and eliciting normal equilibrium responses with control of the involved parts rather than teach compensatory movement techniques.

6. **Gait with body weight support**: Provides a symmetrical removal of weight from the lower extremities thereby facilitating walking in neurological patients who are typically unable to cope with bearing full weight on their lower extremities.

7. **Involved upper extremity addressed**: Any functional PT activity in which the PT addresses the upper extremity.

8. **Constrained induced movement therapy**: The immobilization of the unaffected extremity during the therapy session with intense repetitive exercise, used within a functional application.
Musculoskeletal Interventions

9. **Strengthening**: Strength-building exercises in which the physical therapist does one of the following: applies resistance through the range of active movement (active); assists the patient/client through active movement (assistive); or a static or dynamic muscular contraction is resisted by an outside force applied manually or mechanically (resistive).

10. **Mobilization**: A passive therapeutic movement at the end of the available range of motion at variable amplitudes and speed.

11. **PROM/Stretching**: Passive range of motion (PROM) is a form of bodily movement that is carried through by the therapist, assistant, aid, or patient that does not include the assistance or resistance of the effected body part. Stretching is a sustained, long duration lengthening of soft tissue such as muscle or tendon applied to increase range of motion at least 12-15 seconds. Stretching may be applied by therapist, assistant, or aide or by the patient independently.

12. **Manual Therapy**: A broad group of skilled hand movements including but not limited to mobilization and manipulation used by the physical therapist to mobilize or manipulate soft tissues and joints for the purpose of modulating pain, increasing range of motion; reducing or eliminating soft tissue swelling, inflammation, or restriction; including relaxation; improving contractile and noncontractile tissue extensibility; and improving pulmonary function.

13. **Motor Control**: The ability of the central nervous system to control or direct the neuro-motor system in purposeful movement and postural adjustment by selective allocation of muscle tension across appropriate joint segments.

Cardiopulmonary Interventions

14. **Breathing**: Coordinating inhalation and exhalation exercises with movement during exercise.

15. **Aerobic/Conditioning exercises**: Performance of therapeutic exercise and activities to increase endurance.

Cognitive/Perceptual/Sensory Interventions

16. **Cognitive Training**: Interventions aimed at improving the act or process of knowing, including both awareness and judgment.

17. **Perceptual Training**: The remediation of adaptation of the mechanisms by which the brain interprets sensory information from the environment through teaching specific perceptual skills or through functional activities such as ADLs.

18. **Visual Training**: The process of treating visual deficits through training of visual skills, developing awareness and compensation strategies for visual deficits practice of skills and strategies in functional context.
19. Sensory training: The process of developing tactile, auditory, or kinesthetic awareness or compensation strategies in deficit areas to maximize patient safety.

Education Interventions

20. Patient: Patient who receives specific instructions/training through means of writing, verbalization, and/or demonstration form the PT and is asked to repeat the information via writing, verbalization, and/or demonstration. The information included in patient education is as follows: Mobility training (including gait, transfers, bed mobility, stairs, community, wheelchair), safety, wheelchair management, exercise programs, balance training, coordination training, and functional endurance.

21. Family/Caregiver: Family member or personal caregiver (not facility staff) who receives specific instructions/training from the PT through means of writing, verbalization, and/or demonstration and is asked to repeat the information via writing, verbalization, and/or demonstration. The information included in family/caregiver education is as follows: Mobility training (including gait, transfers, bed mobility, stairs, community, wheelchair), safety, wheelchair management, exercise programs, balance training, coordination training, and functional endurance.

22. Staff: Facility staff who receives specific instructions/training through means of writing, verbalization, and/or demonstration by the PT and is asked to repeat the information via writing, verbalization, and/or demonstration. The information included in staff education is as follows: Mobility training (including gait, transfers, bed mobility, stairs, community, wheelchair), safety, wheelchair management, exercise programs, balance training, coordination training, and functional endurance.

Equipment Interventions

23. Prescription/selection: A written direction or order for administering durable medical equipment or specific activity. Identifying items that meet the patient’s need and financial resources. Writing justification for these items and obtaining doctor’s approval. Done in conjunction with patient and/or caregiver.

24. Application: Putting to practical or specific use devices or treatments that were prescribed. Placing edema control garments and/or splints on the patient’s body. Making adjustments or modifications to patient equipment.

25. Fabrication: The making or constructing of a device. Obtaining necessary supplies and forming supplies into equipment, i.e., splints.

26. Ordering: Arranging or requesting of medical supplies needed by the patient. Seeking insurance authorizations, calling/faxing equipment prescriptions and orders.

Modality Interventions

28. Biofeedback: A training technique that enables an individual to gain some element of voluntary control over muscular or autonomic nervous system functions using a device that produces auditory or visual stimuli.

29. Ultrasound: A treatment technique using high-frequency sound waves to produce heat.

Pet Therapy

30. Use of a specially trained dog to facilitate a PT activity. Not to include having a patient’s pet come from home.

31. Use of other specially trained animal to facilitate a PT activity. Not to include having a patient’s pet come from home.

Area Involved – Non-functional

60. Upper extremity is involved in a non-functional activity, e.g., range of motion, strengthening, mobility, modalities, etc.

61. Lower extremity is involved in a non-functional activity, e.g., range of motion, strengthening, mobility, modalities, etc.

62. Trunk is involved in a non-functional activity, e.g., range of motion, strengthening, mobility, modalities, etc.

63. The head/neck is involved in a non-functional activity, e.g., range of motion, strengthening, mobility, modalities, etc.

Co-treat

Therapists from two or more disciplines working together to form a treatment plan for the patient or to perform multiple treatment plans during a patient session. Multiple therapists may also provide additional skilled assistance for handling patient and performing tasks.

Patient Assessment

Formal Assessment (initial, reevaluation, discharge): comprised of an *Examination and/or an *Evaluation. This examination/evaluation is performed upon admission to the rehab facility, when there is a significant change in patient status, and upon discharge from the rehab facility.

*Examination: The process of obtaining a history, performing relevant systems reviews, and selecting and administering specific tests and measures.

*Evaluation: A dynamic process in which the physical therapist makes clinical judgments based on data gathered during the examination.
Home evaluation: Assessment of patient's home to determine accessibility and to make recommendations to maximize patient's functioning in the home.

Work site evaluation: Assessment of patient's work site to determine accessibility and environmental demands and to make recommendations to maximize patient's functioning at work.

Group Physical Therapy Time:

Group: Ratio of ≥1 PT staff member to ≥3 patients for a therapy session.

Dovetail: Therapy session that involves 1 PT staff member and 2 patients.
Appendix 4. Qualitative questionnaires

Questionnaire 1: Evaluation of patient experience

<table>
<thead>
<tr>
<th></th>
<th>Not at all</th>
<th>Small amount</th>
<th>Moderate amount</th>
<th>Great deal</th>
<th>Extreme amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. To what extent did the program address your goals?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>2. How much do you feel the program contributed to you achieving your goals?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>3. Were you able to use skills learnt during the program in your everyday life (short-term, up to 6 months)?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>4. To what extent do you feel benefits of the program have been maintained in the long-term?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Very dissatisfied</th>
<th>Fairly dissatisfied</th>
<th>Neither Satisfied nor dissatisfied</th>
<th>Satisfied</th>
<th>Very Satisfied</th>
</tr>
</thead>
<tbody>
<tr>
<td>How satisfied were you with the program?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

1. Were there any problems or difficulties you encountered with the program?

2. Other comments or changes you would recommend?
**Questionnaire 2: Evaluation of therapist experience during therapy program**

<table>
<thead>
<tr>
<th>Question</th>
<th>Not at all</th>
<th>Small amount</th>
<th>Moderate amount</th>
<th>Great deal</th>
<th>Extreme amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. To what extent were the outpatient therapy programs implemented as planned (consistency, time)?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>2. To what extent were the therapy programs relevant to the patient goals?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>3. Given the resources allocated to the programs to what extent did they benefit the patients overall?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>4. How satisfied were you with delivery of therapy programs?</td>
<td>Very dissatisfied</td>
<td>Fairly dissatisfied</td>
<td>Neither Satisfied nor dissatisfied</td>
<td>Satisfied</td>
<td>Very Satisfied</td>
</tr>
<tr>
<td>5. What were the a) strengths and b) weaknesses of the programs?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>6. What were the a) barriers and b) enablers to program delivery?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>7. What were your attitudes and beliefs towards the intervention?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>8. Other comments or changes you would make to implementing the programs?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>
**Questionnaire 3: Evaluation of therapist experience using therapy documentation forms**

<table>
<thead>
<tr>
<th>Question</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. To what extent did the therapy documentation forms (physical and occupational therapy) capture details of the program (activities/interventions)? (Domain completeness)</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>2. To what extent were the forms applicable to the patient group*?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>3. How burdensome were the forms to complete for each therapy session? (time/difficulty)</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

*outpatients following BoNT-A for post stroke spasticity

4. Any limitations in using the form/s or recommended changes for this patient
Appendix 5. Cochrane search strategies

Cochrane review search strategies

Databases searched (Chapter 4)

- Cochrane Stroke Group Trials Register (8 February 2012)
- Cochrane Central Register of Controlled Trials (The Cochrane Library 2011, Issue 12)
- MEDLINE (1948 to December 2011)
- EMBASE (1980 to January 2012)
- CINAHL (1982 to January 2012)
- Allied and Complementary Medicine Database (1985 to January 2012)
- Physiotherapy Evidence Database at www.pedro.org.au/ (September 2012)
- REHABDATA at www.naric.com/research/rehab/ (September 2012).

Ongoing trials registers searched

- ClinicalTrials.gov (www.clinicaltrials.gov/)
- EU Clinical Trials Register (www.clinicaltrialsregister.eu)
- Stroke Trials Registry (www.strokecenter.org/trials/)
- Current Controlled Trials (www.controlled-trials.com)
- WHO International Clinical Trials Registry Platform (http://apps.who.int/trialsearch/)
- Australian New Zealand Clinical Trials Registry (www.anzctr.org.au).

Cochrane review search strategies

Cochrane Central Register of Controlled Trials (CENTRAL)

#1.MeSH descriptor Cerebrovascular Disorders explode all trees #2.stroke or poststroke or post-stroke or cerebrovasc* or brain vasc* or cerebral vasc* or eva* or apoplex* or SAH
#3.brain* or cerebr* or cerebell* or intracerebral or
#4.ischemi* or ischaemi* or infarct* or thrombo* or emboli* or
#5.(#3 AND #4) #6.brain* or cerebr* or cerebell* or intracerebral or
intracranial or subarachnoid #7.haemorrhage* or hemorrhage* or haematoma* or hematoma* or bleed* #8. (#6 AND #7) #9.hemipleg* or hemipar* or paresis or paretic #10.MeSH descriptor Hemiplegia, this term only #11.MeSH descriptor Paresis explode all trees #12. (#1 OR #2 OR #5 OR #8 OR #9 OR #10 OR #11) #13.MeSH descriptor Muscle Spasticity, this term only #14.MeSH descriptor Muscle Hypertonia, this term only #15.MeSH descriptor Muscle Rigidity, this term only #16.MeSH descriptor Muscle Tonus, this term only #17.MeSH descriptor Spasm, this term only #18.MeSH descriptor Dystonia, this term only #19.MeSH descriptor Paraparesis, Spastic, this term only #20.spastic* or high tone #21.muscle* #22.spasm or spasms or rigid* or tone or tonus or hyperton* or hypermyoton* or dyston* or contracture* #23. (#21 AND #22) #24. (#13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #23) #25.MeSH descriptor Botulinum Toxins explode all trees #26.MeSH descriptor Phenols explode all trees #27.MeSH descriptor Ethanol, this term only #28.MeSH descriptor Injections, Intramuscular, this term only #29.MeSH descriptor Nerve Block, this term only #30.botulinum* or botulin or botox or BoNT* or BTX* or dysport or xeomin or myobloc or neurobloc or oculinum or onabotulinum* or abobotulinum* or incobotulinum* or rimabotulinum* #31.phenol or ethanol or alcohol or nerve block* or motor point block* #32.intramuscular #33.injection* or treatment* or medication* or neurolysis #34. (#32 AND #33) #35. (#25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #34) #36. (#12 AND #24 AND #35)

MEDLINE (Ovid)
1. cerebrovascular disorders/ or exp basal ganglia cerebrovascular disease/ or exp brain ischemia/ or exp carotid artery diseases/ or exp intracranial arterial diseases/ or exp “intracranial embolism and thrombosis”/ or exp intracranial hemorrhages/ or stroke/ or exp brain infarction/ or vertebral artery dissection/ 2. (stroke or poststroke or post-stroke or cerebrovasc$ or brain vasc$ or cerebral vasc$ or cva$ or apoplex$ or SAH).tw.
3. ((brain$ or cerebr$ or cerebell$ or intracran$ or intracerebral) adj5 (isch?emi$ or infarct$ or thrombo$ or emboli$ or occlus$)).tw. 4. ((brain$ or
cerebr$ or cerebell$ or intracerebral or intracranial or subarachnoid) adj5
(haemorrhage$ or hemorrhage$ or haematoma$ or hematoma$ or bleed$)).tw. 5.
hemiplegia/ or exp paresis/
6. (hemipleg$ or hemipar$ or paresis or paretic).tw.
7. 1 or 2 or 3 or 4 or 5 or 6  8. muscle spasticity/ or muscle hypertonia/ or muscle
rigidity/ or muscle tonus/  9. spasm/ or dystonia/ or paraparesis, spastic/  10.
(spastic$ or high tone).tw.  11. (muscle$ adj5 (spasm or spasms or rigid$ or tone
or tonus or hyperton$ or hypermyoton$ or dyston$ or contracture$)).tw.  12. 8 or
9 or 10 or 11  13. exp botulinum toxins/ or exp phenols/ or ethanol/ or injections,
imtramuscular/ or nerve block/  14. (botulinum$ or botulin or botox or BoNT$ or
BTX$ or dysport or xeomin or myobloc or neurobloc or oculinum or
onabotulinum$ or abobotulinum$ or incobotulinum$ or rimabotulinum$).tw.  15.
(phenol or ethanol or alcohol or nerve block$ or motor point block$).tw.  16.
(intramuscular adj3 (injection$ or treatment$ or medication$ or neurolysis)).tw.
17. 13 or 14 or 15 or 16  18. 7 and 12 and 17  19. cerebral palsy/ or cerebral
palsy.tw.  20. 18 not 19  21. Randomized Controlled Trials as Topic/  22. random
allocation/  23. Controlled Clinical Trials as Topic/  24. control groups/  25.
Placebos/  29. placebo effect/  30. Multicenter Studies as Topic/  31. Therapies,
Investigational/  32. Research Design/  33. Program Evaluation/  34. evaluation
studies as topic/  35. randomized controlled trial.pt.  36. controlled clinical trial.pt.
37. clinical trial.pt.  38. multicenter study.pt.  39. (evaluation studies or
comparative study).pt.  40. random$.tw.  41. (controlled adj5 (trial$ or stud$)).tw.
42. (clinical$ adj5 trial$).tw.  43. ((control or treatment or experiment$ or
intervention) adj5 (group$ or subject$ or patient$)).tw.  44. (quasi-random$ or
quasi random$ or pseudo-random$ or pseudo random$).tw.  45. ((multicenter or
multicentre or therapeutic) adj5 (trial$ or stud$)).tw.  46. ((control or
experiment$ or conservative) adj5 (treatment or therapy or procedure or
manage$)).tw.  47. ((singl$ or doubl$ or tripl$ or trebl$) adj5 (blind$ or
mask$)).tw.  48. versus.tw.  49. placebo$.tw.  50. sham.tw.  51. (assign$ or
alternate or allocate$.tw. 52. controls.tw. 53. or/21-52 54. 20 and 53 55. exp animals/ not humans.sh. 56. 54 not 55
EMBASE (Ovid)
1. cerebrovascular disease/ or basal ganglion hemorrhage/ or cerebral artery disease/ or cerebrovascular accident/ or stroke/ or exp carotid artery disease/ or exp brain hematoma/ or exp brain hemorrhage/ or exp brain infarction/ or exp brain ischemia/ or exp intracranial aneurysm/ or exp occlusive cerebrovascular disease/ 2. stroke unit/ or stroke patient/
3. (stroke or poststroke or post-stroke or cerebrovasc$ or brain vasc$ or cerebral vasc$ or eva$ or apoplex$ or SAH).tw. 4. ((brain$ or cerebr$ or cerebell$ or intracran$ or intracerebral) adj5 (isch?emi$ or infarct$ or thrombo$ or emboli$ or occlus$)).tw. 5. ((brain$ or cerebr$ or cerebell$ or intracerebral or intracranial or subarachnoid) adj5 (haemorrhage$ or hemorrhage$ or hematoma$ or haematoma$ or hemorrhage$ or haematoma$ or bleed$)).tw. 6. hemiplegia/ or paresis/ 7. (hemipleg$ or hemipar$ or paresis or paretic).tw. 8. 1 or 2 or 3 or 4 or 5 or 6 or 7 9. muscle hypertonia/ or muscle rigidity/ or spastic paresis/ or spasticity/ 10. muscle spasm/ or muscle tone/ or dystonia/ or paraplegia/ 11. (spastic$ or high tone).tw. 12. (muscle$ adj5 (spasm or spasms or rigid$ or tone or tonus or hyperton$ or hypermyoton$ or dyston$)).tw. 13. 9 or 10 or 11 or 12 14. botulinum toxin/ or botulinum toxin a/ or botulinum toxin b/ or botulinum toxin c/ or botulinum toxin f/ 15. phenol/ or alcohol/ or intramuscular drug administration/ or exp nerve block/ 16. (botulinum$ or botulin or botox or BoNT$ or BTX$ or dysport or xeomin or myobloc or neurobloc or oculinum or onabotulinum$ or abobotulinum$ or incobotulinum$ or rimabotulinum$).tw. 17. (phenol or ethanol or alcohol or nerve block$ or motor point block$).tw. 18. (intramuscular adj3 (injection$ or treatment$ or medication$ or neurolysis$)).tw. 19. 14 or 15 or 16 or 17 or 18 20. 8 and 13 and 19 21. cerebral palsy/ or cerebral palsy.tw. 22. 20 not 21 23. Randomized Controlled Trial/ 24. Randomization/ 25. Controlled Study/ 26. control group/ 27. clinical trial/ 28. Double Blind Procedure/ 29. Single Blind Procedure/ or triple blind procedure/ 30. placebo/ 31. Multicenter Study/ 32. experimental design/ or experimental study/ or quasi experimental study/ 33.
experimental therapy/ 34. evaluation/ or “evaluation and follow up”/ or evaluation research/ or clinical evaluation/ 35. “types of study”/ 36. Comparative Study/ 37. random$.tw. 38. (controlled adj5 (trial$ or stud$)).tw. 39. (clinical$ adj5 trial$).tw. 40. ((control or treatment or experiment$ or intervention) adj5 (group$ or subject$ or patient$)).tw. 41. (quasi-random$ or quasi random$ or pseudo-random$ or pseudo random$).tw. 42. ((multicenter or multicentre or therapeutic) adj5 (trial$ or stud$)).tw. 43. ((control or experiment$ or conservative) adj5 (treatment or therapy or procedure or manage$)).tw. 44. ((singl$ or doubl$ or tripl$ or trebl$) adj5 (blind$ or mask$)).tw. 45. versus.tw. 46. placebo$.tw. 47. sham.tw. 48. (assign$ or alternate or allocat$).tw. 49. controls.tw. 50. or/23-49 51. 22 and 50

CINAHL (EBSCO)
S37 .S33 not S36 S36 .S34 or S35 S35 .TI cerebral palsy OR AB cerebral palsy S34 .(MH “Cerebral Palsy”) S33 .S22 and S32 S32 .S23 or S24 or S25 or S26 or S27 or S28 or S29 or S30 or S31 S31 .AB intramuscular AND AB ( injection* or treatment* or medication* or neurolysis ) S30 .TI intramuscular AND TI ( injection* or treatment* or medication* or neurolysis ) S29 .TI ( phenol or ethanol or alcohol or nerve block* or motor point block* ) OR AB ( phenol or ethanol or alcohol or nerve block* or motor point block* ) S28 .TI ( botulinum* or botulin or botox or BoNT* or BTX* or dysport or xeomin or myobloc or neurobloc or occlusion or onabotulinum* or abobotulinum* or incobotulinum* or rimabotulinum* ) OR AB ( botulinum* or botulin or botox or BoNT* or BTX* or dysport or xeomin or myobloc or neurobloc or occlusion or onabotulinum* or abobotulinum* or incobotulinum* or rimabotulinum* ) S27 .(MH “Nerve Block”) S26 .(MH “Injections, Intramuscular+”) S25 .(MH “Ethanol”) S24 .(MH “Phenols”) S23 .(MH “Botulinum Toxins”) S22 .S12 and S21 S21 .S13 or S14 or S15 or S16 or S17 or S20 S20 .S18 and S19 S19 .TI ( spasm or spasms or rigid* or tone or tonus or hyperton* or hypermyoton* or dyston* ) or AB ( spasm or spasms or rigid* or tone or tonus or hyperton* or hypermyoton* or dyston* ) S18 .TI muscle* or AB muscle* S17 .TI ( spastic* or high tone ) or AB
(spastic* or high tone) S16. (MH “gait disorders, neurologic”) S15. (MH “dystonia”) S14. (MH “spasm”) S13. (MH “Muscle Spasticity”) OR (MH “Muscle Hypertonia”) OR (MH “Muscle Tonus”) S12. S1 or S2 or S5 or S8 or S9 or S10 or S11. (MH “Brain Injuries”) S10. TI (hemipleg* or hemipar* or paresis or paretic) or AB (hemipleg* or hemipar* or paresis or paretic) S9. (MH “Hemiplegia”) S8. S6 and S7 S7. TI (haemorrhage* or hemorrhage* or haematoma* or hematoma* or bleed*) or AB (haemorrhage* or hemorrhage* or haematoma* or hematoma* or bleed*) S6. TI (brain* or cerebr* or cerebell* or intracerebral or intracranial or subarachnoid) or AB (brain* or cerebr* or cerebell* or intracerebral or intracranial or subarachnoid) S5. S3 and S4 S4. TI (ischemi* or ischaemi* or infarct* or thrombo* or emboli* or oclus*) or AB (ischemi* or ischaemi* or infarct* or thrombo* or emboli* or oclus*) S3. TI (brain* or cerebr* or cerebell* or intracran* or intracerebral) or AB (brain* or cerebr* or cerebell* or intracran* or intracerebral) S2. TI (stroke or poststroke or post-stroke or cerebrovasc* or brain vasc* or cerebral vasc or cva or apoplex or SAH) or AB (stroke or poststroke or post-stroke or cerebrovasc* or brain vasc* or cerebral vasc or cva or apoplex or SAH) S1. (MH “Cerebrovascular Disorders”) or (MH “stroke patients”) or (MH “stroke units”) AMED (Ovid)

1. cerebrovascular disorders/ or cerebral hemorrhage/ or cerebral infarction/ or cerebral ischemia/ or cerebrovascular accident/ or stroke/ 2. (stroke or poststroke or post-stroke or cerebrovasc$ or brain vasc$ or cerebral vasc$ or cva$ or apoplex$ or SAH).tw. 3. ((brain$ or cerebr$ or cerebell$ or intracran$ or intracerebral) adj5 (isch?emi$ or infarct$ or thrombo$ or emboli$ or oclus$)).tw. 4. ((brain$ or cerebr$ or cerebell$ or intracerebral or intracranial or subarachnoid) adj5 (haemorrhage$ or hemorrhage$ or haematoma$ or hematoma$ or bleed$)).tw.

5. (hemipleg$ or hemipar$ or paresis or paretic).tw. 6. hemiplegia/ 7. 1 or 2 or 3 or 4 or 5 or 6 8. exp muscle spasticity/ or muscle hypertonia/ or muscle tonus/ 9. spasm/ or dystonia/

10. (spastic$ or high tone).tw. 11. (muscle$ adj5 (spasm or spasms or rigid$ or tone or tonus or hyperton$ or hypermyoton$ or dyston$ or contracture$)).tw. 12.
8 or 9 or 10 or 11 13. botulinum toxins/ or phenols/ or alcohol ethyl/ or nerve block/  14. (botulinum$ or botulin or botox or BoNT$ or BTX$ or dysport or xeomin or myobloc or neurobloc or oculinum or onabotulinum$ or abobotulinum$ or incobotulinum$ or rimabotulinum$).tw.  15. (phenol or ethanol or alcohol or nerve block$ or motor point block$).tw.  16. (intramuscular adj3 (injection$ or treatment$ or medication$ or neurolysis)).tw.  17. 13 or 14 or 15 or 16  18. 7 and 12 and 17

LILACS
(MH:”cerebrovascular disorders” or MH:”basal ganglia cerebrovascular disease” or MH:”brain ischemia” or MH:”carotid artery diseases” or MH:”intracranial arterial diseases” or MH:”intracranial embolism and thrombosis” or MH: “intracranial hemorrhages” or MH: “stroke” or MH:”brain infarction” or MH:”vertebral artery dissection” or TW:”stroke” or TW:”poststroke” or TW:”post-stroke” or TW: cerebrovasc$ or TW:brain vasc$ or TW:cerebral vasc$ or TW:cva$ or TW:apoplex$ or TW:”SAH” or TW:cerebr$ or TW:cerebell$ or TW:intracran$ or TW:intracerebral or TW:”subarachnoid” or MH:”hemiplegia” or MH:”paresis” or TW:hemipleg$ or TW:hemipar$ or TW:paresis or TW:paretic)

AND
(MH:”muscle spasticity” or MH:”muscle hypertonia” or MH:”muscle rigidity” or MH:”muscle tonus” or MH:”spasm” or MH: “dystonia” or MH:”paraparesis, spastic” or TW:spastic$ or TW:”high tone” or MH:spasm$ or TW:rigid$ or TW:”tone” or TW:”tonus” or TW:hyperton$ or TW:hypermyoton$ or TW:dyston$ or TW:contracture$)

AND
(MH:”botulinum toxins” or MH:”phenols” or MH:”ethanol” or MH:”injections, intramuscular” or MH:”nerve block” or TW:bo- tulinum$ or TW:”botulin” or TW:”botox” or TW:BoNT$ or TW:BTX$ or TW:”dysport” or TW:”xeomin” or TW:”myobloc” or TW:”neurobloc” or TW:”oculinum” or TW:onabotulinum$ or TW:abobotulinum$ or TW:incobotulinum$ or TW:rimabotulinum$ or TW:”phenol” or TW:”ethanol” or TW:”alcohol” or TW:nerve block$ or TW:”motor point block$ or TW:intramuscular or TW: injection$ or TW:”treatment$ or TW:medication$ or TW:”neurolysis”)

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PEDro
Search completed in advanced search using the abstract and title field using the following terms:
spasticity ethanol spasticity phenol spasticity rimabotulinum* spasticity
incobotulinum* spasticity abobotulinum* spasticity onabotulinum* spasticity
oculinum spasticity neurobloc spasticity myobloc spasticity xeomin spasticity
dysport spasticity BTX*
spasticity BoNT* spasticity botox spasticity botulin spasticity botulinum*
REHABDATA
Botulinum* botulin botox BoNT* BTX* dysport xeomin myobloc neurobloc
oculinum onabotulinum* abobotulinum* incobo- tulinum* rimabotulinum*
phenol ethanol
“nerve block”, “motor point block”, “intramuscular injection”
Appendix 6. Data collection sheets

Rehabilitation Spasticity Study 2011 - Royal Melbourne Hospital
Data Collection Sheets
(For all enquiries please contact Dr Marina Demetrios on (03)38372000)

PART A
RESEARCHER ________________________________
PARTICIPANT CODE ________________________________

DATE OF VISIT _______ _______ _______ _______ _______ _______
DAY MONTH YEAR

GENDER □ Male □ Female

DATE OF BIRTH _______ _______ _______ _______ _______ _______ AGE _______ years
DAY MONTH YEAR

MARITAL STATUS □ Married/partner □ divorced/separated □ single □ widowed
LIVING ARRANGEMENTS □ Alone □ With others □ HLC □ LLC □ Other supported accom
CARERS □ No □ Yes, if Yes what is the type of support: □ family/ friends □ External
YEARS OF EDUCATION □ primary □ secondary □ tertiary □ other_________

COUNTRY OF BIRTH ________________________________ NEED FOR INTERPRETER □ Yes □ No

WAITING TIME TO REHAB AX □ < 3 months □ 3 to 6 months □ 6 to 12 months □ > 12 months

DATE OF STROKE _______ _______ _______ _______ _______ _______ AGE _______ years
DAY MONTH YEAR

DURATION OF SPASTICITY □ < 3 months □ 3 to 6 months □ 6 to 12 months □ > 24 months

SITE OF SPASTICITY □ Upper limb (UL) □ Lower limb (LL) □ Both

AFFECTED SIDE □ Left □ Right
HAND DOMINANCE □ Dominant side affected □ Non-dominant side affected □ Ambidextrous

AETIOLOGY OF STROKE (Tick one box only)
□ Infarct □ Haemorrhage □ Mixed - haemorrhage and infarct

LOCALISATION OF BRAIN LESION (Tick all boxes that apply)
□ MCA □ ACA □ Basal ganglia □ Thalamus □ Posterior circulation / brain stem
**IMPAIRMENTS**

**Category of deficit (mandatory):**

<table>
<thead>
<tr>
<th>Motor</th>
<th>Type (Tick all boxes that apply)</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ NO</td>
<td>☐ Tetraparesis</td>
</tr>
<tr>
<td>☐ YES</td>
<td>☐ Hemiparesis</td>
</tr>
<tr>
<td></td>
<td>☐ Monoparesis UL LL</td>
</tr>
<tr>
<td></td>
<td>☐ Ataxia</td>
</tr>
<tr>
<td></td>
<td>☐ Fatigue</td>
</tr>
<tr>
<td></td>
<td>☐ Other</td>
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</table>

<table>
<thead>
<tr>
<th>Sensory</th>
<th>Somatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ NO</td>
<td>☐ Proprioception</td>
</tr>
<tr>
<td>☐ YES</td>
<td>☐ Dysesthesia</td>
</tr>
<tr>
<td></td>
<td>☐ Other</td>
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<tr>
<th>Restricted joint mobility/contracture</th>
<th>Mild (&lt;1/4 range restricted)</th>
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<tr>
<td>☐ NO</td>
<td>☐ Moderate</td>
</tr>
<tr>
<td>☐ YES</td>
<td>☐ Severe (≥3/4 range restrict)</td>
</tr>
<tr>
<td></td>
<td>☐ Other</td>
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<tr>
<th>Cortical/Perceptual</th>
<th>Inattention/neglect</th>
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<tbody>
<tr>
<td>☐ NO</td>
<td>☐ Visuospatial perceptual</td>
</tr>
<tr>
<td>☐ YES</td>
<td>☐ Dysesthesia</td>
</tr>
<tr>
<td></td>
<td>☐ Other</td>
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<th>Communication</th>
<th>Expressive</th>
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<tr>
<td>☐ NO</td>
<td>☐ Receptive (comprehension)</td>
</tr>
<tr>
<td>☐ YES</td>
<td>☐ Dysarthria</td>
</tr>
<tr>
<td></td>
<td>☐ Cognitive speech</td>
</tr>
<tr>
<td></td>
<td>☐ Other</td>
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<table>
<thead>
<tr>
<th>Cognitive</th>
<th>Orientation</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ NO</td>
<td>☐ Attention/concentration</td>
</tr>
<tr>
<td>☐ YES</td>
<td>☐ Memory</td>
</tr>
<tr>
<td></td>
<td>☐ Inattention</td>
</tr>
<tr>
<td></td>
<td>☐ Executive function eg insight, problem solving</td>
</tr>
<tr>
<td></td>
<td>☐ Other</td>
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<tr>
<th>Emotional</th>
<th>Depression</th>
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<td>☐ Anxiety</td>
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<tr>
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<td>☐ Emotional lability</td>
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<tr>
<td></td>
<td>☐ Pain</td>
</tr>
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<td>☐ Other</td>
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<table>
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<tr>
<th>Visual</th>
<th>Hemianopia</th>
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<tbody>
<tr>
<td>☐ NO</td>
<td>☐ Uncorrectable acuity</td>
</tr>
<tr>
<td>☐ YES</td>
<td>☐ Diplopia</td>
</tr>
<tr>
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<td>☐ Other</td>
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<td>☐ NO</td>
<td>☐ Physical aggression</td>
</tr>
<tr>
<td>☐ YES</td>
<td>☐ Disinhibition</td>
</tr>
<tr>
<td></td>
<td>☐ Other</td>
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**NIH Stroke Scale score 1, 2, 3, 4, 5**

**OTHER CONFOUNDERING FACTORS (Tick all boxes that apply)**

- ☐ Prior surgery of the limb to treat
- ☐ Medical comorbidities likely to impact upon spasticity (eg, chronic pain, UTI)
- ☐ Other active medical comorbidities
- ☐ Non-spastically related pain of the upper/ lower limb to treat
- ☐ Site type
- ☐ Fixed contractures on the upper/ lower limb to treat
- ☐ Site
- ☐ Antagonist over activity
- ☐ Medications
- ☐ Other
UMN PATTERNS

1) Dystonia  □ NO  □ YES
2) Clonus  □ NO  □ YES

ASSOCIATED REACTIONS

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<tr>
<th>Type</th>
<th>When</th>
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<tbody>
<tr>
<td>□ NO</td>
<td>□ When walking</td>
</tr>
<tr>
<td>□ YES (tick all boxes that apply)</td>
<td>□ When standing up</td>
</tr>
<tr>
<td>□ Upper limb flexion</td>
<td>□ Other</td>
</tr>
<tr>
<td>□ Lower limb extension</td>
<td></td>
</tr>
<tr>
<td>□ Other</td>
<td></td>
</tr>
</tbody>
</table>

FALLS HISTORY

'An event, which results in a person coming to rest inadvertently on the ground or other lower level' - World Health Organisation

a) NUMBER OF FALLS in last 6 months ________

b) NUMBER OF FALLS RESULTING IN INJURIES REQUIRING MEDICAL ATTENTION in last 6 months ________

USE OF GAIT AID

□ NO  □ YES  If yes, what type: □ SPS  □ 4PS  □ FAC/AC
□ 4WF  □ 3WF  □ PUP
□ Man W/C  □ Elbow W/C
□ Other ________
TREATMENTS FOR SPASTICITY (OTHER THAN BOTOXINUM TOXIN) (Tick one box per line)

<table>
<thead>
<tr>
<th></th>
<th>Pre existing and stopped</th>
<th>Pre existing and continued</th>
<th>Not pre existing but planned</th>
<th>Not pre existing and not planned</th>
<th>Unknown</th>
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<tbody>
<tr>
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<td>☐</td>
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</tr>
<tr>
<td>Occupational Therapy</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
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</tr>
<tr>
<td>Exercise</td>
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<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
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<tr>
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<td>☐</td>
<td>☐</td>
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<tr>
<td>Casting</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
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<tr>
<td>Electrical Stimulation</td>
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<td>☐</td>
<td>☐</td>
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<td>Acupuncture</td>
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<td>☐</td>
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<tr>
<td>Other alternate therapy</td>
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</table>

For patients currently receiving therapy:

A. THERAPY PROGRAM

<table>
<thead>
<tr>
<th>Type of therapy</th>
<th>Frequency of sessions (No/ wk)</th>
<th>Duration of sessions (mins)</th>
<th>Duration of program? (Wks)</th>
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<tbody>
<tr>
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<tr>
<td>Other _______________</td>
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B. THERAPY SETTING

☐ Public Hospital   ☐ Private hospital    ☐ Private therapist    ☐ CHC    ☐ Other _______
OTHER TREATMENTS FOR SPASTICITY (Tick only one box per line)

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<thead>
<tr>
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<th>Pre existing and continued</th>
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<tbody>
<tr>
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<tr>
<td>Anticonvulsants</td>
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<td>□</td>
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<tr>
<td>Other</td>
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<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
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<tr>
<td>Nerve Blockade</td>
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<td></td>
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<tr>
<td>Phonal</td>
<td>□</td>
<td>□</td>
<td>□</td>
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<td>Ethanol</td>
<td>□</td>
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<td>□</td>
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<td>□</td>
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<td>□</td>
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<tr>
<td>Intrathecal Pump</td>
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<tr>
<td>Baclofen</td>
<td>□</td>
<td>□</td>
<td>□</td>
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<tr>
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<tr>
<td>Neurotomy</td>
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<td>Rhizotomy</td>
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Pharmacological

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose mg/ day</th>
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</thead>
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<tr>
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<tr>
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</tbody>
</table>
BOTULINUM TOXIN A INJECTIONS

1. Is it the first administration of Botulinum Toxin A?
   □ YES  □ NO
   A) If NO, time elapsed since the FIRST injection: ___ ___ Months
   B) If NO, time elapsed since the LAST injection: ___ ___ Months
   C) If NO, give details of previous botulinum toxin injection:

<table>
<thead>
<tr>
<th>DATE</th>
<th>SITE (muscles)</th>
<th>PREPARATION (Dysport/ Botox)</th>
<th>TOTAL DOSE (UNITS)</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
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<tr>
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<td>8</td>
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<td></td>
</tr>
<tr>
<td>9</td>
<td></td>
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</tr>
</tbody>
</table>

Overall injection cycles administered (excluding this one): ___ ___ ___ ___

2. What preparation do you plan to inject today to the patient? (Tick one box only)
   □ Dysport  □ Botox  □ Other ______________  Concentration (units/ 1 mL): ___ ___ ___ ___

3. Initials of injector ____________

Rehabilitation Spasticity Study RMM
<table>
<thead>
<tr>
<th>Upper limb</th>
<th>Muscles</th>
<th>Number of injection points</th>
<th>Number of injected units</th>
<th>Nerve stimulation</th>
<th>EMG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shoulder</td>
<td>Supraspinatus</td>
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<td>1</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Infraspinatus</td>
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<tr>
<td></td>
<td>Teres minor</td>
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<td></td>
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<td>Arm</td>
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<td>Triceps brachii</td>
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<td>Anconeus</td>
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<td>No</td>
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<tr>
<td></td>
<td>Flexor digitorum superf</td>
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<td>No</td>
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<tr>
<td></td>
<td>Flexor carpi radialis</td>
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<td>1</td>
<td>Yes</td>
<td>No</td>
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<td></td>
<td>Flexor carpi ulnare</td>
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<td>Forearm post</td>
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<tr>
<td>Hand</td>
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<td>Opponens pollicis</td>
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<td>Adductor pollicis brevis</td>
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<tr>
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<td>Opponens digit minimi</td>
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<td>Flexor digit minimi</td>
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TOTAL DOSE _______ units

Rehabilitation Spasticity Study RMH
### PLANNED TARGET MUSCLES FOR THIS BOTULINUM TOXIN A INJECTION: LOWER LIMB

<table>
<thead>
<tr>
<th>Lower Limb</th>
<th>Muscles</th>
<th>Number of Injection Points</th>
<th>Number of Injected Units</th>
<th>Nerve Stimulation</th>
<th>EMG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thigh</td>
<td>Adductor brevis</td>
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<tr>
<td></td>
<td>Adductor longus</td>
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<tr>
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<td>Adductor magnus</td>
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<td>Sartorius</td>
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<td>Vastus medialis</td>
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<td>Vastus intermedius</td>
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<td>Leg</td>
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<td>Flexor hallucis longus</td>
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<td></td>
<td>Extensor digitorum longus</td>
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<td>No</td>
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<td>Extensor digitorum brevis</td>
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<td>Flexor digitorum brevis</td>
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<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

**TOTAL DOSE** [units]
PLANNED OUTCOME EVALUATION

RESEARCHER: ____________________________

PARTICIPANT CODE NUMBER: ____________________________

DATE OF VISIT ____________________________

DAY MONTH YEAR

Time interval of current evaluation?

☐ Baseline  ☐ Follow up 1  ☐ Follow up 2

Next review date ____________________________

DAY MONTH YEAR
PART B: OUTCOME MEASURES

A. IMPAIRMENT

a) Spasticity

<table>
<thead>
<tr>
<th>Modified Ashworth Scale Upper Limb</th>
<th></th>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shoulder</td>
<td>0</td>
<td>1</td>
<td>1+</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Elbow flexors</td>
<td>0</td>
<td>1</td>
<td>1+</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Wrist flexors</td>
<td>0</td>
<td>1</td>
<td>1+</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>FDS</td>
<td>0</td>
<td>1</td>
<td>1+</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>FDP</td>
<td>0</td>
<td>1</td>
<td>1+</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>FPL</td>
<td>0</td>
<td>1</td>
<td>1+</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Other thumb</td>
<td>0</td>
<td>1</td>
<td>1+</td>
<td>2</td>
<td>3</td>
<td>4</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Modified Ashworth Scale Lower Limb</th>
<th></th>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
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</thead>
<tbody>
<tr>
<td>Hip</td>
<td>0</td>
<td>1</td>
<td>1+</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Knee extensors</td>
<td>0</td>
<td>1</td>
<td>1+</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Knee flexors</td>
<td>0</td>
<td>1</td>
<td>1+</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Gastrocnemius</td>
<td>0</td>
<td>1</td>
<td>1+</td>
<td>2</td>
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<td>4</td>
</tr>
<tr>
<td>Soleus</td>
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<td>1</td>
<td>1+</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Tibialis post</td>
<td>0</td>
<td>1</td>
<td>1+</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Toes</td>
<td>0</td>
<td>1</td>
<td>1+</td>
<td>2</td>
<td>3</td>
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</table>
### Upper limb

<table>
<thead>
<tr>
<th>Joint</th>
<th>Abduction</th>
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<th>2</th>
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</thead>
<tbody>
<tr>
<td>Shoulder</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Int Rotation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elbow</td>
<td>Flexion</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Extension</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Forearm</td>
<td>Pronation</td>
<td>0</td>
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<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
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<td></td>
<td>Supination</td>
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<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Wrist</td>
<td>Flexion</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Extension</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Finger</td>
<td>Flexion</td>
<td>0</td>
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<td>2</td>
<td>3</td>
<td>4</td>
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<tr>
<td></td>
<td>Extension</td>
<td></td>
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</tr>
<tr>
<td>Thumb</td>
<td>Flexors</td>
<td>0</td>
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<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Extensors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Adductors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Abductors</td>
<td></td>
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</tr>
</tbody>
</table>

### Lower limb

<table>
<thead>
<tr>
<th>Joint</th>
<th>Flexors</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hip</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Extensors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Adductors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Knee</td>
<td>Flexors</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Flexors</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Adductors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ankle</td>
<td>Dorsiflexors</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Plantarflexors</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Invertors</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Evertors</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Toe</td>
<td>Flexors</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Extensors</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>
B. ACTIVITY LIMITATION

a) ArmA (upper limb participants only)

Total Score  |  Section A  |  Section B

b) 10 metre walk test (lower limb participants only)

I. Time: _______ seconds
II. Time: _______ seconds

GAIT AID USED

☐ NO  ☐ YES
If yes, what type:  ☐ SPS  ☐ 4PS  ☐ FAC/AC  ☐ 4WF  ☐ 3WF  ☐ PUD
☐ Other _______
ARM ACTIVITY MEASURE - ARMA

Please indicate who completed this questionnaire.

- Completed by yourself
- Completed by your carer (a family member)
- Completed by your carer (not a family member)
- Completed by yourself and your carer (a family member) together
- Completed by yourself and your carer (not a family member) together
- Completed by yourself with the assistance of another person (not your carer)

This section of the questionnaire asks for general information about you and the person who cares for you.

<table>
<thead>
<tr>
<th>Yourself</th>
<th>The person who cares for you</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age:</td>
<td>Age: Not known</td>
</tr>
<tr>
<td>Gender:</td>
<td>Male</td>
</tr>
<tr>
<td>Male</td>
<td>Female</td>
</tr>
</tbody>
</table>

My neurological medical condition is:

- Stroke
- Traumatic Brain Injury
- Anoxic Brain Injury
- Tumour
- Multiple Sclerosis

Other: [ ]

If other, please state: [ ]

Which arm is affected? [ ] Right [ ] Left [ ] Both

Were you right handed? [ ] Right handed [ ] Left handed [ ] Both

Date of completion: DD MM YY Thank you

Guidance for completion of the ArMA questionnaire:

- Section A asks about "saving" 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 you or your carer experience in doing the activity, based on your activity over the last 7 days. Please estimate if you have not done the activity in the last 7 days.
2. If the task is never done, but this has nothing to do with your arm please score difficulty as 0 – No difficulty.

1. If you are unable to complete the questionnaire independently you may:
   - Receive assistance from a carer or professional to either act as scribe
   - To facilitate understanding and completion question by question.

Rehabilitation Spasticity Study RMH
Section A: Caring for your affected arm (not using it in tasks or activities)

In each column, please CIRCLE as appropriate

<table>
<thead>
<tr>
<th>Activities (affected arm)</th>
<th>Difficulty</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Cleaning palm</td>
<td>0</td>
</tr>
<tr>
<td>Cutting finger nails</td>
<td>0</td>
</tr>
<tr>
<td>Cleaning armpit</td>
<td>0</td>
</tr>
<tr>
<td>Positioning arm on a cushion or support in sitting (if not used circle 0)</td>
<td>0</td>
</tr>
<tr>
<td>Putting arm through a sleeve</td>
<td>0</td>
</tr>
<tr>
<td>Putting on a glove</td>
<td>0</td>
</tr>
<tr>
<td>Put on a splint (if not used circle 0)</td>
<td>0</td>
</tr>
</tbody>
</table>

Section B: Using your affected arm to complete tasks or activities

<table>
<thead>
<tr>
<th>Activities</th>
<th>Difficulty</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Difficulty with balance when walking due to your arm</td>
<td>0</td>
</tr>
<tr>
<td>Hold an object still while using unaffected hand</td>
<td>0</td>
</tr>
<tr>
<td>Open a previously opened jar</td>
<td>0</td>
</tr>
<tr>
<td>Pick up a glass, bottle or can</td>
<td>0</td>
</tr>
<tr>
<td>Drink from cup or mug</td>
<td>0</td>
</tr>
<tr>
<td>Brush your teeth</td>
<td>0</td>
</tr>
<tr>
<td>Tuck in your shirt</td>
<td>0</td>
</tr>
<tr>
<td>Write on paper</td>
<td>0</td>
</tr>
<tr>
<td>Eat with a knife and fork</td>
<td>0</td>
</tr>
<tr>
<td>Dial a number on home phone</td>
<td>0</td>
</tr>
<tr>
<td>Do up buttons on clothing</td>
<td>0</td>
</tr>
<tr>
<td>Comb or brush your hair</td>
<td>0</td>
</tr>
<tr>
<td>Use a key to unlock the door</td>
<td>0</td>
</tr>
</tbody>
</table>

Total Score

Section A

Section B

Totaling Section A and B separately produces a total score for each sub scale of the measure. The sub scales should not be combined.
### C. RESTRICTION IN PARTICIPATION

a) WHOQoL – BREF (patient to complete questionnaires)


This assessment asks how you feel about your quality of life, health, & other areas of your life. Please answer all the questions. If unsure about which response to give to a question, please choose the one that appears most appropriate. This can often be your first response.

We ask that you think about your life in the last two weeks.

Please read each question and assess your feelings, for the last two weeks, and circle the number on the scale for each question that gives the best answer for you.

<table>
<thead>
<tr>
<th>1. How would you rate your quality of life?</th>
<th>Very poor</th>
<th>Poor</th>
<th>Neither Poor nor Good</th>
<th>Good</th>
<th>Very Good</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2. How satisfied are you with your health?</th>
<th>Very dissatisfied</th>
<th>Fairly dissatisfied</th>
<th>Neither satisfied nor dissatisfied</th>
<th>Satisfied</th>
<th>Very Satisfied</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

The following questions ask about how much you have experienced certain things in the last two weeks:

<table>
<thead>
<tr>
<th>3. To what extent do you feel that physical pain prevents you from doing what you need to do?</th>
<th>Not at all</th>
<th>Small amount</th>
<th>Moderate amount</th>
<th>Great deal</th>
<th>Extreme amount</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>4. How much do you need any medical treatment to function in your daily life?</th>
<th>Not at all</th>
<th>Slightly</th>
<th>Moderately</th>
<th>Very</th>
<th>Extremely</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>5. How much do you enjoy life?</th>
<th>Not at all</th>
<th>Slightly</th>
<th>Moderately</th>
<th>Very</th>
<th>Extremely</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>6. To what extent do you feel your life to be meaningful?</th>
<th>Not at all</th>
<th>Slightly</th>
<th>Moderately</th>
<th>Very</th>
<th>Extremely</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>7. How well are you able to concentrate?</th>
<th>Not at all</th>
<th>Slightly</th>
<th>Moderately</th>
<th>Very</th>
<th>Extremely</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>8. How safe do you feel in your daily life?</th>
<th>Not at all</th>
<th>Slightly</th>
<th>Moderately</th>
<th>Very</th>
<th>Extremely</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>9. How healthy is your physical environment?</th>
<th>Not at all</th>
<th>Slightly</th>
<th>Moderately</th>
<th>Very</th>
<th>Extremely</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>
The following questions ask you how good or satisfied you have felt about various aspects of your life over the last two weeks.

<table>
<thead>
<tr>
<th>Question</th>
<th>Not at all</th>
<th>Slightly</th>
<th>Somewhat</th>
<th>A great extent</th>
<th>Completely</th>
</tr>
</thead>
<tbody>
<tr>
<td>10. Do you have enough energy for everyday life?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>11. Are you able to accept your body appearance?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>12. Have you enough money to meet your needs?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>13. How available to you is the information you need in daily life?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>14. To what extent do you have the opportunity for leisure activities?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question</th>
<th>Not at all</th>
<th>Slightly</th>
<th>Moderately</th>
<th>Very</th>
<th>Extremely</th>
</tr>
</thead>
<tbody>
<tr>
<td>15. How well are you able to get around physically?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question</th>
<th>Very dissatisfied</th>
<th>Fairly dissatisfied</th>
<th>Neither satisfied nor dissatisfied</th>
<th>Satisfied</th>
<th>Very satisfied</th>
</tr>
</thead>
<tbody>
<tr>
<td>16. How satisfied are you with your sleep?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>17. How satisfied are you with your ability to perform your daily living activities?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>18. How satisfied are you with your capacity for work?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>19. How satisfied are you with yourself?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>20. How satisfied are you with your personal relationships?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>21. How satisfied are you with your sex life?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>22. How satisfied are you with the support you get from your friends?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Question</td>
<td>Very dissatisfied</td>
<td>Fairly dissatisfied</td>
<td>Neither satisfied nor satisfied</td>
<td>Satisfied</td>
<td>Very satisfied</td>
</tr>
<tr>
<td>-------------------------------------------------------------------------</td>
<td>-------------------</td>
<td>---------------------</td>
<td>--------------------------------</td>
<td>-----------</td>
<td>---------------</td>
</tr>
<tr>
<td>23. How satisfied are you with the conditions of your living place?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>24. How satisfied are you with your access to health services?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>25. How satisfied are you with your transport?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question</th>
<th>Never</th>
<th>Infrequently</th>
<th>Sometimes</th>
<th>Frequently</th>
<th>Always</th>
</tr>
</thead>
<tbody>
<tr>
<td>26. How often do you have negative feeling such as blue mood, despair, anxiety, depression?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

Total score: 130
### D. Patient Centred Outcomes

#### Goal Dimensions

**Primary Goals** (Tick as many as relevant)

<table>
<thead>
<tr>
<th>Goal Dimension</th>
<th>Possible Goals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Passive function</td>
<td>- Hygiene (eg, palm hygiene or nail care)</td>
</tr>
<tr>
<td></td>
<td>- Skin integrity (eg, shoulder or axilla)</td>
</tr>
<tr>
<td></td>
<td>- Dressing</td>
</tr>
<tr>
<td></td>
<td>- Aesthetic</td>
</tr>
<tr>
<td></td>
<td>- Prevention of contracture</td>
</tr>
<tr>
<td></td>
<td>- Sling/orthotic application</td>
</tr>
<tr>
<td></td>
<td>- Other (please specify)</td>
</tr>
<tr>
<td>Active function</td>
<td>- Auxiliary hand</td>
</tr>
<tr>
<td></td>
<td>- Grasp</td>
</tr>
<tr>
<td></td>
<td>- Precise grasp</td>
</tr>
<tr>
<td></td>
<td>- Release</td>
</tr>
<tr>
<td></td>
<td>- Reach</td>
</tr>
<tr>
<td></td>
<td>- Balance (Standing/dynamic)</td>
</tr>
<tr>
<td></td>
<td>- Transfers</td>
</tr>
<tr>
<td></td>
<td>- Walking</td>
</tr>
<tr>
<td></td>
<td>- Sitting posture</td>
</tr>
<tr>
<td></td>
<td>- Other (please specify)</td>
</tr>
<tr>
<td>Pain</td>
<td>- During active movement</td>
</tr>
<tr>
<td></td>
<td>- During passive movement</td>
</tr>
<tr>
<td></td>
<td>- At rest</td>
</tr>
<tr>
<td></td>
<td>- Other (please specify)</td>
</tr>
<tr>
<td>Associated reaction</td>
<td>- When walking</td>
</tr>
<tr>
<td></td>
<td>- When standing up</td>
</tr>
<tr>
<td></td>
<td>- Other (please specify)</td>
</tr>
<tr>
<td>Impairment</td>
<td>- Range of movement</td>
</tr>
<tr>
<td></td>
<td>- Other (please specify)</td>
</tr>
<tr>
<td>Other</td>
<td>- Other (please specify)</td>
</tr>
</tbody>
</table>
a) Goal Attainment Scaling

Identify 3 goals prior to injections and commencement of therapy.

<table>
<thead>
<tr>
<th>Goal Attainment Level</th>
<th>Score</th>
<th>GOAL 1</th>
<th>GOAL 2</th>
<th>GOAL 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Best anticipated outcome</td>
<td>+2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>More than expected outcome</td>
<td>+1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Expected outcome</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than expected outcome</td>
<td>-1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unfavourable outcome</td>
<td>-2</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Level at Intake

Level at Follow Up
Circle visit:
6, 12 or 24 wks
Importance
Difficulty
b) Global Assessment Scale (patient satisfaction)

**Aim:** patient or caregiver to assess benefit/improvement from treatment (please circle)

+4 = very marked improvement  
+3 =  
+2 =  
+1 =  
0 = no change  
-1 =  
-2 =  
-3 =  
-4 = very marked worsening

E. CARER BURDEN

a) Self rated burden (SRB) (enlarged version on page 29)

On the scale below ‘0’ means that you feel that caring for or accompanying ……. at the moment is not hard at all; ‘100’ means that you feel that caring for or accompanying ……. at the moment is much too hard. Please indicate with an ‘x’ on the scale how burdensome you feel caring for or accompanying your partner is at the moment.

<table>
<thead>
<tr>
<th>Not at all trying</th>
<th>Much too straining</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>1</td>
<td>20</td>
</tr>
<tr>
<td>2</td>
<td>30</td>
</tr>
<tr>
<td>3</td>
<td>40</td>
</tr>
<tr>
<td>4</td>
<td>50</td>
</tr>
<tr>
<td>5</td>
<td>60</td>
</tr>
<tr>
<td>6</td>
<td>70</td>
</tr>
<tr>
<td>7</td>
<td>80</td>
</tr>
<tr>
<td>8</td>
<td>90</td>
</tr>
<tr>
<td>9</td>
<td>100</td>
</tr>
</tbody>
</table>

F. SAFETY AND ADVERSE EFFECTS

To be recorded at follow up visits.

a) Reactions following injection

☐ Localised pain  ☐ Localised skin reaction  ☐ Flu like symptoms

☐ Weakness  Site: ☐ injected limb  ☐ Generalised  ☐ Contralateral limbs

☐ Other __________________________

b) Recent illnesses

☐ NO  ☐ YES  If YES, specify diagnosis __________________________

Hospitalisation required ☐ NO  ☐ YES

If YES, LOS _______ days

c) Change in medications since last assessment

☐ NO  ☐ YES  Commenced new medication (name/dose) __________________________

Ceased previous medication (name/dose) __________________________

d) Falls

Number of falls (since last assessment) __________________________

Number of falls causing injuries needing medical attention __________________________
e) Change in gait aid

☐ NO  ☐ YES  If yes, what type: ☐ SPS  ☐ 4PS  ☐ FAC/AC
☐ 4WF  ☐ 3WF  ☐ PUF
☐ Man W/C  ☐ Elec W/C  ☐ None
☐ Other ____________________

f) Other issues

________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
Self rated burden (SRB)

On the scale below ‘0’ means that you feel that caring for or accompanying …….. at the moment is not hard at all; ‘100’ means that you feel that caring for or accompanying …….. at the moment is much too hard. Please indicate with an ‘X’ on the scale how burdensome you feel caring for or accompanying your partner is at the moment.

Not at all straining       Much too straining

0  10  20  30  40  50  60  70  80  90  100
Appendix 7. Characteristics of excluded studies (ordered by study author)

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barchich 2008</td>
<td>Intervention not multidisciplinary (electrical stimulation, stretching or taping)</td>
</tr>
<tr>
<td>Bayram 2006</td>
<td>Intervention not multidisciplinary (short-term electrical stimulation)</td>
</tr>
<tr>
<td>Borg 2011</td>
<td>Comparator BoNT-A versus placebo, rehabilitation program (standard care) in both groups</td>
</tr>
<tr>
<td>Carda 2011</td>
<td>Intervention not multidisciplinary (casting, stretching or taping)</td>
</tr>
<tr>
<td>Childers 2004</td>
<td>Comparator 3 doses of BoNT-A, splinting and physical therapy in both groups</td>
</tr>
<tr>
<td>Clark 2011</td>
<td>Comparator BoNT-A versus placebo, upper limb rehabilitation program in both groups</td>
</tr>
<tr>
<td>Clarke 2003</td>
<td>Intervention not multidisciplinary (Functional electrical stimulation)</td>
</tr>
<tr>
<td>Cui 2006</td>
<td>Comparator BoNT-A + rehabilitation therapy versus rehabilitation therapy</td>
</tr>
<tr>
<td>Duarte 2011</td>
<td>Intervention not multidisciplinary (electrical stimulation)</td>
</tr>
<tr>
<td>Farina 2008</td>
<td>Intervention not multidisciplinary (casting)</td>
</tr>
<tr>
<td>Guo 2006</td>
<td>Comparator BoNT-A versus placebo, rehabilitation program in both groups</td>
</tr>
<tr>
<td>Hesse 1995</td>
<td>Intervention not multidisciplinary (short-term electrical stimulation)</td>
</tr>
<tr>
<td>Hesse 1998</td>
<td>Intervention not multidisciplinary (physiotherapy only with short-term electrical stimulation)</td>
</tr>
<tr>
<td>Johnson 2004</td>
<td>Intervention not multidisciplinary (physiotherapy only with electrical stimulation)</td>
</tr>
<tr>
<td>Karadag-Saygi 2010</td>
<td>Intervention not multidisciplinary (kinesiotaping versus sham taping)</td>
</tr>
<tr>
<td>Kent 2006</td>
<td>Intervention not multidisciplinary (physiotherapy only and resting splint/orthotic)</td>
</tr>
<tr>
<td>Lagalla 1997</td>
<td>Intervention not multidisciplinary (forearm splint)</td>
</tr>
<tr>
<td>Marco 2007</td>
<td>Comparator BoNT-A versus placebo, inpatient rehabilitation program and transcutaneous electrical nerve stimulation in both groups</td>
</tr>
<tr>
<td>Reference</td>
<td>Description</td>
</tr>
<tr>
<td>-----------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Mawson 2007</td>
<td>Intervention not multidisciplinary (BoNT-A + physiotherapy versus BoNT-A + stretching advice versus placebo + physiotherapy)</td>
</tr>
<tr>
<td>McCrory 2009</td>
<td>Comparator BoNT-A versus placebo, physiotherapy and occupational therapy as per ‘routine practice’ in both groups</td>
</tr>
<tr>
<td>Meythaler 2009</td>
<td>Comparator BoNT-A versus placebo, occupational therapy program both groups</td>
</tr>
<tr>
<td>Pieber 2011</td>
<td>Intervention not multidisciplinary (functional electrical stimulation only), participants were children with mixed neurological diagnoses</td>
</tr>
<tr>
<td>Pisano 2002</td>
<td>Intervention not multidisciplinary (physiotherapy only with short-term electrical stimulation)</td>
</tr>
<tr>
<td>Reiter 1998</td>
<td>Intervention not multidisciplinary (ankle taping)</td>
</tr>
<tr>
<td>Shaw 2011</td>
<td>Comparator BoNT-A versus placebo, upper limb therapy program in both groups</td>
</tr>
<tr>
<td>Sheikh 2006</td>
<td>Comparator BoNT-A versus placebo, neurodevelopmental therapy program in both groups</td>
</tr>
<tr>
<td>Sisto 2001</td>
<td>Intervention not multidisciplinary (acupressure)</td>
</tr>
<tr>
<td>Van Wijck 2006</td>
<td>Intervention not multidisciplinary (task specific therapy program was physiotherapy only)</td>
</tr>
<tr>
<td>Werner 2011</td>
<td>Comparator BoNT-A versus placebo, inpatient rehabilitation program in both groups</td>
</tr>
<tr>
<td>Wolf 2007</td>
<td>Comparator BoNT-A versus placebo, rehabilitation program (modalities, repetitive task practice, strengthening and functional activities) in both groups</td>
</tr>
</tbody>
</table>

BoNT-A: botulinum toxin type A

Note: for references please see attached publication in Appendix 1: Demetrios M, Khan F, Turner-Stokes L, Brand C, McSweeney S. Multidisciplinary rehabilitation following botulinum toxin and other focal intramuscular treatment for post-stroke spasticity. Cochrane Database of Systematic Reviews 2013, Issue 6. Art. No.: CD009689. DOI: 10.1002/14651858.CD009689.pub2. References to studies excluded from this review (page 17).