Increasing the Amount of Practice Improves Upper Limb Activity in Adults After Stroke

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List of abbreviations

AUC	Area under the curve
CI	Confidence interval
COM-B	Capability, Opportunity, Motivation-Behaviour Model
GRASP	Graded Repetitive Supplementary Arm Program
ICF	International Classification of Functioning, Disability and Health
IQR	Interquartile range
kg	Kilogram
LL	Lower limb
n	Number
N	No
m	Metre
Med	Median
Min	Minute
MMSE	Mini-Mental Status Examination
PEDro	Physiotherapy Evidence Database
Q-RCT	Quasi-randomised clinical trial
RCT	Randomised clinical trial
RCS	Rehabilitation Complexity Scale
Reps	Repetitions
ROC	Receiver operating characteristic
s	Second
SD	Standard deviation
SMD	Standardised mean difference
TIDieR	Template for Intervention Description and Replication
TMS	Transcranial magnetic stimulation
UL	Upper limb
wk	Week
Y	Yes
yr	Year

Abstract

Background: A large amount of task-specific practice is essential for motor learning yet it remains unknown how much extra practice is needed to improve outcome over usual care in terms of upper limb activity for adults after stroke.

Aims: To determine the amount of practice required to improve upper limb outcome and how to best measure upper limb activity, and to investigate the potential of two methods whereby inpatient rehabilitation services could deliver this extra practice to adults after stroke.

Method: Four interrelated studies were conducted using a range of research methods. A systematic review with meta-analysis examined the effect of an increase in the amount of usual rehabilitation on upper limb activity (Study 1). A psychometric study was conducted to determine the clinical utility of two common tests of upper limb activity (Study 2). A pre-post study was conducted to investigate the potential of a professional development program to increase the intensity of practice (Study 3). Finally, another pre-post study was conducted to investigate the feasibility of a semi-supervised upper limb program to increase the duration of practice (Study 4).

Results: Study 1 included 14 studies, comprising 15 comparisons, and found that at least an extra 240% of rehabilitation was needed for significant likelihood that extra rehabilitation would improve activity above that of usual care. Study 2 found that while both the Box and Block and Nine-Hole Peg Tests measure upper limb activity in adults after stroke, the Nine-Hole Peg Test may be a more accurate reflection of the upper limb activity required in everyday life. Study 3 found that a professional development program was associated with an increased intensity of practice during an inpatient, upper limb rehabilitation class. And finally, Study 4 found that it is feasible to use a semi-supervised upper limb program to increase the duration of practice in an inpatient rehabilitation service.

Conclusion: More than tripling the amount of usual rehabilitation improves outcome over usual care in adults after stroke. Methods for inpatient rehabilitation services to increase the amount of practice above the usual amount of practice through increasing the intensity and duration of practice appear to be promising.

Statement of authorship

Except where reference is made in the text of the thesis, this thesis contains no material published elsewhere or extracted in whole or in part from a thesis accepted for the award of any other degree or diploma. No other person's work has been used without due acknowledgement in the main text of the thesis. This thesis has not been submitted for the award of any degree or diploma in any other tertiary institution.

Emma Schneider is the sole author of Chapter 1 (Introduction), Chapter 2 (Background), and Chapter 7 (Discussion). The remaining chapters (listed in Dissemination of Findings) are multi-authored publications on which Emma Schneider was the lead author and completed the majority of the work. The conception, design and management of studies; data collection and analysis; writing and subsequent revisions of publications; as well as response to journal peer-review was led by the PhD candidate. Co-authors provided advice and/or assistance with study planning, design and revision of the final draft of publications. Publication permissions are provided in Appendix A.

All research procedures reported in this thesis were approved by relevant Ethics Committees prior to the commencement of each study. Copies of ethics approvals are provided in Appendix B. Copies of study registrations are provided in Appendix C.

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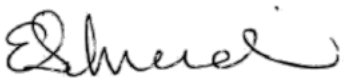
Signature: 

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Dissemination of findings

Peer-reviewed publications

Schneider EJ, Ada L, White M, English C, Crotty M, Lannin NA (under review). Clinical utility of the Box and Block Test and the Nine-Hole Peg Test in adults after stroke. *Brazilian Journal of Physical Therapy*.

Schneider EJ, Lannin NA, Ada L (2014). Increasing the intensity of rehabilitation to improve activity after stroke: a systematic review protocol. *Journal of Clinical Trials* 4:195. doi: 10.4172/2167-0870.1000195

Schneider EJ, Lannin NA, Ada L, Schmidt J (2016). Increasing the amount of usual rehabilitation improves activity after stroke: a systematic review. *Journal of Physiotherapy, 62(4):182-187.* doi: 10.1016/j.jphys.2016.08.006

Schneider EJ, Lannin NA, Ada L (2019). A professional development program increased the intensity of practice undertaken in an inpatient, upper limb rehabilitation class: a pre-post study. *Australian Occupational Therapy Journal*, 66 (3):362-368. doi: 10.1111/1440-1630.12562

Schneider EJ, Ada L, Lannin NA (2019). Extra upper limb practice after stroke: a feasibility study. *Pilot and Feasibility Studies*, 5,156. doi: 10.1186/s40814-019-0531-5

Published abstracts

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Schneider EJ, Lannin NA, Ada L, Schmidt J (2017). A systematic review of providing extra rehabilitation on top of usual rehabilitation to improve activity after stroke. *International Journal of Stroke, 12 (Suppl.2): 3-31.*

Schneider EJ, Lannin NA, Ada L (2017). Feasibility and benefit of providing extra upper limb practice during inpatient rehabilitation after stroke. *Australian Occupational Therapy Journal, 64 (Suppl.2): 5-31.*

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Oral conference presentations

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Schneider EJ, Lannin NA, Ada L, Schmidt J (2014). Increasing the intensity of rehabilitation for improved activity after stroke: A systematic review. *Oral presentation at the World Federation of Occupational Therapy Conference, 18-21st June 2014, Yokahama, Japan.*

Schneider EJ, Lannin NA, Ada L (2015). Does attending a motor training workshop improve the quality and amount of upper limb practice provided in neurorehabilitation? O*ral presentation at the Occupational Therapy National Conference, July 2015, Melbourne.*

Schneider EJ, Lannin NA, Ada L (2017). Feasibility and benefit of providing extra upper limb practice during inpatient rehabilitation after stroke. *Oral presentation at the Occupational Therapy National Conference, 19-21st July 2017, Perth.*

Schneider EJ, Lannin NA, Ada L, Schmidt J (2017). A systematic review of providing extra rehabilitation on top of usual rehabilitation to improve activity after stroke. *Oral presentation at the Smart Strokes Conference, 10-11th August 2017, Surfers Paradise.*

Schneider EJ, Lannin NA, Ada L (2018). Feasibility of extra semi-supervised upper limb practice in adults after stroke. *Oral presentation at the SSA/ Smart Strokes Conference, 8-10th August 2087, Sydney.*

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Chapter 1: Introduction

Stroke is the third most common cause of death and the leading cause of adult disability worldwide (Langhammer et al., 2015; Medis, 2013; World Health Organization, 2018). While there has been a decline in stroke death rate over the past decade, there has been a significant increase in overall disease burden (World Health Organization, 2018). From 2000 to 2016, stroke has moved from the sixth to the second leading cause of disability-adjusted life years lost globally, i.e., more people survive stroke but live with complex disability (Australian Bureau of Statistics, 2017; World Health Organization, 2018). One of the most common limitations after stroke is the loss of upper limb activity, with up to 66% of adults after stroke unable to use their arm in the same way as prior to their stroke (Andrenelli et al., 2015; Medis, 2013). In Australia, just over one-third of adults after stroke experience the inability to engage in activities (activity limitations) from their stroke, of whom 55% are left profoundly limited in core daily activities such as toileting, dressing, and eating (Australian Institute of Health and Welfare, 2013).

These activity limitations are as a result of changes to body structures and functions caused by damage to the motor cortex at the time of stroke (Sacco et al., 2013). When a stroke occurs the blood supply to the brain is either blocked (ischaemic stroke) or ruptured (haemorrhagic stroke), the oxygen supply to the brain is disrupted and brain tissue dies (Sacco et al., 2013). It is the death of brain tissue within the motor cortex (Sacco et al., 2013) that prevents the generation of neural impulses, and ultimately leads to motor impairments and activity limitations (Nudo, 2014). Motor impairment is a loss or limitation of muscle strength and control and is the most common and widely recognised impairment caused by stroke (Langhorne, Coupar, & Pollock, 2009; Yu, Prado, Quinlan, Cramer, & Ombao, 2016). A loss of control of the face, arm, or leg of one side of the body are common motor impairments that can affect up to 80% of adults after stroke (Hendricks, van Limbeek, Geurts, & Zwarts, 2002). This motor impairment leads to activity limitations and the inability to engage in activities (Geyh et al., 2004; Hendricks et al., 2002) (Figure 1.1). Because of upper limb motor impairments, limitations in activities of daily living (showering, dressing, toileting, eating, drinking), and restrictions in participation in household tasks (cooking, cleaning), community life (shopping, driving, leisure), and other major life areas (education, employment) often arise (Geyh et al., 2004; World Health Organization, 2001).

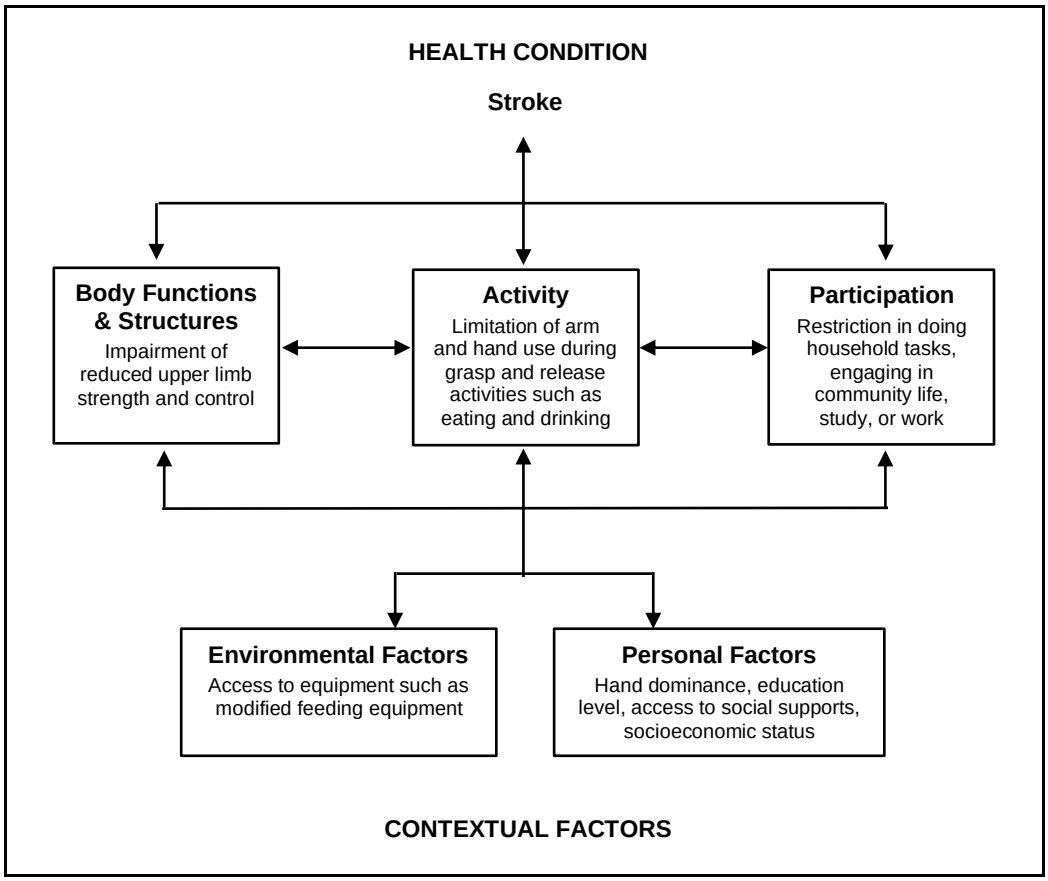


Figure 1.1. *The International Classification of Functioning, Disability and Health (ICF) (World Health Organization, 2001), as applied to the upper limb after stroke.*

While up to 80% of adults after stroke are left with impairments that affect their upper limb activity and participation (Hendricks et al., 2002), some recovery does occur after stroke. A small amount of damage is thought to be reversible through spontaneous neurological recovery (Cassidy & Cramer, 2017; Paciaroni, Caso, & Agnelli, 2009; Teasell, 2012; Wieloch & Nikolich, 2006). But neurological reorganisation is required to compensate for permanent damage (Cassidy & Cramer, 2017; Nilsson, Pekny, & Pekny, 2012; Wieloch & Nikolich, 2006). This neurological reorganisation, or brain plasticity, demonstrates the capacity of the brain to generate new or more refined motor skill (Winstein, Lewthwaite, Blanton, Wolf, & Wishart, 2014) in response to tailored practice (Birkenmeier, Prager, & Lang, 2010; Langhorne et al., 2009; Nilsson et al., 2012).

Motor learning theory suggests that activities are re-learned through repetitive practice (Carr & Shepherd, 1989; Hendricks et al., 2002), with research indicating that a large amount of task-specific practice is needed to produce a benefit (Langhorne, Wagenaar, & Partridge, 1996). Motor learning is thought to occur if the practice is goal-oriented, task-

specific (Plautz, Milliken, & Nudo, 2000), and challenging (Birkenmeier et al., 2010; Langhorne et al., 2009). The type (DeKeyser, 2014; Hayward, Barker, Carson, & Brauer, 2014) and amount (Carr & Shepherd, 2010; McCluskey, Lannin, & Schurr, 2009) of practice likely influences motor learning and therefore the outcome of upper limb activity for adults after stroke (Veerbeek et al., 2014). Rehabilitation programs designed to address upper limb activity limitations, therefore, should be structured to provide repetitive practice of specific upper limb tasks that are challenging, progressive and skill-based (Lohse, Lang, & Boyd, 2014; Stroke Foundation, 2010).

While researchers have concluded that a large amount of practice is essential for motor learning (Carr & Shepherd, 1989; Lohse et al., 2014; Veerbeek, Koolstra, Ket, van Wegen, & Kwakkel, 2011; Veerbeek et al., 2014), the actual amount of practice needed to achieve best outcome remains unknown, causing guidelines to recommend the amount of practice during stroke rehabilitation to be 'as much practice as possible' (Canadian Stroke Network, 2013; Scottish Intercollegiate Guidelines Network, 2010; Stroke Foundation, 2010). This thesis is concerned with the amount of extra practice provided in inpatient rehabilitation programs designed to achieve an improved outcome of upper limb activity over that achieved by usual practice in adults after stroke. In this thesis, I define an increase in the amount of practice as adding extra practice of the same content as usual practice, where usual practice aims to reduce activity limitations of the upper limb after stroke.

Recovery of upper limb activity after stroke is often poor (Dean & Mackey, 1992); and adults after stroke perceive that their time spent in upper limb rehabilitation was not sufficient (Barker & Brauer, 2005). Given the time-sensitive nature of neural plasticity and motor learning (Cassidy & Cramer, 2017; Cramer et al., 2011; Nudo, 2014; Teasell, 2012), the amount of practice provided in the shortest number of days during rehabilitation may be most beneficial. While there is evidence that more practice is needed (Cooke, Mares, Clark, Tallis, & Pomeroy, 2010; Kwakkel, van Peppen, et al., 2004; Langhorne et al., 1996; Lohse et al., 2014; Veerbeek et al., 2011; Veerbeek et al., 2014), it remains unknown *how much* extra practice on top of usual practice is needed to guarantee an improvement in outcome of upper limb activity for adults after stroke.

There are two key aspects of *amount* of practice: the *intensity* and *duration*. The *intensity* of practice refers to the amount of practice undertaken within a set time, i.e., the number

of repetitions completed within a rehabilitation session. The *duration* of practice refers to the amount of practice time across the day or week, i.e., the duration of a rehabilitation session. There are, therefore, two methods to increase the amount of practice provided in rehabilitation. First, to increase the *intensity* of practice undertaken within the usual rehabilitation session by increasing the number of repetitions within the session (English, Bernhardt, & Hillier, 2014). Second, to increase the *duration* of practice time by providing an additional opportunity for practice over the day or week. Both aspects can be used to increase the amount of usual practice provided in rehabilitation.

The studies that comprise this thesis were planned in 2014 and were conducted over the past six years. Hence, review of the evidence (Chapter 2) incorporates research up to the end of 2014. At this time, there was general agreement that a dose-response relationship for motor learning exists, where the greater the amount of practice, the greater the benefit to activities of daily living, walking ability and walking speed (Cooke, Mares, et al., 2010; Kwakkel, van Peppen, et al., 2004; Langhorne et al., 1996; Lohse et al., 2014; Veerbeek et al., 2011; Veerbeek et al., 2014). However, no studies had determined *how much* extra practice on top of usual practice is needed to guarantee improved outcome of upper limb activity for adults after stroke. Therefore, a systematic review was planned to address this research question (Study 1).

Researchers and clinicians need to know the relationship between upper limb activity in real life and scores on common, standardised tests of upper limb activity (Alt Murphy, Resteghini, Feys, & Lamers, 2015; Smart, 2006) to ensure that the amount of practice targets real recovery rather than compensation (Connell & Tyson, 2012). Two common, standardised tests of upper limb activity are the Box and Block Test (Mathiowetz, Volland, Kashman, & Weber, 1985) and the Nine-Hole Peg Test (Mathiowetz, Weber, Kashman, & Volland, 1985). However, no studies have determined if performance on the Box and Block Test (Mathiowetz, Volland et al., 1985) or the Nine-Hole Peg Test (Mathiowetz, Weber et al., 1985) relates to real life upper limb use. Therefore, a measurement study with psychometric analysis was planned to address this research question (Study 2).

Rehabilitation programs for adults after stroke struggle to deliver the guideline-recommended amount of practice (Grimshaw, Eccles, Lavis, Hill, & Squires, 2012; Stroke Foundation, 2014) or they fail to deliver sufficient amounts of practice for motor

learning to occur (Bernhardt, Dewey, Thrift, & Donnan, 2004; Janssen et al., 2014; Kaur, English, & Hillier, 2013; King, McCluskey, & Schurr, 2011). While studies have investigated the use of professional development programs to increase staff adherence to guideline recommendations (e.g. Cusick & McCluskey, 2000; French et al., 2012; Michie et al., 2005), no studies had investigated the use of a professional development program to specifically increase the amount of upper limb practice within an inpatient clinical population. Therefore, a pre-post study of the potential benefit of training clinicians was designed to address this research question (Study 3).

Furthermore, research has consistently shown that many of the opportunities for practice occur during time with a therapist (Ada, Mackey, Heard, & Adams, 1999; Skarin et al., 2013). Most studies of extra practice to date have delivered the extra practice in one-on-one sessions outside the usual rehabilitation service (Burgar et al., 2011; Cooke, Tallis, Clark, & Pomeroy, 2010; Donaldson et al., 2009; GAPS, 2004; Han, Wang, Meng, & Qi, 2013; Kim, Cho, & Lee, 2014; Kwakkel, Wagenaar, Twisk, Lankhorst, & Koetsier, 1999a; Lincoln, Parry, & Vass, 1999; Partridge et al., 2000; Rodgers et al., 2003; Ross, Harvey, & Lannin, 2009) despite this being a resource intensive way to increase the amount of practice (Aprile et al., 2011; Trahey, 1991). What remains unknown is how to deliver the extra practice while considering staff and resource constraints. Therefore, a pre-post study of the feasibility of using two self-directed upper limb programs as a way of increasing the amount of practice during an inpatient phase of stroke rehabilitation was planned to address this research gap (Study 4).

Consequently, the research reported in this thesis furthers the understanding of the amount of extra practice required to improve upper limb activity above usual, how to best measure upper limb activity, and presents two methods by which inpatient rehabilitation services could deliver this extra practice to adults after stroke. The results of these studies have significant implications for the delivery of stroke rehabilitation given the growing burden of stroke disability and the benefit of providing rehabilitation with improved efficiency (Jackson, McCrone, Mosweu, Siegert, & Turner-Stokes, 2014; Slade, Tennant, & Chamberlain, 2002).

To set the scene for the four studies reported in this thesis, research pertaining to the significant role that amount of practice plays during the reorganisation of neural networks and motor learning in retraining upper limb activity in adults after stroke is

summarised in Chapter 2. Furthermore, the two key aspects of amount of practice (*intensity* and *duration*) will be reviewed. Finally, the measurement of the amount of practice and the outcome of practice on upper limb activity will be summarised.

Chapter 2: Background

Neural reorganisation and motor learning form the basis for neurological rehabilitation (Winstein et al., 2014). Through the application of evidence to practice, neurological rehabilitation broadly aims to reduce impairment, drive recovery of activity, and ultimately improve participation and quality of life for adults after stroke (Langhorne et al., 2009; McCluskey et al., 2009; Winstein et al., 2014). Effective interventions for the recovery of activity after stroke are based on pre-clinical (i.e., animal) (Nudo, Wise, SiFuentes, & Milliken, 1996) and clinical (i.e., human) (Taub & Uswatte, 2003) studies about motor learning and the activation of practice-dependent neuronal plasticity (Birkenmeier et al., 2010). Recovery of upper limb activity after stroke has been shown to be dependent on both reorganisation of neural networks (Winstein et al., 2014) and motor learning (Birkenmeier et al., 2010; Carr & Shepherd, 2010; Langhorne et al., 2009; Nilsson et al., 2012). Despite evidence of effective interventions (Barreca, Sigouin, Lambert, & Ansley, 2004; Hubbard, Parsons, Neilson, & Carey, 2009; Stroke Foundation, 2014), upper limb recovery for adults after stroke often remains poor (Kwakkel, Kollen, van der Grond, & Prevo, 2003; Nakayama, Jorgensen, Raaschou, & Olsen, 1994). Challenges remain to integrate the principles of motor learning into clinical practice. While the focus of this thesis is on the amount of extra practice designed to guarantee an improved outcome of upper limb activity for adults after stroke, the way the brain may recover after stroke must first be reviewed. So as to highlight the importance of how the *amount of practice* is an integral factor for neural reorganisation and motor learning, the research pertaining to the key concepts will be summarised.

REORGANISATION OF NEURAL NETWORKS AND MOTOR LEARNING

Neurological recovery is considered to have occurred when neurological impairments (Cassidy & Cramer, 2017; Wieloch & Nikolich, 2006) have resolved after stroke. Recovery involves either spontaneous neurological recovery (Paciaroni et al., 2009), or specialised practice of a specific task to generate a neurological response (Nilsson et al., 2012; Nudo, 2014; Wieloch & Nikolich, 2006).

Spontaneous neurological recovery occurs during the immediate hours following a stroke when blood flow returns to the area of brain tissue surrounding the stroke site (Paciaroni et al., 2009; Teasell, 2012; Wieloch & Nikolich, 2006). This non-ischaemic area of brain

tissue surrounding the stroke site consists of the brain tissue that survived the primary stroke, known as the penumbra (Wieloch & Nikolich, 2006). The spontaneous cell regeneration and general recovery from oedema and inflammation that occur in the days to weeks following stroke are often incomplete (Cassidy & Cramer, 2017; Paciaroni et al., 2009; Teasell, 2012). Without targeted rehabilitation, the remaining motor impairments lead to activity limitations and participation restrictions (Alia et al., 2017).

A neurological response involves the initiation of brain repair by changing the properties of existing neuronal pathways and modifying brain structure leading to the formation of new neuronal connections (Wieloch & Nikolich, 2006). These processes of establishing and consolidating existing and new neural networks are known as neurological reorganisation or neural plasticity (Birkenmeier et al., 2010; Cramer et al., 2011; Nudo, 2014; Nudo et al., 1996; Plautz et al., 2000; Wieloch & Nikolich, 2006). Neural pathways in the brain are established in response to the repetitive practice of a task-specific movement (Birkenmeier et al., 2010; Langhorne et al., 2009; Nilsson et al., 2012; Wieloch & Nikolich, 2006). This specialised learning of new movement generates increased recruitment of neurons and the creation of neural pathways in the surrounding areas (Teasell, Bayona, & Bitensky, 2005). The more a movement is repeated, the more defined the neural pathway becomes (Nudo, 2014; Wieloch & Nikolich, 2006; Winstein et al., 2014), and the larger the amount of brain tissue in the brain dedicated to controlling this activity (Cramer et al., 2011; Nudo, 2014). This theory of plasticity, or the ability for the brain to change over time, forms the basis of neurological recovery after stroke.

The most convincing evidence for plasticity is the observation of brain reorganisation demonstrated in the homunculus (Cicinelli et al., 2003; Cicinelli, Traversa, & Rossini, 1997; Harrison, Silasi, Boyd, & Murphy, 2013; Liepert et al., 1998; Nudo et al., 1996; Traversa, Cicinelli, Bassi, Rossini, & Bernardi, 1997), an area within the primary motor cortex that represents every part of the human body. Within the homunculus, areas of the brain evoking similar body parts cluster together to form a topographical representation of body parts where the amount of cortex dedicated to each body part is dependent on the amount of motor control the brain has over that part (Nilsson et al., 2012; Nudo, 2014). Topographical reorganisation of the homunculus in response to targeted practice has been observed in both pre-clinical (animal) (Harrison et al., 2013; Nudo et al., 1996; Plautz et al., 2000) and clinical (human) models (Cicinelli et al., 1997; Liepert et al.,

1998; Traversa et al., 1997) after stroke and is known to represent change in motor control (Nudo, 2014), e.g., an improved ability to pick up a piece of food after targeted training. This is because the information generated in the primary motor cortex by the homunculus is sent to the rest of the body via the corticospinal tract (Nudo, 2014), the only direct pathway from the brain to the spinal cord and the main pathway for voluntary movement in humans (Nudo, 2014; Stinear et al., 2007).

Plasticity for motor learning and re-learning following stroke is influenced by several factors (Cassidy & Cramer, 2017; Cramer et al., 2011; Lindenberg et al., 2010; Nudo, 2014; Plautz et al., 2000; Riley et al., 2011; Teasell et al., 2005). Neural plasticity is dependent on the location and extent of the damage (Cramer et al., 2011; Lindenberg et al., 2010; Riley et al., 2011; Teasell et al., 2005), the specific activity, the challenge of the activity to force new learning to occur (Nudo, 2014; Plautz et al., 2000), time since stroke (Cassidy & Cramer, 2017), and features of the environment (Cramer et al., 2011). For example, in response to complex activity-specific learning, significant long-term changes in neuronal plasticity are seen in the primary motor cortex, whereas changes in the prefrontal cortex disappear after only a few days (Comeau, McDonald, & Kolb, 2010; Kolb, Gorny, Soderpalm, & Robinson, 2003). While most neurological reorganisation is thought to occur in the first three months after stroke, it has been shown to continue at a much slower rate for months or even years after stroke (Cassidy & Cramer, 2017; Cramer et al., 2011; Nudo, 2014; Teasell, 2012).

Neurological reorganisation can occur over an extended period of time after stroke (Cassidy & Cramer, 2017; Cramer et al., 2011; Nudo, 2014; Teasell, 2012), however, neural plasticity may occur at a greater rate early after stroke (Wolf et al., 2006). Longitudinal studies (Kwakkel, Kollen, & Lindeman, 2004; Kwakkel, Kollen, & Wagenaar, 2002; Parker, Wade, & Langton Hewer, 1986; Wade, Wood, & Hewer, 1985) and studies designed to measure the outcome of motor learning on activity (Bonita & Beaglehole, 1988; Duncan, Goldstein, Matchar, Divine, & Feussner, 1992; Heller et al., 1987; Parker et al., 1986; Rathore, Hinn, Cooper, Tyroler, & Rosamond, 2002; Skilbeck, Wade, Hewer, & Wood, 1983) have found that the majority of recovery experienced by adults after stroke occurs in the first six months. So while the opportunity for ongoing recovery can continue for months and even years after stroke (Dam et al., 1993; Pereira et al., 2012) best upper limb outcome is achieved by 95% of adults after stroke within nine weeks of stroke onset (Nakayama et al., 1994). Fewer than 20% of adults after

stroke experience sufficient motor recovery for a completely useful upper limb activity (Kwakkel et al., 2003; Nakayama et al., 1994). Therefore, there is a need for motor recovery to be driven *early* after stroke (Nudo, 2014) to achieve best outcomes for adults after stroke. As neurological reorganisation and motor recovery occur in response to learning new or lost movements, the concept of motor learning is central to neural plasticity (Birkenmeier et al., 2010; Langhorne et al., 2009; Nudo, 2014; Wieloch & Nikolich, 2006). This thesis focuses on the early, inpatient phase of rehabilitation because neural plasticity (Wolf et al., 2006) and motor recovery (Nudo, 2014) must be addressed early after stroke to achieve best outcomes for adults after stroke.

Motor Learning

Learning is the acquisition of knowledge or skill through study, instruction, or experience ("Learning definition," 2020). *Motor* learning describes the neurological process of learning movements that are required to complete a specific activity. The process involves the acquisition of skill through repeated performance and practice and motor adaptation (Birkenmeier et al., 2010; Langhorne et al., 2009). Motor learning occurs when neuronal pathways are created or strengthened in the brain in response to practice or experience of a specific activity (Nudo, 2014; Wieloch & Nikolich, 2006). Motor learning is, therefore, a prerequisite factor in driving plasticity in the primary motor cortex. Motor learning, or skill acquisition, occurs over three stages: (i) verbal cognitive, (ii) motor, and (iii) autonomous (DeKeyser, 2014; Fitts & Posner, 1967) (Figure 2.1).

Within the motor stage, the learner attempts to master the task through repeated trials. Within this stage, the declarative knowledge gained within stage one (verbal cognitive stage) is turned into procedural knowledge, meaning the cognitive knowledge translates into physical knowledge. A large amount of practice is required for this translation to occur. With this intensive practice, the physical knowledge becomes more refined and procedural to allow for automatic recognition and correction of errors, a decrease in time to complete the task, reduced percentage of error, and reduced amount of attention required to complete the task (DeKeyser, 2014; Fitts & Posner, 1967; McCluskey et al., 2009). Within the autonomous stage, the learner completes the activity automatically, without error or conscious thought (DeKeyser, 2014; Fitts & Posner, 1967). For this

transfer to occur a set of abstract rules, concrete examples, and the opportunity to practice the activity in many different situations is required (DeKeyser, 2014).

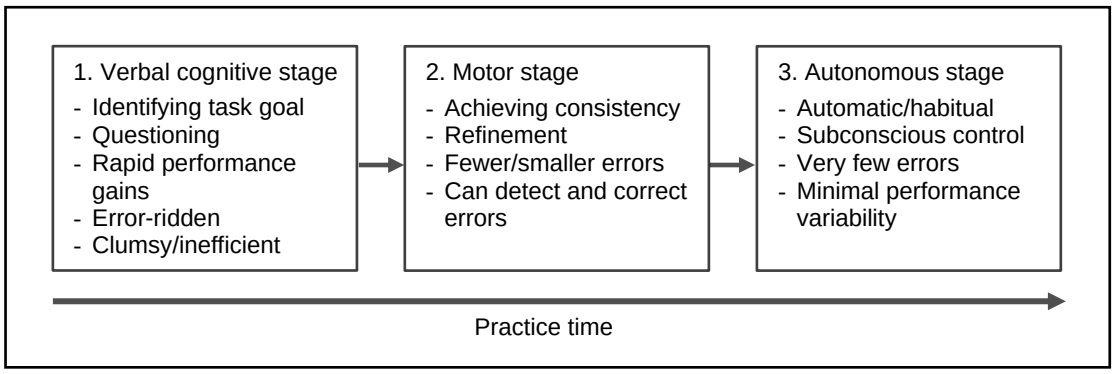


Figure 2.1. *The three-stage model describes motor learning as a continuous process with gradual changes in information processing in response to repeated performance and practice (adapted from Davids, Button, & Bennett, 2008, p. 9).*

Within the verbal cognitive stage, the learner is applying cognitive thought or awareness on how to complete the task (DeKeyser, 2014; Fitts & Posner, 1967). The learner gains knowledge about a task until the goal of the task is clear, and the factors that make the movement correct are communicated and understood (McCluskey et al., 2009). This stage requires supervision for feedback, correction, and additional instruction until the learner has learnt the set of movements required to carry out the task (DeKeyser, 2014; Fitts & Posner, 1967; McCluskey et al., 2009).

Experience and repetitive training are critical elements for neural plasticity (Carey, Polatajko, Tabor Connor, & Baum, 2012) and motor learning (DeKeyser, 2014; Fitts & Posner, 1967) to occur after stroke, similar to how healthy people learn through repetition and targeted practice. Plasticity and motor learning are therefore directly related as one cannot occur without the other. Although recovery of motor control and activity occurs in almost all individuals in response to intense training (Liepert et al., 1998; Luft et al., 2004), the application of neural plasticity and motor learning principles via specialised training and repeated practice immediately following stroke can influence and optimise neural reorganisation and motor learning (Hosp & Luft, 2011).

Pre-clinical models of neurological reorganisation and motor learning

Pre-clinical (i.e., animal) models were first to identify that neural plasticity can occur in response to a large amount of activity-specific practice of a task that is challenging, progressive, and skill-based (Nudo et al., 1996; Plautz et al., 2000). Following targeted cortical damage, individual non-human primates learned to retrieve small food pellets from either a small container using a challenging precision grasp (Nudo et al., 1996) or a large container using a typical prehensile grip pattern (Plautz et al., 2000). Within these pre-clinical studies, food withdrawal increased the motivation to complete the task (Nudo et al., 1996; Plautz et al., 2000) and the amount of activity-specific practice was very high, approximately 1,000 finger flexions each day (Nudo et al., 1996). Brain scans have been used to determine the amount of cortical reorganisation of the homunculus in response to the training in non-human primates (Nudo et al., 1996; Plautz et al., 2000). Following training, the amount of brain tissue devoted to controlling individual fingers was observed to increase in size in direct response to a task that presents a high level of challenge (Nudo et al., 1996; Plautz et al., 2000). Individual non-human primates trained to retrieve small food pellets from a small container using a challenging precision grasp developed neurological reorganisation (Nudo et al., 1996; Plautz et al., 2000). Whereas, individual non-human primates presented with an easy task did not develop neurological reorganisation (Plautz et al., 2000). Neurological reorganisation has thus been shown to occur in pre-clinical models in response to repetitive activity-specific practice of a motor learning task that is challenging, progressive, and skill-based.

Pre-clinical models have also been able to demonstrate that repetitive motor tasks alone do not produce neural plasticity (Nudo, 2014; Nudo et al., 1996; Plautz et al., 2000). Learning something new or difficult is necessary for neurological reorganisation to occur in animals (Plautz et al., 2000), i.e., practice of an activity or task designed to challenge the current level of ability and force new learning is key. The pre-clinical models demonstrate motor learning is dependent on goal-oriented, task-specific practice, i.e., repeated training of a specific challenging activity that has high motivation for success (Nudo et al., 1996; Plautz et al., 2000). Within pre-clinical models, high motivation and high level of challenge is achieved using food withdrawal, forced practice, and confinement (Nudo, 2014; Nudo et al., 1996; Plautz et al., 2000). While these may be used in animal experiments, the use of such methods in clinical (i.e., human) models poses challenging ethical considerations. Nonetheless, application of the key points to

clinical models is possible (Birkenmeier et al., 2010; Liepert et al., 2000; Liepert et al., 1998).

Clinical models of neurological reorganisation and motor learning

Consistent with pre-clinical models, repetitive engagement in an activity designed to promote the learning of a new motor skill also produces neural plasticity in humans (Nudo, 2014; Wieloch & Nikolich, 2006; Winstein et al., 2014). Critical elements for motor learning include goal-oriented movements (Blennerhassett & Dite, 2004; Bosch, O'Donnell, Barreca, Thabane, & Wishart, 2014; Donaldson et al., 2009; Gauggel, Leinberger, & Richardt, 2001; Han et al., 2013; Winstein et al., 2016), task specific movements (or practice) (Boyd, Vidoni, & Wessel, 2010; Jang et al., 2005; Kwakkel, Veerbeek, van Wegen, & Wolf, 2015), feedback (Fu, Knutson, & Chae, 2015; Galea, Mallia, Rothwell, & Diedrichsen, 2015; Jang et al., 2005; Molier, Van Asseldonk, Hermens, & Jannink, 2010; Morris, Taub, & Mark, 2006; Taub & Uswatte, 2003; Taylor, Krakauer, & Ivry, 2014), and a high number of repetitions (Birkenmeier et al., 2010; Fu et al., 2015; Liepert et al., 2000; Winstein et al., 2014). Animal experiments have used strategies which are unethical in humans to motivate practice (Nudo et al., 1996; Plautz et al., 2000), and as such, the application of pre-clinical evidence on plasticity and motor learning to the clinical model requires modification (Lang, MacDonald, & Gnip, 2007; Taub & Uswatte, 2003). As a starting point, the individual must be involved in goal development, be highly motivated to learn the activity (Carr & Shepherd, 2010; McCluskey et al., 2009), and engage in lots of practice (Boyd et al., 2010; Jang et al., 2005; Kwakkel et al., 2015).

The intensive targeted practice of a specific activity is fundamental for motor learning to occur and is considered to be one of the most important modulators of neural plasticity (Nudo, 2014). Practice refers to the involvement of the patient in producing a movement (Lang et al., 2009; "Practice definition," 2020); e.g., the activity required to reach and grasp for a cup. The more a person repeats the activity, the stronger the neural pathway (Nudo, 2014; Wieloch & Nikolich, 2006; Winstein et al., 2014), and the larger the amount of brain tissue in the brain dedicated to controlling this activity (Birkenmeier et al., 2010; Cramer et al., 2011; Langhorne et al., 2009; Nilsson et al., 2012; Nudo, 2014). Models of clinical practice outside of the stroke model also suggest the importance of amount of practice. Professional athletes, musicians, and dancers all spend a large part

of their day engaged in practice to achieve mastery of their specialised activity or skill (Sloboda, Davidson, Howe, & Moore, 1996), as mastery is said to occur after more than three thousand hours of dedicated task practice (Sloboda et al., 1996). Lots of practice is, therefore, essential to generate motor learning and neural plasticity for both healthy adults and adults after stroke (Birkenmeier et al., 2010; French et al., 2016; French et al., 2007; Langhorne et al., 2009; Nilsson et al., 2012; Wieloch & Nikolich, 2006).

AMOUNT OF PRACTICE FOR RE-LEARNING UPPER LIMB ACTIVITY AFTER STROKE

Researchers in the field of neurological rehabilitation have adapted the knowledge of learning a new skill to re-learning lost activities in adults after stroke (Carr & Shepherd, 2010; Langhorne et al., 2009). Consistent with pre-clinical models, repetitive engagement in an activity designed to promote the re-learning of a new motor skill produces neural plasticity in humans (Birkenmeier et al., 2010; Boyd et al., 2010; Jang et al., 2005; Liepert et al., 2000; Liepert et al., 1998; Luft et al., 2004). The retrained activity should be a goal-oriented, purposeful, promote focused attention, and provide knowledge of task completion (Blennerhassett & Dite, 2004; Bosch et al., 2014; Carr & Shepherd, 2010; Gauggel et al., 2001; McCluskey et al., 2009). Goal-oriented practice requires the individual to execute not just the individual movement patterns, but combinations of movement patterns appropriate to achieve the task (Horak, 1991), and for the focus of attention to be on the effect of the movement, not just on the movement itself (Wulf & Prinz, 2001). In fact, setting specific, challenging goals (Gauggel et al., 2001) appears to produce higher cortical activation (Nathan et al., 2012) and more efficient reaching performance than the same movements without a goal (Wu, Trombly, Lin, & Tickle-Degnen, 2000) or without a challenge (Gauggel et al., 2001). For example, reaching to an arbitrary location is meaningless unless there is a target and a purpose, i.e., to reach for and grasp a cup to pick it up and bring it to the mouth, drink and return it to the target location. Motivation for task completion can be provided by setting the level of challenge just above current ability (Gauggel et al., 2001; Kwakkel et al., 2015; Nudo, 2014; Plautz et al., 2000; Taub et al., 1994) or by reward or positive reinforcement (Abe et al., 2011; Galea et al., 2015).

Providing cues to encourage, guide or praise task completion (i.e. positive reinforcement) can improve motor learning (Schmidt & Lee, 2014) and can be delivered by the therapist

(Dobkin, 2004; Hollands, Pelton, Tyson, Hollands, & van Vliet, 2012; Subramanian, Massie, Malcolm, & Levin, 2010), the environment (Luft et al., 2004; Yavuzer, Eser, Karakus, Karaoglan, & Stam, 2006), or technology (Dorsch et al., 2015; Fong et al., 2013) during stroke rehabilitation. Despite the mode of delivery, feedback or instructions should be short, present a clear goal, and provide clarifying information about the critical components of the activity (Carr & Shepherd, 2010; Dorsch et al., 2015; Fong et al., 2013; Hollands et al., 2012; Luft et al., 2004; McCluskey et al., 2009; Yavuzer et al., 2006) so as not to take the learner's focus away from the whole task they are performing (Carey et al., 2012; Dobkin, 2004; Schmidt & Lee, 2014). Demonstration of the activity or a component of the activity allows the individual to see the amplitude of the movement, and appreciate the timing and coordination necessary (Carroll & Bandura, 1982). Observation of another's movement can stimulate the cortical motor areas of the brain (Aziz-Zadeh, Maeda, Zaidel, Mazziotta, & Iacoboni, 2002; Fadiga, Fogassi, Pavesi, & Rizzolatti, 1995) and it has been suggested that this may apply after stroke as well (Garrison, Aziz-Zadeh, Wong, Liew, & Winstein, 2013; Kim & Kim, 2015; Pomeroy et al., 2005; Sale, Ceravolo, & Franceschini, 2014). Feedback can provide an external focus of attention during training (Shea & Wulf, 1999; Wulf, Chiviacowsky, Schiller, & Avila, 2010) and enables error correction, and improvement in the next attempt (Carey et al., 2012; Carr & Shepherd, 2010; McCluskey et al., 2009). While all these elements are imperative, a high number of repetitions, i.e., lots of practice, remains the fundamental principle thought to underpin the clinical recovery of activity.

The amount (Carr & Shepherd, 1989; Lohse et al., 2014; Veerbeek et al., 2011; Veerbeek et al., 2014) and type (DeKeyser, 2014; Hayward et al., 2014) of practice provided in rehabilitation can have a direct impact on the amount of neural plasticity, motor learning, and thus, the amount of recovery after stroke. The amount of practice is, therefore, directly linked to retraining activity after stroke. Lots of practice of an activity that will target the underlying impairment could have the most substantial impact on improvement in activity after stroke (Canning, Ada, Adams, & O'Dwyer, 2004; Harris & Eng, 2007). As time is a factor in neural reorganisation and rehabilitation (Nakayama et al., 1994; Wolf et al., 2006), activity retraining programs need to deliver lots of practice of a task that will have the most significant impact on the improvement of the activity (Hubbard et al., 2009; Roby-Brami et al., 2003) early after stroke.

Most interventions for addressing upper limb activity limitations after stroke contain elements of motor learning and lots of practice with active engagement (Barreca et al., 2004; Corbetta, Sirtori, Castellini, Moja, & Gatti, 2015; Howlett, Lannin, Ada, & McKinstry, 2015; Langhorne et al., 2009; Ross et al., 2009). Examples include constraint-induced movement therapy (Morris et al., 2006; Stroke Foundation, 2010; Taub, Uswatte, & Pidikiti, 1999) task-specific training (Carr & Shepherd, 1989; Hubbard et al., 2009; Stroke Foundation, 2010; Winstein & Campbell, 2006) and functional electrical stimulation (Dobkin & Dorsch, 2013; Lohse et al., 2014; Peckham & Knutson, 2005). Functional electrical stimulation is an example of lots of practice with active engagement as, unlike cyclic electrical stimulation, it involves mental practice, facilitated active movement, and active participation required for motor learning (Howlett et al., 2015; Lohse et al., 2014). Repetitive task-specific training is an intervention developed based on the principles of motor learning theory first suggested by Carr and Shepherd (1989) recommended in stroke guidelines across the world (Canadian Stroke Network, 2013; Scottish Intercollegiate Guidelines Network, 2010; Stroke Foundation, 2010). Repetitive task-specific practice, a type of training encouraging a large amount of practice of a specific activity, is shown to result in motor learning and strengthening of neural pathways (French et al., 2016; French et al., 2007; Michaelsen, Dannenbaum, & Levin, 2006; Nelson et al., 1996; Winstein et al., 2004). For example, the cortical map was shown to enlarge in adults with stroke in response to two weeks of constrained induced movement therapy (Liepert et al., 1998) and after six weeks of repetitive upper limb training (Luft et al., 2004). In terms of motor learning, upper limb function improved in adults with stroke in response to task-specific practice when compared to usual care or no practice (Arya et al., 2012; Blennerhassett & Dite, 2004; Kwakkel et al., 1999a; Yen, Wang, Chen, & Hong, 2005). A design limitation of these randomised trials, however, is the variability in the amount of task-specific practice provided, ranging from as little as 20 total hours over four weeks (Arya et al., 2012; Blennerhassett & Dite, 2004), to more than 40 total hours over two weeks (Yen et al., 2005) or 16 weeks (Kwakkel et al., 1999a). In contrast, three similar randomised trials designed to measure the effect of additional task-specific practice compared to usual care or no practice found similar improvement in upper limb function between both groups at the end of the intervention period (Higgins et al., 2006; Ross et al., 2009; Winstein et al., 2004). A lack of difference between the amount (Ross et al., 2009) of intervention provided to the control and experimental intervention groups, or the small amount of task-specific practice provided to the experimental group (Higgins et al., 2006; Winstein et al., 2004)

may explain the contrasting findings. As can be seen from these trials, current research does not yet provide a good understanding for how much extra practice should be provided after stroke.

The amount of practice delivered during stroke rehabilitation is synthesised in national and international stroke guidelines (Canadian Stroke Network, 2013; Scottish Intercollegiate Guidelines Network, 2010; Stroke Foundation, 2010). With regards to the amount, intensity and timing of rehabilitation, guidelines recommend an 'as much as possible' approach. For instance, the Australian Stroke Foundation (2010) clinical guidelines recommended that rehabilitation be structured to provide as much practice as possible within the first six months after stroke (Figure 2.2); while the Scottish Intercollegiate Guidelines Network (2010) stated "every opportunity to increase the intensity of therapy" should be provided (p. 18); and the Canadian Stroke Network (2013) advised that appropriate intensity 'be structured to meet the needs and tolerance levels of each patient'. Overall, the guidelines lack detail regarding the amount of practice provided each day, how the amount of practice is best measured, and do not provide strategies to implement this amount of practice in stroke rehabilitation. It is not surprising that only 51% of stroke patients in Australia receive the recommended amount of upper limb practice during rehabilitation (Stroke Foundation, 2014).

Section 6.1.1 Amount and intensity of rehabilitation		**Grade**
a)	Rehabilitation should be structured to provide as much practice as possible within the first six months after stroke.	A[470]
b)	For patients undergoing active rehabilitation, as much physical therapy (physiotherapy and occupational therapy) should be provided as possible with a minimum of one hour of active practice per day at least five days a week.	GPP
c)	Task-specific circuit class training or video self-monitoring should be used to increase the amount of practice in rehabilitation.	B[471, 472]
d)	For patients undergoing active rehabilitation, as much therapy for dysphagia or communication difficulties should be provided as they can tolerate.	C[476, 477-479]
e)	Patients should be encouraged by staff members, with the help of their family and/or friends if appropriate, to continue to practice skills they learn in therapy sessions throughout the remainder of the day.	GCP

Figure 2.2. *Summarised evidence for the amount of practice taken from the Australian Stroke Foundation Guidelines, section 6.1.1 (Stroke Foundation, 2010).*

The clinical conundrum of how much practice to provide each day has been of interest to clinicians and researchers alike for some time. Several systematic reviews have explored

the effect of the amount of practice on outcome after stroke (Cooke, Mares, et al., 2010; Hayward et al., 2014; Kwakkel, van Peppen, et al., 2004; Langhorne et al., 1996; Lohse et al., 2014; Veerbeek et al., 2011; Veerbeek et al., 2014), and three reviews with meta-analyses have investigated the effect of extra practice (Kwakkel, van Peppen, et al., 2004; Lohse et al., 2014; Veerbeek et al., 2011). Kwakkel, van Peppen and colleagues (2004) found that extra rehabilitation improved activities of daily living (standardised mean difference [SMD] 0.13, 95% CI 0.03 to 0.23, 24 randomised trials). Consistently, Veerbeek and colleagues (2011) found that extra lower limb rehabilitation within six months of stroke improved walking ability (SMD 0.32, 95% CI 0.11 to 0.52, 11 randomised trials) and walking speed (SMD 0.22, 95% CI 0.01 to 0.43, 8 randomised trials). And Lohse and colleagues (2014) found that extra rehabilitation improved outcome (SMD 0.35, 95% CI 0.26 to 0.45, 34 randomised trials). These meta-analyses concluded that there is a dose-response relationship in posts-stroke motor training, where the larger the amount of extra rehabilitation, the greater the benefit (Cooke, Mares, et al., 2010; Kwakkel, van Peppen, et al., 2004; Langhorne et al., 1996; Lohse et al., 2014; Veerbeek et al., 2011; Veerbeek et al., 2014) regardless of time after stroke (Lohse et al., 2014).

Importantly, however, these previous systematic reviews (Kwakkel, van Peppen, et al., 2004; Langhorne et al., 1996; Lohse et al., 2014; Veerbeek et al., 2011; Veerbeek et al., 2014) included trials that did not investigate different doses of the same content of rehabilitation. For example, some reviews (Kwakkel, van Peppen, et al., 2004; Lohse et al., 2014; Veerbeek et al., 2011; Veerbeek et al., 2014) included trials comparing the effect of rehabilitation with no rehabilitation (Green, Forster, Bogle, & Young, 2002; Parker et al., 2001; Walker, Gladman, Lincoln, Siemonsma, & Whiteley, 1999; Wade, Collen, Robb, & Warlow, 1992; Werner & Kessler, 1996). Other reviews (Kwakkel, van Peppen, et al., 2004; Langhorne et al., 1996; Lohse et al., 2014; Veerbeek et al., 2011; Veerbeek et al., 2014) included trials which provided extra rehabilitation that was of different content than the usual rehabilitation (Allison & Dennett, 2007; Askim, Morkved, Engen, Roos, Aas, & Indredavik 2010; Barreca, Sigouin, Lambert, Ansley, 2004; Di Lauro, Pellegrino, Savastano, Ferraro, Fusco et al., 2003; Fang et al., 2003; Feys, De Weerdt, Selz, Cox Steck, Spichiger, et al., 1998; Gilbertson, Langhorne, Walker, Allen, & Murray, 2000; Howe, Taylor, Finn, Jones, 2005; Yang, Yen, Wang, Yen, & Lieu, 2005), thereby confounding the analysis of the *amount* of rehabilitation with the *type* of rehabilitation. Cooke and colleagues (2010) recognised these limitations

and examined seven trials where the extra rehabilitation was delivered on top of usual rehabilitation and was of the same content. A meta-analysis of the seven studies was not performed, but the effect sizes of several trials with the same outcomes suggested that there was some evidence supporting the hypothesis that extra rehabilitation on top of usual rehabilitation improves outcome after stroke (Cooke, Mares, et al., 2010). Given the need for a meta-analysis of the evidence of the amount where the studies delivered consistent *type* of rehabilitation, a systematic review was conducted (Study 1).

Research has consistently shown that rehabilitation programs rarely provide sufficient motor training to induce cortical changes (Lang et al., 2009; Scrivener, Sherrington, Schurr, & Treacy, 2011). Nor is rehabilitation consistent with the amount of practice recommended in national clinical practice guidelines (Bernhardt et al., 2004; Janssen et al., 2014; Kaur, English, & Hillier, 2012; Kaur et al., 2013; King et al., 2011). For example, a systematic review investigating the effect of different doses of rehabilitation found that, on average, rehabilitation participants spend 39 minutes each day engaged in physiotherapy and occupational therapy combined (Kwakkel, van Peppen, et al., 2004). Observational studies of activity levels during rehabilitation found that patients' practice only 45% of the time they are in a therapy area (Mackey, Ada, Heard, & Adams, 1996), complete task-specific upper limb practice in 51% of upper limb rehabilitation sessions, (Lang et al., 2009), and on average, complete 32 repetitions of upper limb activities each session (Lang et al., 2009). In addition, observational behavioural mapping studies designed to describe the time use and activity levels of hospitalised patients after stroke in metropolitan Australia have found patients are inactive and alone for the majority of their day (Bernhardt et al., 2004; King et al., 2011). Patients undergoing rehabilitation spent 11% of their weekday with an allied health or nursing professional, 76% of their weekday in their bedroom, and 62% of their weekday being inactive (King et al., 2011). A systematic review of studies designed to record the amount of time adults after stroke spent physically active during physiotherapy sessions found that patients are engaged in practice for less than two thirds of the session duration (Kaur et al., 2012). Overall, observational studies of inpatient stroke rehabilitation demonstrate conclusively that most practice occurs during time with a therapist (as opposed to time alone or time with a visitor) (Ada et al., 1999; Skarin et al., 2013) and the amount of practice provided is well below the guideline-recommended amount (Bernhardt et al., 2004; King et al., 2011). A small proof-of-concept study has shown, however, that it appears feasible for patients engaged in stroke rehabilitation to increase the intensity of task specific practice to be

more in line with animal studies (Birkenmeier et al., 2010). Further investigation into potential barriers and solutions to the delivery of an increase in the amount of practice provided during stroke rehabilitation is required.

One such barrier is the therapist. Therapist behaviour is known to affect the implementation of guideline recommendations (Eccles, Grimshaw, Walker, Johnston, & Pitts, 2005; McCluskey, Vratsistas-Curto, & Schurr, 2013). The application of specific models or frameworks for changing health professional behaviours have been successful (French et al., 2012; McCluskey et al., 2013; Michie et al., 2005; Novak & McIntyre, 2010; Petzold et al., 2012) when designed to address known barriers for successful implementation of stroke guidelines (French et al., 2012; Michie et al., 2005). Several studies have attempted to change therapist behaviour to increase the amount of practice through ongoing professional development programs (Cunningham, Turton, Van Wijck, & Van Vliet, 2016; Merians, Poizner, Boian, Burdea, & Adamovich, 2006; Ross et al., 2009; Waddell, Birkenmeier, Moore, Hornby, & Lang, 2014), since organisations commonly deliver professional development programs with a goal to increase compliance with evidence-based practice (Cusick & McCluskey, 2000). A systematic review that synthesised 81 studies investigating professional development programs found that educational meetings alone or combined with other interventions improved professional practice (Forsetlund et al., 2009). A professional development program designed to target therapist behaviour may be a potential solution to increase the amount of practice provided during stroke rehabilitation. This potential solution is investigated further in Study 3.

MEASUREMENT OF AMOUNT OF PRACTICE

To understand the effect increasing the amount of practice on upper limb activity in adults after stroke, researchers and clinicians need reliable measurement tools to measure both the *amount* of practice and the *outcome* of practice on upper limb activity. Unfortunately, there is no agreement on how best to measure the amount of practice provided during stroke rehabilitation. There are several methods currently in use that consider the *duration* and *intensity* of practice, yet each has limitations. First, the amount of time participants spend in rehabilitation sessions has been used as an indicator of the amount of practice (Cooke, Mares, et al., 2010; Kwakkel, van Peppen, et al., 2004; Langhorne et al., 1996; Veerbeek et al., 2011; Veerbeek et al., 2014). Prospective review

of rehabilitation timetables, collection of clinician statistics, or observation of how patients spend their time in rehabilitation have been used to indicate of the amount of time spent in practice (Ada et al., 1999; Lang et al., 2007; Lang et al., 2009; Mackey et al., 1996). The time patients spend in rehabilitation sessions, however, has been shown to be a poor proxy for the actual amount of practice (Kaur et al., 2013) as it does not take into account rest breaks and other interruptions to therapy (Scrivener et al., 2011). An observational study investigating how the time in the therapy area was spent by sixteen patients participating in an inpatient stroke rehabilitation program found, on average, patients spent 58% of the hour of scheduled therapy in activities unrelated to stroke recovery, including 11 minutes with no activity occurring and nine minutes in conversation (Ada et al., 1999). This was confirmed in an observational study comparing therapists' estimations of amount of practice and video recordings of therapy sessions, which found therapists systematically overestimated the amount of time adults after stroke spent engaged in active therapy by 28% and underestimated rest time by 36% (Kaur et al., 2013). The time spent in scheduled or intended rehabilitation should thus, not be interpreted as being the same as the amount of rehabilitation.

One strategy to overcome limitations in recording amount of practice has been to record the number of completed repetitions of an activity over the specified time spent in rehabilitation (Lang et al., 2007; Lang et al., 2009; Scrivener et al., 2011). This is not without issues either, however, as generally such methods fail to specify the definition of a repetition of a complex activity. For example, the number of exercise repetitions completed in a 30-minute session can vary significantly depending on task complexity. In an observational study by Scrivener and colleagues (2011), the range of repetitions was extreme; between 4 to 369 repetitions. The number of repetitions may misrepresent the amount of practice if an activity is particularly complex, challenging, or time-consuming to complete. For example, the number of repetitions of a particularly complex and time-consuming activity such as doing up small buttons on a shirt may be low despite the person with impaired co-ordination being engaged in active practice for the entire session duration.

More recently, to address these challenges, researchers have reported the amount of time spent engaged in active practice (Ada et al., 1999; Kuys, Brauer, & Ada, 2011; Kwakkel, Wagenaar, Twisk, Lankhorst, & Koetsier, 1999b; Lohse et al., 2014). For example, an observational study investigating cardiorespiratory training after stroke used video

recording of the therapy session to record the number, type, and duration of each activity completed during physiotherapy intervention (Kuys et al., 2011). While this is an improvement over recording only the session length, or only the number of repetitions, it is very time consuming and rarely used.

MEASUREMENT OF OUTCOME OF UPPER LIMB ACTIVITY

The purpose of upper limb activity is to interact with the environment and objects within it (Lang, Bland, Bailey, Schaefer, & Birkenmeier, 2013). Upper limb activity is complex and varies with the individual task (McCluskey et al., 2009). For example, the position of the shoulder, elbow, wrist, and shaping of the hand will be different when eating a steak with a knife and fork, eating a sandwich, or eating popcorn. Unlike the upper limb, there are a smaller number of lower limb activity tasks (such as walking, sitting and standing) and thus, classifying performance of the lower limb is acknowledged to be more straightforward. Being able to measure upper limb activity after stroke is essential not only for evaluating the efficacy of upper limb rehabilitation (Santisteban et al., 2016) but also for making decisions regarding clinical rehabilitation (Chen, Chen, Hsueh, Huang, & Hsieh, 2009). Researchers and clinicians need tests that are relevant, meaningful, and appropriate to ensure that test results reflect upper limb activity in real/everyday life (Connell & Tyson, 2012; Coster, 2013; Smart, 2006). While there are several measurement tools available that purport to measure upper limb activity, there is general agreement that no single measurement tool adequately measures upper limb activity across the spectrum of stroke (Connell & Tyson, 2012; Coster, 2013; Thompson-Butel, Lin, Shiner, & McNulty, 2014). The need to compensate for the limitations of one measurement tool by using additional tools has contributed to the vast array of measurement tools currently used (Ali & Elhameed, 2012).

Factors that are associated with good outcome measures include being quick and easy to administer (Hatem et al., 2016), involve direct observation at the level of activity or participation (Lang et al., 2013), having good psychometric properties (Connell & Tyson, 2012), and involve timed-performance producing interval data that make changes in scores more readily interpretable (Alt Murphy et al., 2015). Another essential factor to consider is the clinical utility of outcome measures (Smart, 2006). Understanding what measure is most able to reflect upper limb activity in real life is imperative to ensure measurement of an accurate change over time due to intervention (Ashford, Slade,

Malaprade, & Turner-Stokes, 2008). The selection of an appropriate outcome measure is, therefore, difficult but essential.

Broadly speaking, tests measuring upper limb activity can be divided into two categories: (i) tests that measure performance of multiple tasks that categorise level of difficulty and produce ordinal data; or (ii) tests that measure the timed performance of a set task and produce interval data (Nunnally & Bernstein, 1994). The Arm Activity Measure (Ashford, Slade, & Turner-Stokes, 2013) and the Action Research Arm Test (Hsieh, Hsueh, Chiang, & Lin, 1998) are measurement tools that produce ordinal data to categorise upper limb activity. Two common tests of upper limb activity that measure the timed performance of a set task are the Box and Block Test (Mathiowetz, Volland, et al., 1985) (a measure of the ability to grasp, transport, and release small blocks) and the Nine-Hole Peg Test (Mathiowetz, Weber, et al., 1985) (a measure of the ability to grasp, transport, manipulate, and release small pegs).

While both tests produce interval data, there are, however, key differences between their psychometric properties. First, the Box and Block Test is more responsive at detecting change in upper limb activity than the Nine-Hole Peg Test (Lin, Chuang, Wu, Hsieh, & Chang, 2010). Second, the floor effect of the Nine-Hole Peg Test (Jacob-Lloyd, Dunn, Brain, & Lamb, 2005; Lin et al., 2010) appears to be larger than the floor effect of the Box and Block Test (Vratsistas-Curto, Sherrington, & McCluskey, 2018). These differences between the psychometric properties of the two tests may be because the Box and Block Test was developed to measure gross, inaccurate upper limb activity (Mathiowetz, Volland, et al., 1985), whereas the Nine-Hole Peg Test was developed to measure fine, accurate activity (Kellor, Frost, Silberberg, Iversen, & Cummings, 1971). The disadvantage of timed tests such as the Box and Block Test and the Nine-Hole Peg Test, is that they require a certain amount of upper limb activity before one can record a score, leading to a floor effect (Jacob-Lloyd et al., 2005; Lin et al., 2010; Vratsistas-Curto et al., 2018). Tests designed to measure upper limb activity over a set duration, however, are able to be reported as a rate of performance (Alt Murphy et al., 2015) which alleviates this issue since inability to do the test can be recorded as zero.

Timed tests, such as the Box and Block Test (Mathiowetz, Volland, et al., 1985) and the Nine-Hole Peg Test (Mathiowetz, Weber, et al., 1985) are measurement tools that produce interval data and quantify upper limb activity on a linear scale. A disadvantage

of ordinal data is that, other than higher or lower, the difference between orders is not consistent and does not allow for comparison on a sliding scale (Nunnally & Bernstein, 1994). Interval data, on the other hand, is sequential and can quantify performance even when performance is very poor (Nunnally & Bernstein, 1994). This is demonstrated in measures of lower limb activity. Lower limb activity performance is commonly quantified as gait speed (Richards, Malouin, & Dean, 1999). Gait speed is represented as a rate of performance by dividing the total distance by the time taken (metres per second) (Fulk & Echternach, 2008; Richards et al., 1999) and is determined by recording either the time taken to walk a set distance (ten-metre Walk Test) (Scrivener, Schurr, & Sherrington, 2014) or the distance one can walk in a set duration (six-minute Walk Test) (Dunn et al., 2015). By recording the distance one can walk in a set duration (six-minute walk test) the linear (interval) data is sequential and can quantify performance even when performance is very poor. Gait speed can, therefore, reflect the amount of lower limb activity in real life by comparing to the values for categorisation as household (<0.40 m/s), limited community (0.40–0.80 m/s), and full community (>0.80 m/s) ambulators (Perry, Garrett, Gronley, & Mulroy, 1995). Researchers and clinicians can determine lower limb activity in real life over the continuum of stroke recovery through this interval data (Fulk, Reynolds, Mondal, & Deutsch, 2010; Perry et al., 1995; Schmid et al., 2007) . To date, however, there is no method to categorise upper limb activity outcome using interval data.

In summary, upper limb activity is necessary for participation in meaningful everyday tasks (Australian Institute of Health and Welfare, 2013). Repetitive targeted practice of a specific activity designed to promote the re-learning of a motor skill after stroke produces neural plasticity in humans in the presence of a challenge (Birkenmeier et al., 2010; Carr & Shepherd, 2010; Langhorne et al., 2009; Nilsson et al., 2012). The amount of practice is, therefore, directly linked to the motor outcomes of adults after stroke. Nevertheless, rehabilitation programs rarely provide sufficient motor training to induce cortical changes (Lang et al., 2009; Scrivener et al., 2011) and the amount of extra practice needed to guarantee a better upper limb outcome than usual care is unknown. Furthermore, it is not yet known how the scores obtained on two common tests of upper limb activity reflect upper limb activity in real life (Connell & Tyson, 2012; Coster, 2013; Smart, 2006).

To increase the amount of practice provided during stroke rehabilitation, strategies to facilitate change in clinical practice are needed. Rehabilitation designed to improve upper limb activity after stroke must be based on evidence and involve task-specific practice of an activity that is challenging, progressive, and meaningful. As inpatient rehabilitation programs are resource-intensive (Dewey et al., 2001), there is a need to identify strategies to deliver this increase in the amount of practice within the current resources. Four research questions were developed to address these important issues.

RESEARCH QUESTIONS

The research questions addressed in this thesis were:

1. Does the research evidence suggest that an increase in the amount of usual rehabilitation will improve upper limb activity in adults after stroke (Study 1, Chapter 3)?

2. Does performance on the Box and Block Test or the Nine-Hole Peg Test relate more closely to upper limb activity in real life (Study 2, Chapter 4)?

3. Can a professional development program increase the intensity of upper limb practice undertaken in an inpatient upper limb rehabilitation class (Study 3, Chapter 5)?

4. Is it feasible for adults who are undergoing inpatient rehabilitation and have some movement in the upper limb after stroke to follow a semi-supervised program to increase the duration of upper limb practice each day (Study 4, Chapter 6)?

OUTLINE OF THE THESIS

Research questions 1-4 are presented as four independent but interrelated studies, with each study representing one chapter in this thesis (Chapter 3-6). Three chapters (Chapter 3, Chapter 5, and Chapter 6) present work which has been published in peer-review journals, and one other chapter (Chapter 4) presents a manuscript which is currently under review. For ease of reading, the published chapters and associated references have been reformatted to achieve consistency across the thesis, with the numbering of figures and tables kept continuous throughout.

Study 1 (Chapter 3) comprises a systematic review with meta-analyses examining the effect of an increase in the amount of usual rehabilitation on upper limb activity (Research Question 1). Subsequent threshold calculations of the minimum amount of extra rehabilitation required to guarantee an improvement in upper limb activity over usual care is presented.

Study 2 (Chapter 4) presents a psychometric analysis to determine the clinical utility of two common tests of upper limb activity in adults after stroke. Subsequent determination of the minimum performance on each test required to pick up a cup is presented (Research Question 2).

Two methods to increase the amount of practice in inpatient rehabilitation services are explored and presented separately in Study 3 and Study 4. First, to increase the *intensity* of practice, and second, to increase the *duration* of practice time. Study 3 (Chapter 5) presents a pre-post study of a professional development program to increase the *intensity* of practice undertaken in an inpatient, upper limb rehabilitation class (Research Question 3). Study 4 (Chapter 6) presents a pre-post study of the feasibility of using a semi-supervised upper limb program to increase the *duration* of practice in an inpatient rehabilitation program for adults after stroke (Research Question 4).

Chapter 7 discusses all studies to form conclusions about the amount of practice to improve upper limb activity in adults after stroke. Clinical implications and recommendations for future research directions are also provided.

Chapter 3: Increasing the amount of practice: a systematic review

The work covered in this chapter has been published as:

Schneider EJ, Lannin NA, Ada L (2014). Increasing the intensity of rehabilitation to improve activity after stroke: a systematic review protocol. *Journal of Clinical Trials* 4:195. doi: 10.4172/2167-0870.1000195

Schneider EJ, Lannin NA, Ada L, Schmidt J (2016). Increasing the amount of usual rehabilitation improves activity after stroke: a systematic review. *Journal of Physiotherapy, 62 (4):182-187.* doi: 10.1016/j.jphys.2016.08.006

Trial registration: Prospective Register of Systematic Reviews (PROSPERO) registration number CRD42012003221.

See Appendix A for publication permission, Appendix C for trial registration, Appendix D for supplementary material, and Appendix H for published manuscript.

BACKGROUND AND RESEARCH QUESTIONS

Research evidence (Cooke, Mares, et al., 2010; Kwakkel, van Peppen, et al., 2004; Langhorne et al., 1996; Lohse et al., 2014; Veerbeek et al., 2014) and clinical practice guidelines (Canadian Stroke Network, 2013; Scottish Intercollegiate Guidelines Network, 2010; Stroke Foundation, 2010) recommend an 'as much practice as possible' approach to retraining upper limb activity in adults after stroke. Past systematic reviews investigating the amount of practice (see Chapter 2) were confounded by including trials which provided extra rehabilitation that was of different content than usual rehabilitation. For example, some of the included trials compared the effect of rehabilitation with no rehabilitation (Green et al., 2002; Parker et al., 2001; Walker et al., 1999; Wade et al., 1992; Werner & Kessler, 1996) whereas other included trials provided extra rehabilitation that was of different content to the usual rehabilitation (Allison & Dennett, 2007; Askim et al., 2010; Barreca et al., 2004; Di Lauro et al., 2003; Fang et al., 2003; Feys et al., 1998; Gilbertson et al., 2000; Howe et al., 2005; Yang et al.,2005). These prior systematic reviews of the amount of practice have therefore been confounded by the *type* of rehabilitation, leaving a gap in the research evidence to date (Cooke, Mares, et al., 2010).

Rehabilitation is resource intensive (Dewey et al., 2001), both on the part of the patient and the healthcare system. It is therefore important to determine the effect of increasing the amount of usual rehabilitation after stroke, and to ensure that this estimate is not confounded by the effect of extra rehabilitation of different content. The aim of this systematic review was to examine the effect of extra rehabilitation of the same content on top of usual rehabilitation. The specific research questions which guided this systematic review were:

1. In people receiving rehabilitation aimed at reducing activity limitations of the lower and/or upper limb after stroke, does adding extra rehabilitation (of the same content as usual rehabilitation) aimed at reducing activity limitations (of lower and/or upper limb) improve activity?
2. What is the amount of extra rehabilitation that needs to be provided to achieve a beneficial effect?

METHOD

Identification and selection of studies

A systematic review of randomised and quasi-randomised trials was undertaken, including research of the highest levels of evidence (Howick et al., 2011). Searches were conducted of Medline, EMBASE, CINAHL, and the Cochrane Register of Controlled Trials (CENTRAL) databases from the earliest date available until October 2015, for relevant articles available in English. Search terms included words related to stroke, physical therapy, occupational therapy, rehabilitation and intensity (such as dose, frequency, quantity, duration, and amount) (see Appendix D for full search strategy). Titles and abstracts were screened by one reviewer to identify potentially relevant studies. Full-text of all potentially relevant papers were then retrieved. Reference lists of articles included in this review and of similar systematic reviews were also screened by one reviewer to identify any additional studies meeting the inclusion criteria. The eligibility of retrieved papers was determined independently by two reviewers using predetermined criteria (Figure 3.1). An independent reviewer adjudicated any disagreements.

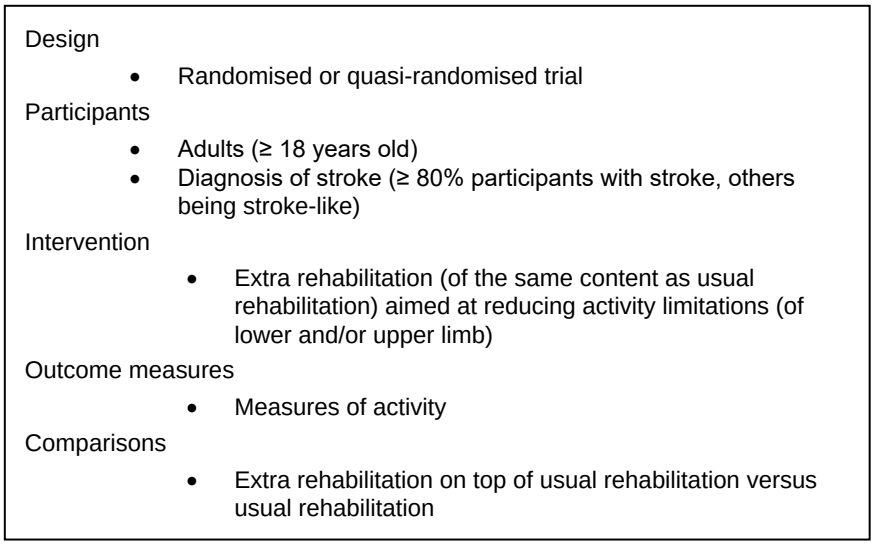


Figure 3.1. *Inclusion criteria.*

Assessment of characteristics of studies

Quality

The quality of the included studies was assessed by extracting PEDro scores from the Physiotherapy Evidence Database (www.pedro.org.au). The PEDro scale generates a

score out of 10 depending on whether the quality of each study meets each item of the tool (Maher, Sherrington, Herbert, Moseley, & Elkins, 2003). Where a study was not included on the database, two reviewers independently scored the study, and a third reviewer resolved any disagreements.

Participants

Studies were included if ≥ 80% participants were adults with stroke (with the remainder being stroke-like conditions such as cerebral aneurysm). Characteristics of participants, including age, sex, time since stroke and type of rehabilitation service, were examined to assess the similarity of the studies.

Intervention

Studies were included if they examined the effect of an increased dose of rehabilitation. That is, the experimental group received extra rehabilitation (of the same content as usual rehabilitation) on top of usual rehabilitation aimed at improving lower limb activity or upper limb activity or both. The control group received usual rehabilitation alone. The dose of usual rehabilitation was calculated as the amount of time dedicated to rehabilitation of the activity included in the extra rehabilitation. For example, if the experimental group received 30 min of extra upper limb rehabilitation, and the control group received 60 min of rehabilitation consisting of 30 min upper limb and 30 min lower limb, the comparison of the same content would be 30 min extra upper limb rehabilitation plus 30 min usual upper limb rehabilitation (60 min) versus 30 min usual upper limb rehabilitation.

Outcome measures

Measures involving direct observation of upper or lower limb activity were used, regardless of whether they produced continuous data (e.g., Box and Block Test, 10-m Walk Test) or ordinal data (e.g., Action Research Arm Test, Functional Ambulation Category).

Data analysis

Information about the method (ie, design, participants, intervention, measures) and results (ie, number of participants and mean (standard deviation [SD]) of outcomes) were extracted by one reviewer and cross-checked by another reviewer. Data were converted,

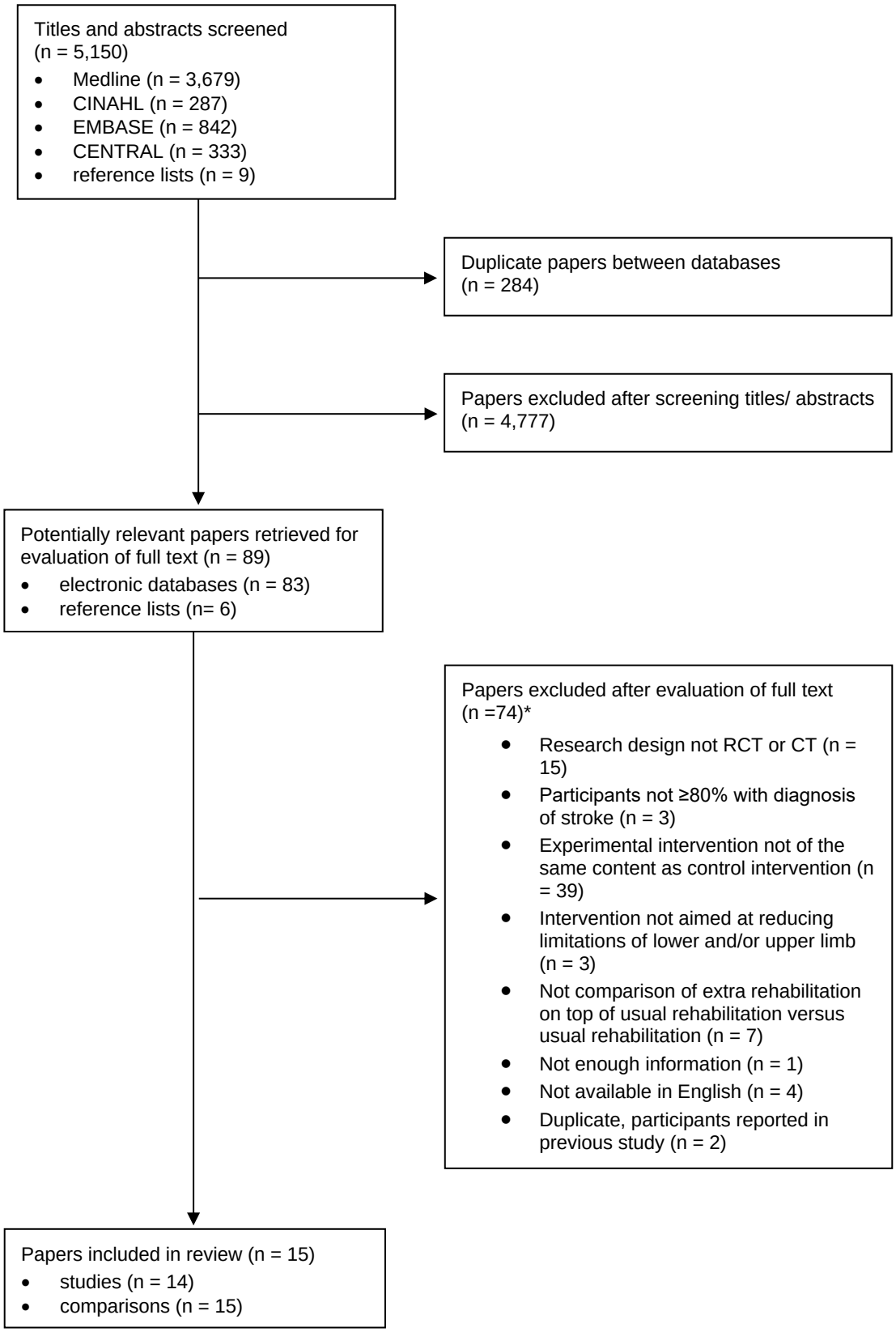
where necessary, using methods recommended by the Cochrane Handbook of Systematic Review (Higgins & Green, 2011). Authors were contacted where information was not available.

Post intervention scores were used to obtain the pooled estimate of the effect of the extra rehabilitation using RevMan 5.1 software (The Nordic Cochrane Centre, 2011). Since different outcome measures were used, the effect size was reported as Cohen's SMD (95% confidence interval [CI]). A random-effects model was used and in the case of significant heterogeneity ($I^2 > 50\%$), a sensitivity analysis was carried out to confirm the source of heterogeneity. Sub-group analyses according to the time after stroke (acute versus chronic) and body part (upper versus lower limb) were planned a priori where there were a sufficient number of comparable studies. The relationship between percentage of extra rehabilitation provided and the effect size was calculated using Pearson correlation coefficient. The amount of extra rehabilitation needed to provide a beneficial effect was determined from a receiver-operator characteristic (ROC) curve.

RESULTS

Flow of studies through the review

The electronic search strategy identified 5141 studies, of which 284 were duplicates. After screening titles, abstracts and reference lists, 89 potentially relevant papers were retrieved. Of these, 74 papers did not meet the inclusion criteria (see Appendix D for a summary of excluded papers), and therefore, 15 papers reporting 14 studies were included in this review (Figure 3.2).



* Papers may have been excluded for failing to meet more than one inclusion criterion.

Figure 3.2. *Flow of studies through the review.*

Characteristics of included studies

The 14 included studies involved 954 participants in 15 comparisons which investigated the effect of extra rehabilitation on top of usual rehabilitation for improving activity (Burgar et al., 2011; Cooke, Tallis, et al., 2010; Donaldson et al., 2009; English et al., 2015; GAPS, 2004; Han et al., 2013; Kim et al., 2014; Kowalczewski, Gritsenko, Ashworth, Ellaway, & Prochazka, 2007; Kwakkel et al., 2002; Kwakkel et al., 1999a; Lincoln et al., 1999; Page, Levin, Hermann, Dunning, & Levine, 2012; Partridge et al., 2000; Rodgers et al., 2003; Ross et al., 2009) (Table 3.1). Additional information was requested from the authors for four studies (English et al., 2015; Lincoln et al., 1999; Page et al., 2012; Rodgers et al., 2003).

Quality

The mean PEDro score of included papers was 6.9 out of 10.0, with individual study scores ranging from five to eight (Table 3.2). All of the papers reported random allocation, baseline similarity, between-group difference, and point estimate variability. The majority of papers reported concealed allocation (80%), assessor blinding (87%), and $<$ 15% loss to follow-up (87%). No papers reported participants or therapist blinding and 40% reported performing an intention-to-treat analysis.

Table 3.1. *Summary of included studies (n=14).*

Study	Design	Participants	Intervention	Outcome measures *
Burgar et al (2011)	QRCT	n = 36 Age (yr) = 61 (SD not stated) Sex = not stated Time since stroke < 6 mth	Extra = UL rehabilitation 60 min x 5/wk x 3 wk (↑ 100%) Usual = UL rehabilitation 60 min x 5/wk x 3 wk	• UL activity = Wolf Motor Function Test (ability, 0-5) • Timing = 0, 3, 26 wk
Cooke et al (2010)	RCT	n = 73 Age (yr) = 67 (SD 13) Sex = 59% male Time since stroke < 6 mth	Extra = LL rehabilitation 60 min x 4/wk x 6 wk (↑ 240%) Usual = LL rehabilitation 20 min x 5/wk x 6 wk	• LL activity = 10-m Walking Test (comfortable speed, m/s) • Timing = 0, 6, 12 wk
Donaldson et al (2009)	RCT	n = 20 Age (yr) = range 44-90 Sex = 50% male Time since stroke < 6 mth	Extra = UL rehabilitation 60 min x 4/wk x 6 wk (↑ 240%) Usual = UL rehabilitation 20 min x 5/wk x 6 wk	• UL activity = Action Research Arm Test (0-57) • Timing = 0, 6, 12 wk
English et al (2015)	RCT	n = 190 Age (yr) = 69 (SD 13) Sex = 58% male Time since stroke < 6 mth	Extra = LL rehabilitation 12 min x 2/wk x 4 wk (↑ 40%) Usual = LL rehabilitation 12 min x 5/wk x 4 wk	• LL activity = 6-min Walking Test (m/s) • Timing = 0, 4, 26 wk
GAPS (2004)	RCT	n = 70 Age (yr) = 68 (SD 11) Sex = 59% male Time since stroke < 6 mth	Extra = UL + LL rehabilitation 30-40 min x 5/wk x 10 wk (↑ 100%) Usual = UL + LL rehabilitation 30-40 min x 5/wk x 10 wk	• LL activity = Rivermead Mobility Index (0-15) • Timing = 0, 12, 26 wk
Han et al (2013)	RCT	n = 20 Age (yr) = 49 (SD 6) Sex = 75% male Time since stroke < 6 mth	Extra = UL rehabilitation 120 min x 5/wk x 6 wk (↑ 200%) Usual = UL rehabilitation 60 min x 5/wk x 6 wk	• UL activity = Action Research Arm Test (0-57) • Timing = 0, 6 wk
Kim et al (2014)	RCT	n = 22 Age (yr) = 51 (SD 9) Sex = 59% male Time since stroke > 6 mth	Extra = LL rehabilitation 30 min x 5/wk x 4 wk (↑ 300%) Usual = LL rehabilitation 10 min x 5/wk x 4 wk	• LL activity = 10-m Walking Test (comfortable speed, m/s) • Timing = 0, 4 wk
Kowalczewski et al (2007)	RCT	n = 19 Age (yr) = 61 (SD 16) Sex = 53% male	Extra = UL rehabilitation 60 min x 4/wk x 3-4 wk (↑ 400%) Usual = UL rehabilitation	• UL activity = Wolf Motor Function Test (ability, 0-5) • Timing = 0, 4, 26 wk

Study	Design	Participants	Intervention	Outcome measures *
		Time since stroke < 6 mth	60 min x 1/wk x 3-4 wk	
Kwakkel et al (1999 & 2002)	RCT	n = 101 Age (yr) = 66 (SD 12) Sex = 43% male Time since stroke < 6 mth	Extra 1 = UL rehabilitation 30 min x 5/wk x 20 wk (↑ 200%) Extra 2 = LL rehabilitation 30 min x 5/wk x 20 wk (↑ 200%) Usual = LL rehabilitation 15 min x 5/wk x 20 wk UL rehabilitation 15 min x 5/wk x 20 wk	• UL activity = Action Research Arm Test (0-57) • LL activity = 10-m Walking Test (comfortable speed, m/s) • Timing = 0, 20, 26 wk
Lincoln et al (1999)	RCT	n = 189 Age (yr) = 73 (SD not stated) Sex = 51% male Time since stroke < 6 mth	Extra = UL rehabilitation 24 min x 5/wk x 5 wk (↑ ?%) Usual = UL + LL rehabilitation 30-45 min x 5/wk x 5 wk	• UL activity = Action Research Arm Test (0-57) • Timing = 0, 6, 26 wk
Page et al (2012)	RCT	n = 17 Age (yr) = range 38-75 Sex = 59% male Time since stroke > 6 mth	Extra = UL rehabilitation 90 min x 5/wk x 8 wk (↑ 300%) Usual = UL rehabilitation 30 min x 5/wk x 8 wk	• UL activity = Action Research Arm Test (0-57) • Timing = -1, 9 wk
Partridge et al (2000)	RCT	n = 55 Age (yr) = range 60-94 Sex = not stated Time since stroke = not stated	Extra = UL + LL rehabilitation 30 min x 5/wk x 6 wk (↑ 100%) Usual = UL + LL rehabilitation 30 min x 5/wk x 6 wk	• LL activity = 5-m Walking Test (comfortable speed, m/s) • Timing = 0, 6, 26 wk
Rodgers et al (2003)	RCT	n = 105 Age (yr) = 75 (SD not stated) Sex = 55% male Time since stroke < 6 mth	Extra = UL rehabilitation 30 min x 5/wk x 6 wk (↑ ?%) Usual = UL + LL rehabilitation 45 min x 5/wk x 6 wk	• UL activity = Action Research Arm Test (0-57) • Follow up = 0, 26 wk
Ross et al (2009)	RCT	n = 37 Age (yr) = 59 (SD 19) Sex =57% male Time since stroke < 6 mth	Extra = UL rehabilitation 60 min x 5/wk x 6 wk (↑ 200%) Usual # = UL rehabilitation 30 min x 5/wk x 6 wk	• UL activity = Action Research Arm Test (0-57) • Timing = 0, 6 wk

RCT = randomized clinical trial, Q-RCT = quasi-randomised clinical trial, UL = upper limb, LL = lower limb, * = outcome measures and their timing listed are those analysed in the review, there may have been other measures reported in the paper, # = information provided by author

Table 3.2. *PEDro criteria and scores for included papers (n=15).*

Study	Random allocation	Concealed allocation	Groups similar at baseline	Participant blinding	Therapist blinding	Assessor blinding	< 15% dropouts	Intention-to-treat analysis	Between-group difference reported	Point estimate and variability reported	Total (0 to 10)
Burgar et al (2011)	Y	N	Y	N	N	Y	Y	N	Y	Y	6
Cooke et al (2010)	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8
Donaldson et al (2009)	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8
English et al (2015)	Y	Y	Y	N	N	Y	Y	N	Y	Y	7
GAPS (2004)	Y	Y	Y	N	N	N	Y	Y	Y	Y	7
Han et al (2013)	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8
Kim et al (2014)	Y	Y	Y	N	N	Y	N	N	Y	Y	6
Kowalczewski et al (2007)	Y	N	Y	N	N	Y	Y	N	Y	Y	6
Kwakkel et al (2002)	Y	N	Y	N	N	N	Y	N	Y	Y	5
Kwakkel et al (1999)	Y	Y	Y	N	N	Y	Y	N	Y	Y	7
Lincoln et al (1999)	Y	Y	Y	N	N	Y	N	N	Y	Y	6
Page et al (2012)	Y	Y	Y	N	N	Y	Y	N	Y	Y	7
Partridge et al (2000)	Y	Y	Y	N	N	Y	Y	N	Y	Y	7
Rodgers et al (2003)	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8
Ross et al (2009)	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8

Y = yes, N = no

Participants

Across the studies, the mean age ranged from 49 to 75 years. Time after stroke ranged from a few weeks to > 6 months, with 86% of the studies carried out within 6 months after stroke.

Intervention

All the studies involved the experimental group receiving extra rehabilitation on top of usual rehabilitation and the control group receiving usual rehabilitation. Furthermore, the extra rehabilitation was the same content as usual (or a component of usual) rehabilitation. Extra rehabilitation included upper limb activity (nine comparisons), lower limb activity (four comparisons), and both upper and lower limb activity (two comparisons). One included study involved three trial arms; only the experimental group receiving therapy seven days per week and the control group receiving usual care were included (Cooke, Tallis, et al., 2010).

Outcome measures

Upper limb activity was measured using the Wolf Motor Function Test (two comparisons) or the Action Research Arm Test (seven comparisons). Lower limb activity was measured using: timed tests of walking speed (five comparisons) and the Rivermead Mobility Index (one comparison).

Effect of extra rehabilitation on top of usual rehabilitation

The immediate effect of extra rehabilitation on top of usual rehabilitation was examined by pooling post-intervention data using a random effects model from 11 comparisons that measured activity immediately after the intervention period. These comparisons were of good quality (PEDro score 7.2 out of 10.0) and comprised 577 participants. Extra rehabilitation improved activity immediately after the intervention period (SMD 0.39, 95% CI 0.07 to 0.71) (Figure 3.3). Four comparisons could not be included in the analysis: two because there was no immediate data (Burgar et al., 2011; Rodgers et al., 2003), and two because the data were too skewed to enable conversion from non-parametric data to parametric data (Kwakkel et al., 1999a; Lincoln et al., 1999).

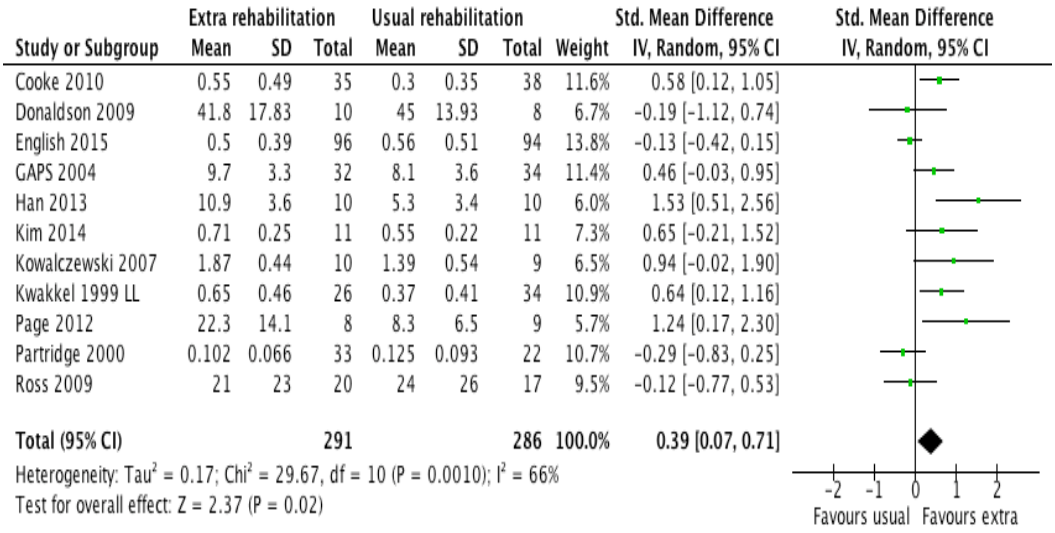


Figure 3.3. *Standardised mean difference (95% CI) of the effect of extra rehabilitation on top of usual rehabilitation compared with usual rehabilitation for activity immediately after the period of intervention (n=577 participants).*

There was substantial statistical heterogeneity (I^2 = 66%), indicating that the variation between the results of the trials was above the variation expected by chance. A sensitivity analysis revealed that the heterogeneity was not explained by the quality of the trials (PEDro score > 6/10), assessor blinding (yes or no), sample size (> 20 participants per trial), severity of participants (> 20% normal activity), chronicity of participants (> 6 months post stroke) or limb rehabilitated (upper vs lower). Heterogeneity, however, was partially explained by the amount of extra practice. In order to standardise extra rehabilitation across the comparisons, it was expressed as percentage increase per week. When reanalysed, separating trials into small (≤ 100%) or large (> 100%) increases in amount of practice, only the large increase in rehabilitation improved activity (SMD 0.59, 95% CI 0.23 to 0.94, I^2 = 44%) (Figure 3.4).

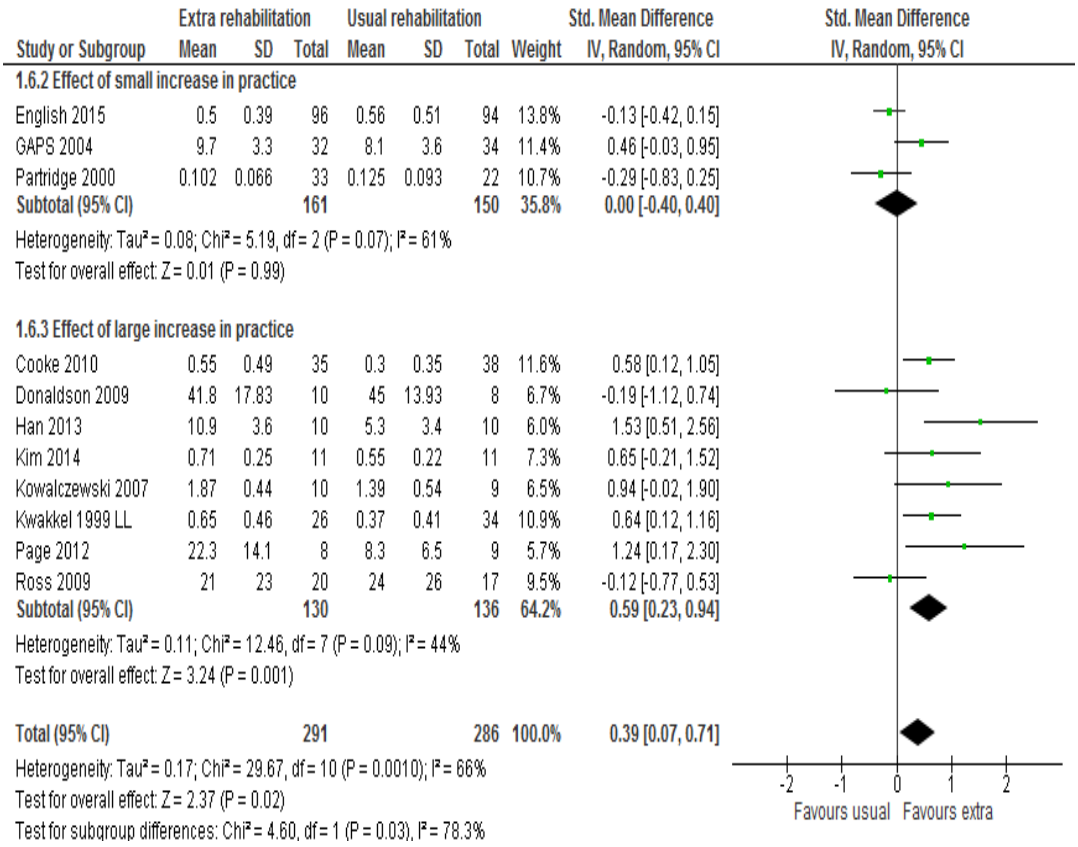


Figure 3.4. *Standardised mean difference (95% CI) of the effect of amount of extra rehabilitation on top of usual rehabilitation compared with usual rehabilitation for activity.*

Amount of extra rehabilitation needed to achieve a beneficial effect

There was a trend towards a positive relationship (r = 0.53, p = 0.09) between the amount of extra rehabilitation and improved activity when examining the 11 comparisons with data available immediately after the intervention period. Extra rehabilitation was expressed as percentage increase per week and deemed beneficial when the SMD was 0.5 in favour of the experimental group. The turning point on the ROC curve of false versus true benefit (area under the curve [AUC] = 0.88, p = 0.04) indicated that at least an extra 240% rehabilitation is needed for significant likelihood that the amount of rehabilitation will improve activity in adults after stroke (Figure 3.5). That is, the amount of practice required would need to be more than tripled from what is usually provided.

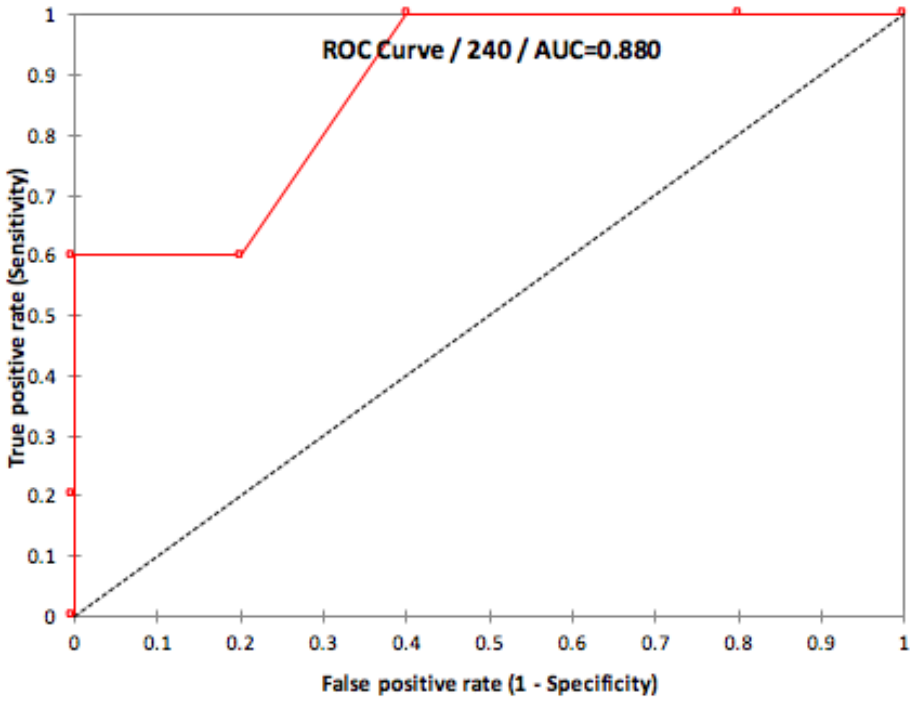


Figure 3.5. *ROC curve of the true versus false benefit for amount of extra rehabilitation per week immediately after the period of intervention (n=11 comparisons).*

CONCLUSION

This systematic review shows that there is sufficient research evidence that an increase in the amount of usual rehabilitation will improve upper limb activity in adults after stroke. The included studies provided evidence of immediate benefits to increasing the amount of rehabilitation aimed at reducing activity limitations in either the upper or lower limb. When added to usual rehabilitation, this increase in the amount of practice, on average, improves activity in people after stroke. The amount of extra rehabilitation that needs to be provided to achieve a beneficial effect is large. An increase of three times the amount of usual rehabilitation needs to be provided to improve upper or lower limb activity. There is, however, still much that remains unknown about how to provide this amount of usual rehabilitation, as well as implications for how to measure real life upper limb activity improvements. For example, understanding the meaning of improved upper limb activity in real life will benefit adults after stroke, therapists, and health services to understand the importance of finding new methods to deliver this increase in the amount of practice. Only with this research will therapists and health services be able to make informed choices about increasing the amount of task-specific practice intervention to

improve upper limb activity for adults undergoing stroke rehabilitation programs. Findings of this systematic review thus led to the development of new research questions for Studies 2, 3, and 4, which are reported in subsequent chapters.

Chapter 4: Measuring the outcome of practice: a psychometric study

The work covered in this chapter has been submitted as:

Schneider EJ, Ada L, White M, English C, Crotty M, Lannin NA (under review). Clinical utility of the Box and Block Test and the Nine-Hole Peg Test in adults after stroke. *Brazilian Journal of Physical Therapy*.

See Appendix B for ethics approval and Appendix E for supplementary material.

BACKGROUND AND RESEARCH QUESTION

Researchers and clinicians need tests that are relevant, meaningful, and appropriate to ensure that test results reflect upper limb activity in real/everyday life (Connell & Tyson, 2012; Coster, 2013; Smart, 2006). Tests involving direct observation with timed-performance that produce interval data make changes in scores more readily interpretable (Alt Murphy et al., 2015). Two such tests commonly used are the Box and Block Test (Mathiowetz, Volland, et al., 1985) (a measure of the ability to grasp, transport, and release small blocks) and the Nine-Hole Peg Test (Mathiowetz, Weber, et al., 1985) (a measure of the ability to grasp, transport, manipulate, and release small pegs).

It can be challenging for clinicians to know which test to use in clinical practice, since both the Box and Block Test and the Nine-Hole Peg Test provide similar data (Alt Murphy et al., 2015) and both have reasonable psychometric properties (Croarkin, Danoff, & Barnes, 2004; Heller et al., 1987; Higgins, Mayo, Desrosiers, Salbach, & Ahmed, 2005; Lin et al., 2010; Platz et al., 2005). Since the validity of different tests is known to depend on the activity level of the patient (Thompson-Butel et al., 2014), it would be useful to know the relationship between upper limb activity in real life and scores on each test (Lang et al., 2013). The objective of this study, therefore, was to determine the clinical utility of the Box and Block Test and the Nine-Hole Peg Test in adults after stroke.

METHOD

Design

Deidentified baseline data from studies (Lannin et al, 2019; Schneider, Ada, & Lannin, 2019; White et al., 2019) with consistent inclusion criteria were used in this study. All participants had a diagnosed stroke and were assessed at baseline between July 2015 and July 2018, and it was this baseline data that was used in the present study. Following consent, participants completed the Box and Block Test, the Nine-Hole Peg Test, rated their ability to pick up a cup and provided demographic data in a single measurement session. Only the affected upper limb was assessed. Tests were administered in no specific order by one of three occupational therapists following training; this training included an examination of written instructions and guidelines, as well as repeated practice. Institutional ethics committee approvals were attained prior to commencement of the studies (Alfred Hospital Human Research Ethics Committee approval numbers

442/14, 94/15, 367/17), and all participants gave written, informed consent before data were collected.

Participants

Participants were included if they had a diagnosis of stroke, were aged 18 years or older and had a clinically-assessed upper limb movement deficit. Exclusion criteria included severe cognitive and/or language deficits, comorbid neurological disorders, or non-stroke related upper limb conditions. Consistent demographic and clinical information including age, sex, time since stroke (months), side of hemiplegia, upper limb dominance, living situation, education, sensation (light touch), mobility status, and grip strength (kg) using dynamometry was collected across all studies.

Outcome measures

Box and Block Test

The Box and Block Test is a timed test of the ability to grasp, transport, and release one-inch cubes with one hand. Participants were asked to pick up and move one block at a time, over a barrier, to the other side of the box as quickly as possible (Mathiowetz, Volland, et al., 1985). Participants were asked to move as many blocks as possible in 60 seconds. Upper limb activity was quantified by the number of blocks moved in 60 seconds (number of blocks). The score was then transformed into a rate of performance by dividing the number of blocks moved by 60 seconds (blocks/s).

Nine-Hole Peg Test

The Nine-Hole Peg Test is a timed test of the ability to grasp, transport, manipulate, and release small pegs with one hand. Participants were asked to pick up the nine pegs one at a time and place them in holes until all nine holds were filled, then remove the nine pegs one at a time and return them to the tray (Heller et al., 1987; Mathiowetz, Weber, et al., 1985). Participants ceased the test if they had placed no pegs into holes at 60 seconds (Early Stopping Rule 1) (Chen et al., 2009) or if they had not completed the test, i.e., placed and removed all nine pegs, in 120 seconds (Early Stopping Rule 2). The number of pegs moved was recorded and quantified as zero to 18 pegs, so either zero to nine pegs placed into the holes or 10 to 18 pegs returned to the tray. The score was then transformed into a rate of performance by dividing the number of pegs moved by the

number of seconds to complete or stop the test (pegs/s) (Heller et al., 1987; Sunderland, Tinson, Bradley, & Hewer, 1989).

Upper limb activity in real life

Upper limb activity in real life was measured as 'picking up a cup'. On a five-point scale, participants were asked to rate their ability to independently pick up a glass, bottle or can with the affected upper limb, with zero representing no difficulty and four, unable to do the activity (Ashford et al., 2013). The score was then transformed into a nominal yes (able to pick up a cup) or no (unable to pick up a cup), where a score from zero to three is 'yes' and four is 'no'.

Data analysis

Descriptive statistics were calculated to describe the participants and their performance. Pearson correlation coefficient was used to evaluate the general agreement between scores on the Box and Block Test and the Nine-Hole Peg Test. A strong correlation was indicated by Pearson correlation coefficient value > 0.50 (Nunnally & Bernstein, 1994).

Clinical utility was assessed by examining the threshold difference in performance between scores on the Box and Block Test and the Nine-Hole Peg Test. Initially, Nine-Hole Peg Test scores were dichotomised as those who had or did not have the ability to place at least one peg in 60 seconds on the Nine-Hole Peg Test, then upper limb ability was dichotomised as those who did or did not have the ability to pick up a cup unaided. ROC curves were constructed by plotting sensitivity (vertical) versus one minus specificity (horizontal) in three separate calculations. First, a person's Box and Block Test score (blocks/s) was considered as a predictor of their ability to place at least one peg in 60 seconds on the Nine-Hole Peg Test, then, a person's Box and Block Test score (blocks/s) was considered as a predictor of their ability to pick up a cup unaided. Lastly, a person's Nine-Hole Peg Test score (pegs/s) was evaluated as a predictor of their ability to pick up a cup unaided. For each comparison, the AUC was calculated using non-parametric (Wilcoxon's) statistics as an index to quantify discriminative ability (Fan, Upadhye, & Worster, 2006). Outstanding discrimination was determined by an AUC of 0.90 and excellent discrimination by an AUC of ≥ 0.80 but < 0.90 (Fan et al., 2006). SPSS version 26 was used for analysis and the significance level was set at 0.05.

RESULTS

Sixty participants aged 56 years (SD 16) were recruited to the study. More than half of the participants were male (68%), and the majority experienced right hemiplegia (57%) (see Table 4.1 for participant characteristics). The mean performance on each test was 0.19 (SD 0.24) blocks/s on the Box and Block Test and 0.11 (SD 0.1) pegs/s on the Nine-Hole Peg Test. Of the 60 participants, 26 (43%) were unable to move one block on the Box and Block Test, 36 (60%) were unable to place one peg on the Nine-Hole Peg Test (Figure 4.1), and 38 (63%) were unable to pick up a cup.

Table 4.1. *Baseline characteristics of participants.*

Characteristic	(n = 60)
Age (yr), mean (SD)	56 (16)
Sex, n male (%)	41 (68)
Time since stroke (months), med (IQR)	16 (1-40)
Side of hemiplegia, n right (%)	34 (57)
Dominant upper limb, n right (%)	56 (93)
Living situation, n lives alone (%)	14 (23)
Education, n attended university (%)	18 (30)
Dwelling at time of enrolment, n (%)	
Home	40 (67)
Hospital	20 (33)
Cognitive impairment, n (%)	
None	17 (28)
Mild	38 (63)
Moderate	5 (8)
Loss of sensation, n (%)	
None	31 (52)
Some	18 (30)
Complete	11 (18)
Mobility, n walks unaided (%)	19 (32)
Grip strength (kg), mean (SD)	11 (10)

Abbreviations: n, number; yr, year; SD, Standard Deviation; med, Median; IQR, Interquartile range; kg, kilogram.

There was a very strong correlation (Pearson correlation coefficient 0.88; 95% CI 0.76 to 1.0, $p < 0.001$) between scores obtained on the Box and Block Test and the Nine-Hole Peg Test.

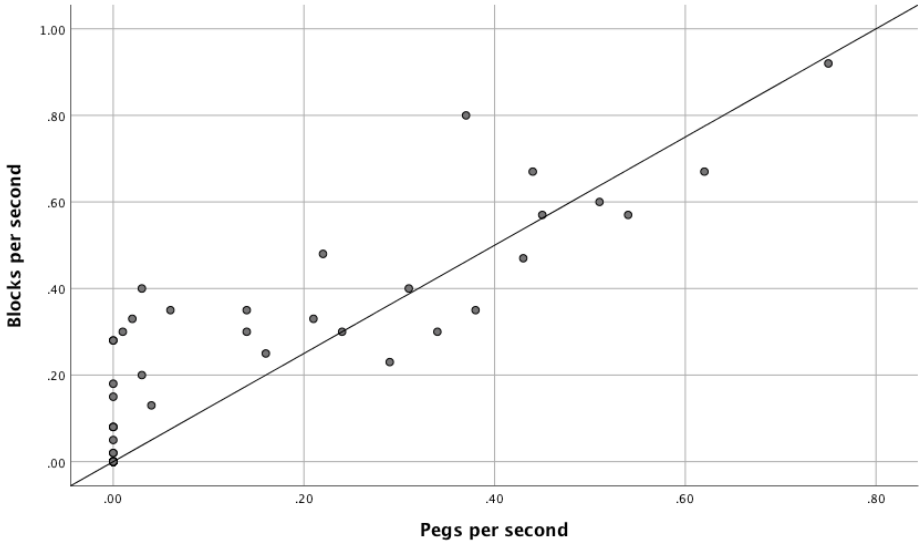


Figure 4.1. *Scatterplot of Box and the Block Test scores versus Nine-Hole Peg Test scores.*

Use of the ROC curve for the Box and Block Test score (blocks/s) to determine a threshold for the ability to place at least one peg in 60 seconds on the Nine-Hole Peg Test is shown in Figure 4.2. The Box and Block Test's discriminative ability regarding the Nine-Hole Peg Test score was outstanding (AUC = 0.99, $p < 0.001$) and suggests that a person will be able to place at least one peg in 60 seconds on the Nine-Hole Peg Test if they can move ≥ 0.29 blocks/s (i.e., ≥ 18 blocks in 60 seconds) on the Box and Block Test. The ROC curves for each test's ability to discriminate between ability to pick up a cup or not are shown in Figure 4.3. The Box and Block Test's discriminative ability was outstanding (AUC = 0.98, $p < 0.001$) and suggests that a person will have the ability to pick up a cup if they can move ≥ 0.29 blocks/s (i.e., 18 blocks in 60 seconds). The Nine-Hole Peg Test's discriminative ability in relation to cup performance was similarly outstanding (AUC = 0.99, $p < 0.001$) and suggests that a person will have the ability to pick up a cup if they can place ≥ 0.04 pegs/s (i.e., two pegs in 60 seconds).

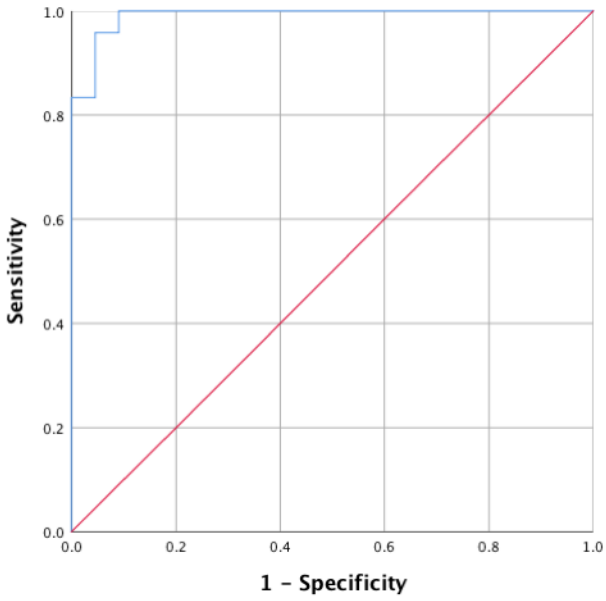


Figure 4.2. *ROC curve (AUC=0.99) for Box and Block Test score (pegs/s) and ability to place at least one peg in 60 seconds on the Nine-Hole Peg Test.*

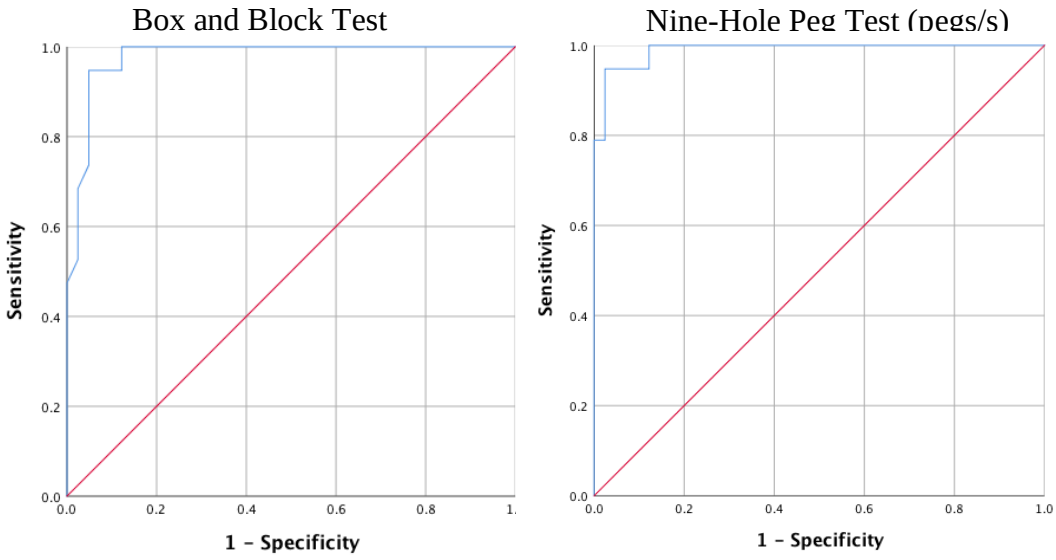


Figure 4.3. *ROC curves for the Box and Block Test score (AUC = 0.99) and the Nine-Hole Peg Test score (AUC=0.99) to discriminate between a person's self-reported ability to pick up or not pick up a cup.*

CONCLUSION

The results of this study confirm that the Box and Block Test and the Nine-Hole Peg Test are both measures that can reflect real world upper limb activity in adults after stroke,

however, the results of the Nine-Hole Peg Test may relate more closely to upper limb activity in real life. For some stroke survivors, despite registering some grip strength, their grip strength did not translate into upper limb activity in real life, i.e., picking up a cup. While the Nine-Hole Peg Test is a more difficult test to complete, the amount of upper limb activity required to move a peg is, therefore, more likely consistent with the upper limb activity required to perform meaningful tasks. While there is still much that remains unknown about how to determine upper limb activity in real life over the continuum of stroke recovery (Chapter 2), the results of this study can guide clinicians about which test to use in clinical practice to evaluate the efficacy of upper limb rehabilitation.

Understanding the true meaning of upper limb use over the recovery process is imperative for making decisions regarding clinical rehabilitation to ensure the amount of practice targets real recovery rather than compensation. Only with this research will researchers and clinicians be able to understand the effect of increasing the amount of practice on upper limb activity in real life and make informed choices about how to deliver this increase in the amount of practice to adults after stroke. As noted in Chapters 1, 2 and 3, the identification of methods to increase the amount of task-specific practice intervention to improve upper limb activity for adults undergoing stroke rehabilitation programs is needed. The following chapter will present the findings of a study specifically designed to determine if a professional development program can increase the intensity of practice undertaken in an inpatient upper limb rehabilitation class.

Chapter 5: Increasing the intensity of practice: a pre-post study

The work covered in this chapter has been published as:

Schneider EJ, Lannin NA, Ada L (2019). A professional development program increased the intensity of practice undertaken in an inpatient, upper limb rehabilitation class: a pre-post study. *Australian Occupational Therapy Journal*, 66 (3):362-368. doi: 10.1111/1440-1630.12562

See Appendix A for publication permission, Appendix B for ethics approval, Appendix F for supplementary material, and Appendix H for published manuscript.

BACKGROUND AND RESEARCH QUESTIONS

Professional development programs occur on a regular basis at most metropolitan hospitals, with the goal of assuring evidence-based practice (Cusick & McCluskey, 2000). Despite this, best-practice recommendations from guidelines are not routinely carried out (Grimshaw et al., 2012). Amount of rehabilitation is one such evidence-practice gap, and only 51% of stroke patients in Australia always receive the recommended amount of motor practice when participating in an upper limb activity training program (Stroke Foundation, 2014). A professional development program on how to provide active practice during rehabilitation sessions may be effective at addressing this evidence-practice gap by targeting the lack of knowledge and skill of staff (Cusick & McCluskey, 2000; French et al., 2012; Michie et al., 2005). Such a professional development program, however, likely needs to address more than simply changing therapist behaviours (i.e. doing things differently), but should also focus on changing organisational expectations for evidence-based practice, and developing local clinical guidelines (Cusick & McCluskey, 2000). Therefore, a professional development program designed to improve the knowledge and skills of staff while also using evidence about how best to get evidence into practice, has the potential to change staff behaviour (Grimshaw et al., 2012).

This chapter presents the process that a rehabilitation team went through to increase the *intensity* of practice undertaken within usual care upper limb rehabilitation. In this setting, most of the upper limb intervention is provided in a group-based format in an inpatient, upper limb rehabilitation class. Occupational therapists facilitate the class for patients with upper limb activity limitations to practice upper limb rehabilitation as part of usual care. This class runs for 60-minutes a day, five days a week. In this setting, we were unable to increase the length of time available for the upper limb rehabilitation class, and so this study sought to increase the intensity of practice as a way of increasing the amount of practice completed.

The research questions for this study were:

1. Does a professional development program increase the intensity of practice undertaken in an inpatient, upper limb rehabilitation class? and
2. Is the intensity of practice maintained 6 months after the cessation of the professional development program?

METHOD

Design

A study was conducted in a metropolitan rehabilitation hospital in Australia where practice was measured pre- and post-delivery of a professional development program. The design is outlined in Figure 5.1. The intensity of practice observed during the 60-minute inpatient, upper limb rehabilitation class during one week was recorded at baseline, 12 months (end of program) and 18 months (6 months later) to determine whether the amount of practice undertaken within the group had increased. The observational data were recorded from either a concealed space within the room or whilst in the room as a treating therapist (but not involved in the upper limb class). All attendees (staff and patients) of the upper limb class were blinded to the purpose of data collection at all three time periods. Institutional Human Research Ethics Committees approved this study (HREC approval number 16-094).

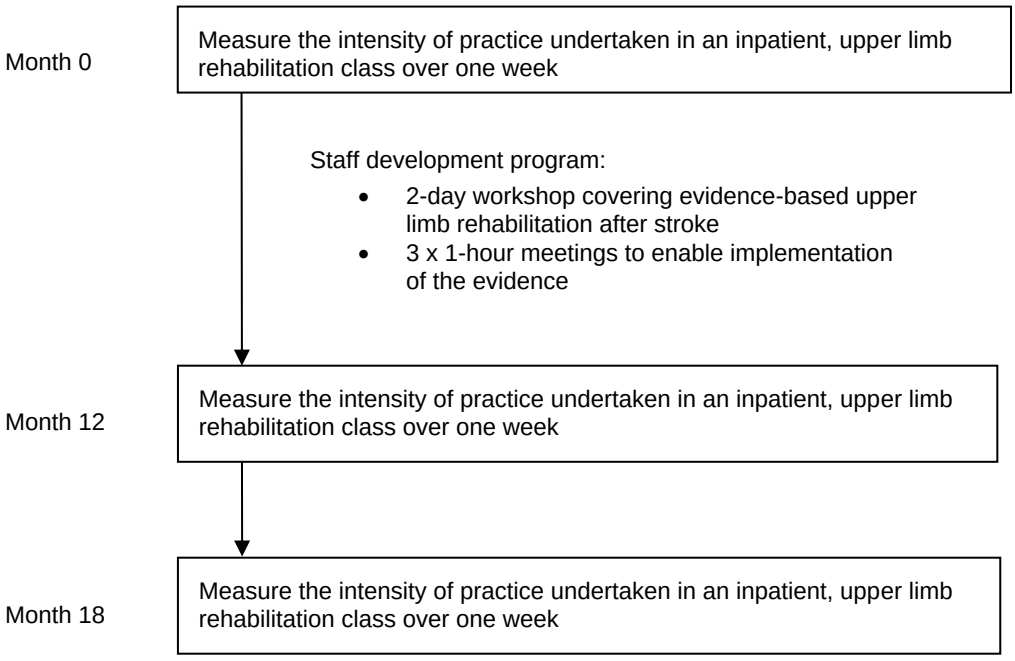


Figure 5.1. *Design and flow of the study.*

Setting

The study was conducted in a 205-bed sub-acute metropolitan rehabilitation hospital. This hospital provides rehabilitation for adults with mixed neurological conditions (e.g. stroke, subarachnoid haemorrhage, transient ischaemic attack, traumatic brain injury, spinal cord injury) and other conditions (orthopedic injuries, burns, amputation and aged

care conditions). Staff consists of an interdisciplinary allied health team (including occupational therapists, physiotherapists, speech pathologists, social workers, clinical psychologists, neuropsychologists, and allied health assistants). The upper limb class runs five days each week and is open to all inpatients with upper limb activity limitations with mixed neurological conditions, irrespective of primary diagnosis so long as they are able to tolerate sitting for 60 minutes. The maximum group size is nine patients, and it is an open class, i.e., inpatients in the class may change daily. The upper limb class is facilitated by three staff (two occupational therapists, one allied health assistant), randomly rostered on across the week. Descriptive characteristics of the upper limb class (such as duration, number of staff, number of patients, and patient diagnosis) were collected.

Intervention

A professional development program aimed at improving the implementation of clinical guidelines was delivered (Table 5.1). The program began with a two-day theoretical and practical workshop delivered by external experts on evidence-based upper limb rehabilitation after stroke. This was followed by three one-hour meetings with all staff to review best practice, identify barriers to putting it into practice, and develop a process for implementing the best-practice guidelines into rehabilitation. During these additional one-hour meetings, occupational therapists discussed the evidence in context of the upper limb class, developed solutions for resource allocation, clinical skill development/upgrading and mentoring, and led solutions to identified barriers. Attendance was recorded.

Table 5.1. *Intervention description using the Template for Intervention Description and Replication (TIDieR) checklist.*

Brief name	Professional development program
Why	A professional development program may increase the intensity of practice undertaken in an inpatient, upper limb rehabilitation class.
What materials	Materials included the stroke-guideline for upper limb activity impairment; specifically section 6.1 Amount, intensity, and timing of rehabilitation, and section 6.3.5 Upper limb activity (Stroke Foundation, 2010). Specifically, materials included a copy of clinical guideline recommended evidence-based upper limb intervention treatment protocols with suggested treatment strategies. Clinical guideline recommended treatment strategies included interventions such as mirror therapy, mental practice, and sensory retraining approaches. A copy of each intervention protocol was left in the treatment room used to provide upper limb rehabilitation as an on-site resource.
What procedures	A professional development program to increase use of clinical guidelines was delivered. The program comprised of theoretical and practical workshop and implementation meetings. It began with a two-day theoretical and practical workshop on evidence-based upper limb rehabilitation after stroke. These sessions were restricted to senior occupational therapy clinicians and was based on guideline recommended evidence-based interventions for upper limb activity impairment (Barker & Brauer, 2005; Birkenmeier et al., 2010; Doyle, Bennett, & Dudgeon, 2014; McCluskey et al., 2009, Stroke Foundation, 2010) and included practical demonstration sessions with patient volunteers. This was followed by three one-hour implementation meetings with all staff to identify barriers and develop a process for implementing the evidence into practice. During these additional one-hour meetings, the occupational therapists discussed the evidence in context of the upper limb class, developed solutions for resource allocation, clinical skill development/upgrading and mentoring, and led solutions to identified barriers. Audit feedback was not provided. Facilitated discussion of the clinical guideline recommendations concerning the recommended amount of rehabilitation and evidence-based interventions for patients with upper limb activity limitations was provided. Clinical skills were imparted to participants via practical demonstration sessions on normal movement and assessment of upper limb motor impairments, the use of task-specific motor training, and functional electrical stimulation with patient volunteers. Demonstrations also included the use of other evidence-based upper limb interventions such as mirror therapy, mental practice, and sensory retraining approaches.
Who provided	The two-day theoretical and practical workshop was delivered by external experts on evidence-based upper limb rehabilitation after stroke. The implementation meetings were delivered and monitored by a qualified occupational therapist employed by the health service.
How	The theoretical and practical workshop was held over two days. The occupational therapy manager supported senior occupational therapy staff to attend during work time. The implementation meetings were held once every week over a three-week period. The meetings ran for one hour during usual work hours. The implementation meetings were scheduled over different days of the week in order to capture the maximum number of staff. Sessions were advertised to all staff internally via email. Attendance was not mandatory but was encouraged by management.
Where	The professional development program was provided on-site at the rehabilitation hospital.
When and how much	Initially, the theoretical and practical workshop was provided over two days. Two months later, the implementation meetings were provided (60 minute duration) once per week for three weeks. As attendance at all sessions was not mandatory, key educational components were repeated across sessions with the result that some participants were exposed to educational topics on more than one occasion.
Tailoring	Staff were supported to identify barriers to the implementation of the evidence. Tailoring was used to develop a process for implementation of the evidence into practice. This included placing clinical guideline recommended intervention protocols into the treatment space.
Modifications	No modifications to the intervention were made.
How well	Staff attendance at the professional development program sessions was recorded.

Outcome measures

Building on prior research undertaken by English and colleagues (2014), intensity of upper limb practice was measured as the proportion of practice time per class (%) and the number of repetitions per practice time (repetitions/min). Proportion of practice time per class was calculated by recording the practice time and class duration for each attendee and dividing the mean number of practice minutes by the mean class duration and expressing this as a percentage. Number of repetitions per practice time was calculated by recording the number of repetitions per class for each attendee and dividing the mean number of repetitions by the mean number of practice minutes and expressing this as a rate (i.e. repetitions/minute). A stopwatch was used to record per patient the number of minutes spent in practice or the number of minutes spent at rest.

Practice was recorded (Appendix F) against activities recommended in the stroke-guideline for upper limb activity impairment; specifically section 6.1 Amount, intensity, and timing of rehabilitation, and section 6.3.5 Upper limb activity (Stroke Foundation, 2010). Practice was defined as the patient being actively involved in producing the upper limb movement (e.g. reach and grasp, functional electrical stimulation) and did not include tasks that did not involve active engagement (e.g. passive range of motion exercises, massage, electrical stimulation). Functional electrical stimulation was included as, unlike cyclic electrical stimulation, it involves mental practice and facilitated active movement such that the patient is engaged in the active participation required for motor learning (Howlett et al., 2015; Lohse et al., 2014).

The number of repetitions was measured by counting the number of repetitions completed per patient during each class (Scrivener, Sherrington, & Schurr, 2012). One repetition was defined as one complete movement of a task, such as reaching plus placing an object to the goal destination, or completing a movement to the desired target and back to the starting position, such as active shoulder forward flexion in standing and returning the arm back to the side of the body.

Data analysis

Data from all attendees of the inpatient, upper limb rehabilitation classes during the week of data recording were used to generate summary data for each of the three time periods. Data from attendees with stroke or stroke-like conditions, the attendees the stroke

guidelines specifically apply to, was used to generate summary data for each of the three time periods. Group characteristics and descriptive statistics are presented as mean (SD) and number (%). The time periods were compared with respect to change from 12 months to baseline and from 18 months to baseline and presented as mean (95% CI) differences.

RESULTS

Characteristics of the professional development program attendees

Twenty-two staff attended at least one professional development session; 18 (82%) were occupational therapists and 4 (18%) were allied health assistants. Five (23%) staff attended the two-day theoretical and practical workshop and up to 22 (100%, range 7 to 22) of staff attended at least one of the three one-hour implementation meetings.

Characteristics of classes

The characteristics of the inpatient upper limb rehabilitation class are detailed in Table 5.2. The duration of the class did not increase across all three time periods. The proportion of staff who facilitated the inpatient, upper limb rehabilitation class and who had attended at least one professional development session changed from 70% at 12 months to 55% at 18 months. The inpatient, upper limb rehabilitation class did not run for 2 of the 15 scheduled days of data collection. Reasons for the scheduled classes to be cancelled included un-scheduled clashes (e.g. x-ray or having a shower) or illness.

Table 5.2. *Characteristics of the inpatient, upper limb rehabilitation class.*

Characteristic	Times		
	Month 0	Month 12	Month 18
Duration of class (min), mean (SD)	52 (3)	50 (5)	42 (9)
Number of staff, mean (SD)*	1.8 (1.3)	2.4 (0.9)	3.0 (0.0)
Number of patients, mean (SD)	5.7 (1.5)	4.2 (1.8)	5.0 (1.6)
Staff to patient ratio	1:1.9	1:1.8	1.1.7
Patient diagnosis, number (%)			
Stroke or stroke-like condition	10 (100)	2 (20)	4 (40)
Progressive neurological condition	0 (0)	2 (20)	2 (20)
Spinal cord or nerve injury	0 (0)	4 (40)	1 (10)
Other (e.g. psychiatric, cardiac, orthopaedic) conditions	0 (0)	2 (20)	3 (30)

* Staff includes occupational therapists and allied health assistant

The intensity of practice

Mean (SD) intensity of practice undertaken at each time, and mean (95% CI) difference between times by all patients are detailed in Table 5.3. Between baseline and 12 months, the mean proportion of practice time per class increased by 52% (95% CI 33 to 70; $p < 0.001$) and the mean number of repetitions per practice time increased by 5.1 repetitions/min (95% CI 1.7 to 8.4; $p < 0.01$). Between baseline and 18 months, the mean proportion of practice time per class increased by 53% (95% CI 36 to 69; $p < 0.01$) and the mean number of repetitions per practice time increased by 4 (2 to 6) repetitions/min (95% CI 1.9 to 5.9; $p < 0.001$).

Table 5.3. *Mean (SD) amount and intensity of practice undertaken at each time by all patients, mean (95% CI) difference between times.*

Practice	Times			Difference between times	
	Month 0	Month 12	Month 18	Month 12 minus Month 0	Month 18 minus Month 0
Amount					
Practice time (min)	17 (16)	45 (13)	40 (13)	29 (19 to 38) *p < 0.001*	23 (13 to 33) *p < 0.001*
Repetitions (n)	53 (73)	348 (335)	250 (181)	295 (139 to 450) *p < 0.01*	197 (103 to 291) *p < 0.001*
Intensity					
Proportion of practice time per class (%)	32 (31)	84 (23)	85 (11)	52 (33 to 70) *p < 0.001*	53 (36 to 69) *p < 0.001*
Repetitions per practice time (reps/min)	2.2 (2.6)	7.2 (6.4)	6.1 (3.5)	5.1 (1.7 to 8.4) *p < 0.01*	3.9 (1.9 to 5.9) *p < 0.001*

Mean (SD) intensity of practice undertaken at each time, and mean (95% CI) difference between times by patients with stroke or stroke-like conditions are detailed in Table 5.4. Between baseline and 12 months, the mean proportion of practice time per class increased by 33% (95% CI) -6 to 72; $p = 0.09$) and the mean number of repetitions per practice time increased by 1.2 repetitions/min (95% CI -1.8 to 4.1; $p = 0.45$). Between baseline and 18 months, the mean proportion of practice time per class increased by 54% (95% CI 34 to 74; $p < 0.001$) and the mean number of repetitions per practice time increased by 1.9 repetitions/min (95% CI -0.1 to 3.8; $p = 0.06$).

Table 5.4. *Mean (SD) amount and intensity of practice undertaken at each time by patients with stroke or stroke-like conditions, mean (95% CI) difference between times.*

Practice	Times			Difference between times	
	Month 0	Month 12	Month 18	Month 12 minus Month 0	Month 18 minus Month 0
Amount					
Practice time (min)	17 (16)	32 (22)	36 (16)	15 (-5 to 35) *p = 0.14*	19 (7 to 32) *p < 0.01*
Repetitions (n)	53 (73)	140 (99)	144 (94)	87 (-3.5 to 178) *p = 0.06*	91 (26 to 156) *p < 0.01*
Intensity					
Proportion of practice time per class (%)	32 (31)	65 (45)	86 (11)	33 (-6 to 72) *p = 0.09*	54 (34 to 74) *p < 0.001*
Repetitions per practice time (reps/min)	2.2 (2.6)	3.3 (2.2)	4.0 (2.2)	1.2 (-1.8 to 4.1) *p = 0.45*	1.9 (-0.1 to 3.8) *p = 0.06*

CONCLUSION

These results showed a professional development program increased the intensity of upper limb practice undertaken in an inpatient upper limb rehabilitation class. This study suggests that a professional development program that includes theoretical, practical and clinical training using both education and implementation discussion meetings could be used by services who wish to increase the intensity of practice undertaken by inpatients in upper limb rehabilitation classes. The increase in the intensity of practice at the site within this study was maintained for 6 months after the cessation of the program. As a large increase in the amount of practice is needed to improve upper limb activity in adults after stroke (Study 1), understanding all the potential methods that clinicians might be able to increase the amount of practice in inpatient rehabilitation services is required. Another way to increase the amount of practice is to increase the duration of practice by creating additional practice sessions. The following chapter will present the findings of a study specifically designed to determine if it is feasible to add extra upper limb practice to usual inpatient rehabilitation and whether it is likely to improve upper limb activity and grip strength.

Chapter 6: Increasing the duration of practice: a pre-post study

The work covered in this chapter has been published as:

Schneider EJ, Ada L, Lannin NA (2019). Extra upper limb practice after stroke: a feasibility study. *Pilot and Feasibility Studies*, 5,156. doi: 10.1186/s40814-019-0531-5

Trial registration: Australian and New Zealand Clinical Trial Registry (ACTRN12615000665538).

See Appendix A for publication permission, Appendix B for ethics approval, Appendix C for trial registration, Appendix G for supplementary material, and Appendix H for published manuscript.

BACKGROUND AND RESEARCH QUESTIONS

There is high-level evidence that an increase in the amount of supervised rehabilitation improves motor outcome for adults after stroke (Lohse et al., 2014; Schneider, Lannin, Ada, & Schmidt, 2016; Veerbeek et al., 2011; Veerbeek et al., 2014). In Study 2, my systematic review found that at least a 240% increase in the amount of usual rehabilitation was needed to ensure that the extra rehabilitation improved activity (Chapter 3). This is almost three times the amount of usual rehabilitation and a large amount of extra practice. Most studies to date have delivered extra rehabilitation in one-on-one sessions outside the usual rehabilitation service (Burgar et al., 2011; Cooke, Tallis, et al., 2010; Donaldson et al., 2009; GAPS, 2004; Han et al., 2013; Kim et al., 2014; Kwakkel et al., 1999a; Lincoln et al., 1999; Partridge et al., 2000; Rodgers et al., 2003; Ross et al., 2009) without using strategies such as gaming (Hijmans, Hale, Satherley, McMillan, & King, 2011; Thomson, Pollock, Bugge, & Brady, 2014), group practice or homework (English et al., 2015; Harris, Eng, Miller, & Dawson, 2009; Page et al., 2012). A model of one-on-one delivery, however, is not an efficient way to increase the duration of practice in an inpatient rehabilitation service.

The challenge facing clinicians and health services alike is to find a feasible way to provide a large amount of extra practice taking into account staff and resource constraints. This study sought to investigate the use of largely self-directed practice within inpatient rehabilitation as one way of increasing the amount of upper limb practice in the subacute phase after stroke. In preparation for a large, fully-powered randomised trial, it is important to first understand the feasibility of recruitment, delivering the intervention and collecting the outcome measures. Therefore, the primary questions of this study were:

1. Is it feasible (in terms of recruitment, intervention and measurement) for people who are undergoing inpatient rehabilitation and have some movement in the upper limb after stroke to undertake an extra hour of upper limb practice, six days per week for four weeks?
2. Is the extra practice likely to improve upper limb activity and grip strength?

METHOD

Design

A prospective single-group, pre-post test study was conducted at a metropolitan inpatient rehabilitation hospital in Melbourne, Australia. The participants received extra upper limb practice for 4 weeks. Outcomes were measured at baseline (Week 0) and at the end of intervention (Week 4). Outcome measures were collected by occupational therapists trained in the procedures who were not blinded to the aims of the study. University and hospital human research ethics committees approved this study. All participants gave written informed consent before data collection began.

Setting

The study was conducted in one sub-acute rehabilitation hospital that has > 25 beds dedicated to multidisciplinary inpatient rehabilitation after stroke.

Participants and therapists

Consecutive patients with stroke admitted for inpatient rehabilitation between July 2015 and June 2016 were screened for eligibility by a researcher within 72 hours of admission. Patients were eligible if they had a medical diagnosis of stroke, were aged over 18 years, had an upper limb activity limitation (defined as < 54 blocks on the Box and Block Test which is a 20% reduction in the normal scores of adults aged 20-80 years) (Mathiowetz, Volland, et al., 1985), and had some upper limb activity (> Grade 1 wrist extension and > Grade 3 shoulder elevation on manual muscle testing) in order to be able to carry out the practice (Kendall, McCreary, & Provance, 1993). Patients were excluded if they had severe cognitive and/or language defects (Mini-Mental Status Examination [MMSE] score ≤ 24) (Folstein, Folstein, & McHugh, 1975), had any medical condition that precluded them participating in a rehabilitation program aimed at upper limb activity, or had a discharge date that precluded them completing the four week program. For patients who were initially ineligible (no upper limb activity), screening was repeated weekly to establish if they became eligible. Age (year), sex (number male), time since stroke (days), side of hemiplegia (number right), living situation (lives alone), education (attended university), cognition (MMSE, 0-30) (Folstein et al., 1975), unilateral spatial neglect (Albert's Line Cancellation Test, number of lines left uncrossed) (Albert, 1973), loss of light touch sensation (none/some/complete), spasticity (Tardieu Scale Quality of

Muscle Reaction, 0-5) (Gracies et al., 2000), contracture (range of motion at the wrist and elbow), complexity of rehabilitation needs (Rehabilitation Complexity Scale – Extended, 0-20) (Turner-Stokes, Scott, Williams, & Siegert, 2012), and ability to pick up a cup unaided (number) and walk unaided (number) were collected at baseline to describe the sample.

Occupational therapists overseeing the extra upper limb practice all had experience in neurological rehabilitation and were trained in delivering the intervention prior to study commencement. One therapist was involved in overseeing the extra upper limb practice, with incidental support from two additional therapists.

Intervention

Participants undertook an extra hour of upper limb practice, six days a week (Monday to Saturday) for four weeks, consisting of two 30-minute self-directed programs designed to be used by adults with stroke: the Graded Repetitive Arm Supplementary Program (GRASP) and the AbleX (Harris et al., 2009). GRASP is a self-directed arm and hand program that incorporates strengthening exercises, part practice and practice of whole upper limb activities (Harris et al., 2009). GRASP has three levels of difficulty. The level of difficulty prescribed was determined by participant performance on weekly clinical outcome measures and ability to complete half of the tasks at the maximum number of set repetitions (Harris et al., 2009). The therapist provided the participant with one of six GRASP kits (manual and equipment) at the start of each session. AbleX is a computer-based upper limb program. Participants hold a controller in their affected hand or bilaterally to play a range of computer games designed to promote target-hitting (Hijmans et al., 2011). The computer system provides participants with immediate feedback on their performance (accuracy), activity time (adherence) and exercise intensity (Hijmans et al., 2011).

Therapists provided direction and encouragement to practice, set-up the equipment, checked the quality of the practice, and progressed the difficulty of practice to ensure the level of challenge was always high. The amount of support was gradually reduced once the participant could follow the self-directed programs. To set-up the equipment the therapist provided the participant with a pre-packed GRASP kit or laptop. The extra practice could be undertaken at any time during usual rehabilitation hours (8 am to 5

pm), individually or in a group, in the therapy area or a common space on the ward. The time of the extra practice session was scheduled on the participant's timetable to ensure the participant was ready for each session. Participants were encouraged to complete the required amount of daily practice but could choose to practice for greater or less than 60 minutes per session. Amount of practice and session duration was tracked and recorded by the participant with assistance from the therapist using a stop watch and paper diary. No other aspects of the multidisciplinary rehabilitation were changed. The amount of usual upper limb rehabilitation that was scheduled on the participant's timetable by the multidisciplinary rehabilitation team was collected. Usual upper limb rehabilitation could include a combination of individual and group sessions provided by occupational therapists and /or physiotherapists targeting task-specific motor training of the affected upper limb.

Outcome measures

Feasibility

Feasibility of the study involved examining recruitment, intervention (adherence, efficiency, acceptability, and safety) and measurement. Feasibility of recruitment was determined by calculating the proportion of enrolled patients from the population who were screened for eligibility. Feasibility of the intervention was determined by examining adherence (the number of sessions attended as a proportion of the number of possible sessions), efficiency (the amount of practice as a proportion of total minutes), acceptability (participants yes/no responses to five statements about the training and rating of their acceptability from 0-5), and safety (the number of adverse events such as fatigue, illness, muscle soreness, or injuries as a proportion of the number of sessions attended). If required, an interpreter or non-verbal communication assisted the participant. Feasibility of measurement involved examining how many participants could be measured for all outcomes.

Clinical

Clinical outcomes were upper limb activity and grip strength. Upper limb activity was measured using the Box and Block Test (number of blocks) and the Nine-Hole Peg Test (s). Grip strength (kg) was measured using dynamometry. The Box and Block Test is a timed test of the ability to grasp and release. The instructions for the test were standardised according to Mathiowetz, Volland, and colleagues (1985). Participants

were asked to pick up and move one block at a time over a barrier to the other side of the box as quickly as possible. The ability to grasp and release was transferred to a rate of performance by dividing the number of blocks moved by 60 seconds (number of blocks/s).

The Nine-Hole Peg Test is a timed test of the ability to gasp, manipulate and place small objects with one hand. The instructions for the test were modified to incorporate additional stopping points (Chen et al., 2009; Mathiowetz, Weber, et al., 1985). Participants were asked to pick up the nine pegs one at a time and place them in the holes until all nine holes were filled; then remove the nine pegs one at a time and return them to the tray. The participants were told not to continue the test if they had placed zero pegs into the holes at 60 seconds (Chen et al., 2009). The participants were told not to continue the test if they had not completed the test (placed and removed all nine pegs) in 120 seconds (Mathiowetz, Weber, et al., 1985). The number of pegs moved was quantified as 0-18 pegs; either 0-9 pegs placed into the holes or 10-18 pegs returned to the tray. The score was then transferred to a rate of performance by dividing the number of pegs moved by the number of seconds to complete or stop the test (pegs/s).

Dynamometry of maximum voluntary contraction of grip measures the strength of muscles in the forearm and hand. The instructions for the test were standardised according to Horowitz, Tollin, and Cassidy (1997). Grip strength was quantified by the number of kilograms achieved. If the participant could register some strength but not enough to reach the first increment on the dynamometer (at two kilograms), the score was recorded as one kilogram.

Data analysis

Due to the nature of a feasibility study, a formal sample size calculation was not performed (Tickle-Degnen, 2013). Twenty participants was considered an adequate number to assess the feasibility (Billingham, Whitehead, & Julious, 2013).

For participant characteristics and feasibility outcomes, descriptive statistics are presented as mean (SD) or number (%). For clinical outcomes, paired between-time differences (Week 4 minus Week 0) are presented as mean difference (95% CI). When a

participant was discharged home or from the study before Week 4, a measure was taken at this time.

RESULTS

The flow of participants though the study is presented in Figure 6.1

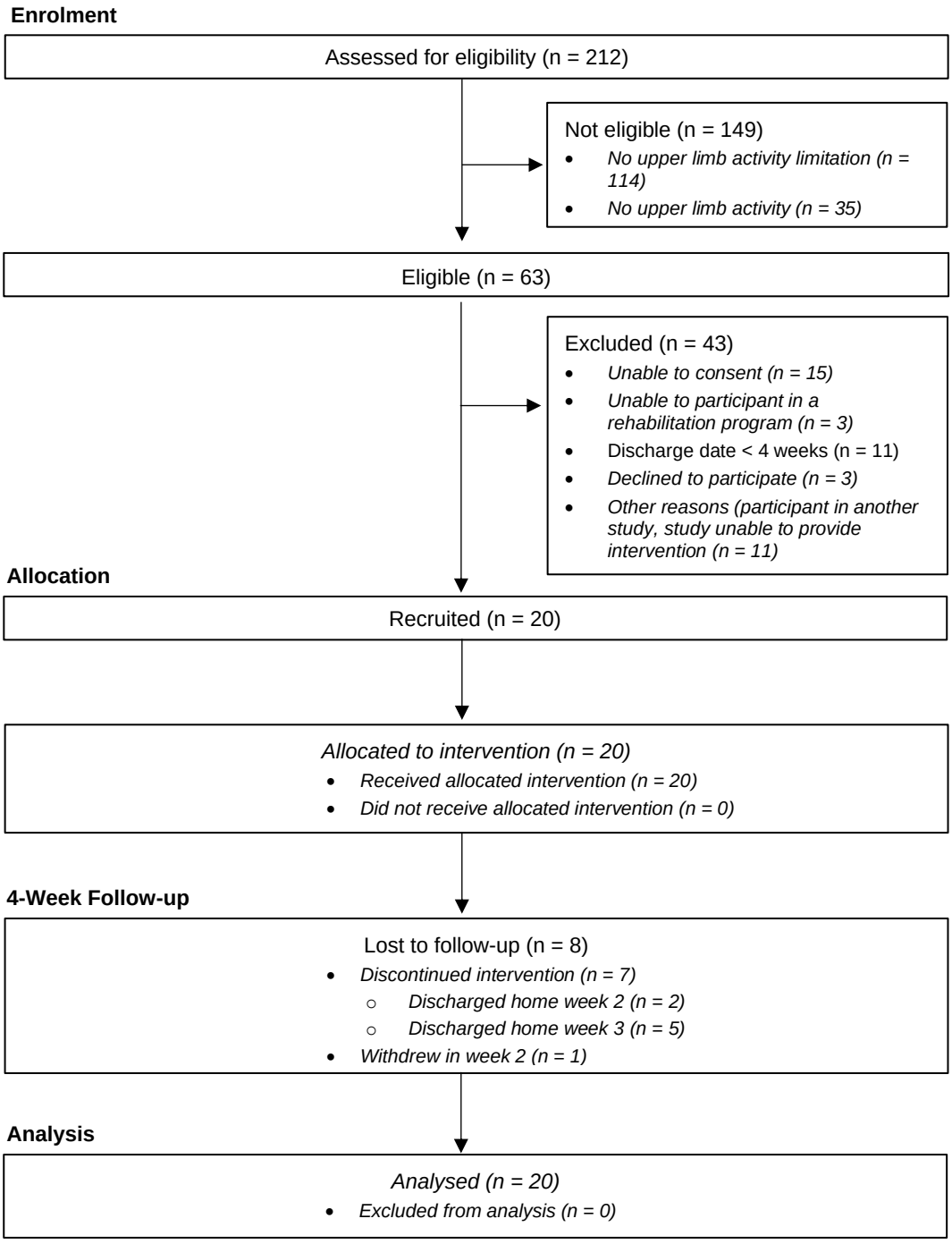


Figure 6.1 *Design and flow of participants through the study.*

Characteristics of participants

Twenty participants aged 63 (SD 17) years, of which 11 (55%) were men, participated in the study. Characteristics of participants are presented in Table 6.1. Usual upper limb rehabilitation was scheduled for a mean of 37 (SD 26) minutes per day with 4 (20%) participants scheduled to receive no upper limb rehabilitation.

Table 6.1. *Baseline characteristics of participants.*

Characteristic	(n = 20)
Age (yr), mean (SD)	63 (17)
Sex, *n* male (%)	11 (55)
Time since stroke (*day*), mean (SD)	38 (87)
Side of hemiplegia, *n* right (%)	12 (60)
Living situation, *n* lives alone (%)	9 (45)
Education, *n* attended university (%)	9 (45)
Cognition (*MMSE, 0-30*), mean (SD)	28 (2)
Neglect (Albert's Line Cancelation Test), n (%)	2 (10)
Loss of light touch sensation, *n* (%)	
None	18 (90)
Some	2 (10)
Complete	0 (0)
Spasticity (Tardieu Scale Quality of Muscle Reaction, 0-4), mean (SD)	
Wrist flexors	0.15 (0.38)
Biceps	0.2 (0.51)
Contracture upper limb, *n* (%)	3 (15)
Complexity of rehabilitation needs (*RCS, 0-20*), mean (SD)	12 (2)
Grasps unaided, *n* (%)	10 (50)
Walks unaided, *n* (%)	2 (10)

MMSE = Mini-Mental Status Exam, RCS = Rehabilitation Complexity Scale-Extended

Feasibility

Recruitment

Over an 11 month period, 212 people were screened, 42 (20%) were eligible, and 20 (9%) were enrolled. In terms of retention, at Week 4, 7 (35%) participants had already been discharged home and one (5%) had withdrawn (co-enrolled in another study and reported fatigue). Participants completed the extra upper limb practice program for a mean of 3 (SD 1) weeks. The flow of participants through the study is presented in Figure 6.1.

Intervention

Removing the 77 sessions missed due to early discharge of seven participants from the study, there were a possible 403 sessions. Adherence to the intervention was 85% (ie, 342 out of a possible 403 sessions). Forty-five (11%) sessions were missed because of non-attendance (illness, fatigue, visitors); and 15 (4%) sessions were missed because the participant withdrew. Efficiency of the intervention was 95%; ie, participants completed 324 hours of practice during a total of 342 hours. Participants undertook a mean of 57 (SD 9) minutes of extra upper limb practice during a mean session of 73 (SD 10) minutes. Acceptability of the intervention is presented in Table 6.2. Overall, the participants were satisfied (4.8 out of 5.0) with their extra practice. In terms of safety, the incidence of fatigue, illness, or muscle soreness during the 342 intervention sessions was 40 (12%); 32 (9%) reports of fatigue; 4 (1%) reports of illness; 4 (1%) reports of localized muscle soreness in the affected arm. There were no injuries or serious adverse events (study related or otherwise).

Table 6.2. *Acceptability of the extra rehabilitation.*

Acceptability	(n=20)
Would you recommend this program to a friend who had suffered a stroke and couldn't move their arm normally, number yes (%)	19 (95)
On average, was the program, number yes (%):	
Too much practice/exercise for your arm and hand?	1 (5)
Too little practice/exercise for your arm and hand?	1 (5)
Just enough practice/exercise for your arm and hand?	18 (90)
Did the practice make you tired, number yes (%)	8 (40)
Did the practice make you so tired that you wanted to stop, number yes (%)	3 (15)
How satisfied are you with the extra practice you received (0-5*), mean (SD)	4.8 (0.5)

* Where 0 is 'strongly not satisfied at all' and 5 is 'very satisfied'

Measurement

Clinical outcomes were collected from all 20 (100%) participants at Week 4 or prior to discharge home or withdrawal.

Clinical

The group clinical outcomes are presented in Table 6.3. There was a mean 0.29 blocks/s (95% CI 0.19 to 0.39) increase on the Box and Block Test from baseline to end of intervention. There was a mean 0.20 pegs/s (95% CI 0.10 to 0.30) increase on the Nine-

Hole Peg Test from baseline to end of intervention. There was a mean 4.4 kg (95% CI 2.9 to 5.9) increase in grip strength from baseline to end of intervention.

Table 6.3. *Mean (SD) for clinical outcomes at each time, mean (95% CI) difference between times and reference values for healthy adults.*

Clinical outcome	Reference value	Times		Difference between times
		Wk 0	Wk 4	Wk 4 minus Wk 0
Box and Block Test *(blocks/s)*	1.3*	0.29 (0.25)	0.58 (0.33)	0.29 (0.19 to 0.39)
Nine-Hole Peg Test (*pegs/s*)	1.0[+]	0.18 (0.20)	0.37 (0.33)	0.20 (0.10 to 0.30)
Grip Strength *(kg)*	32[#]	12 (11)	17 (11)	4 (3 to 6)

*Mathiowetz, Volland, et al. (1985); [+]Mathiowetz, Weber, et al. (1985); [#]Massy-Westropp, Gill, Taylor, Bohannon, and Hill (2011)

CONCLUSION

The results of this study suggest it is feasible for people who are undergoing inpatient rehabilitation and who have some movement in the upper limb after stroke to undertake an extra hour of upper limb practice each day. The extra upper limb practice program was feasible when delivered outside usual therapy time and in a group in the common space of the ward. The magnitude of the clinical outcomes suggests a promising improvement in upper limb activity and grip strength. Adding a self-directed upper limb program to usual rehabilitation appears to be a feasible way to increase the duration of upper limb practice for adults after stroke while considering staff and resource constraints. The results of this study provide useful information for the design of a future large, fully-powered randomised trial designed to investigate the effect of using a self-directed program to increase the duration of practice on upper limb activity in adults after stroke.

Chapter 7: Discussion

This thesis presents a series of studies that sought to better understand the relationship between the amount of practice and improvements in upper limb activity in adults after stroke. This chapter will synthesise the main findings of the four studies presented in this thesis. Directions for future research and the clinical implications from the current research will be given. The limitations of the studies will also be discussed.

SUMMARY OF THE FINDINGS

The systematic review presented in Study 1 provides evidence that extra rehabilitation aimed at reducing activity limitations in either the upper or lower limb on top of usual rehabilitation is effective at improving outcome above that achieved by usual practice. Furthermore, given that the extra practice was of the same content as usual rehabilitation, the effect is purely a result of an increase in the amount of rehabilitation. The amount of extra rehabilitation that needs to be provided to achieve a beneficial effect is large, in the order of 240%.

In Study 2, findings confirm that the Box and Block Test and the Nine Hole Peg can reflect real-world upper limb activity in adults after stroke. There was a threshold difference in performance between the two tests, with the Box and Block Test an easier test to complete than the Nine-Hole Peg Test. The results of this study suggest that an adult after stroke would be able to place at least one peg in 60 seconds on the Nine-Hole Peg Test if they are able to move at least 18 blocks on the Box and Block Test. In addition, an adult after stroke would be able to pick up a cup if they are able to move at least 18 blocks on the Box and Block Test or two pegs on the Nine-Hole Peg Test.

Study 3 demonstrates that a professional development program was associated with an increase in the intensity of practice undertaken during an inpatient, upper limb rehabilitation class. The duration of the class remained unchanged, therefore the results of this study suggests a professional development program focused on evidence-based practice appears to increase the intensity of upper limb rehabilitation. Despite this complexity of changing therapists' behaviour so as to deliver a larger amount of upper limb rehabilitation (Cunningham et al., 2016; Merians et al., 2006; Ross et al., 2009;

Waddell et al., 2014), the observed increase in the intensity of practice remained stable 6 months after the professional development program ended.

Study 4 demonstrates that it appears feasible for people who are undergoing inpatient rehabilitation and have some movement in the upper limb after stroke to undertake an extra hour of upper limb practice, six days per week until discharge or for up to 4 weeks. Participants attended the majority of sessions, practiced for the majority of session duration, rated the acceptability of the intervention as high, and reported a low number of adverse events during the extra upper limb practice. The change observed in the clinical outcomes suggests a promising improvement in upper limb activity and grip strength above what might normally be expected (Kwakkel, Kollen, & Twisk, 2006). For example, it has been suggested that time alone accounts for 16% improvement in impairments over 6-10 weeks (Kwakkel et al., 2006) compared with the 42% improvement in grip strength and 100% improvement in upper limb activity over 4 weeks found in this study.

CONTEXT OF THE FINDINGS

The studies presented in this thesis were carried out in specific contexts which raises issues, and these will now be presented.

The systematic review presented in Study 1 was the first to examine the effect of an extra amount of practice unconfounded by (i) type of practice and (ii) control groups who received no intervention. However, there is another confounding factor that has come to light in the last few years. It is now more possible to predict patients who will not benefit from rehabilitation, i.e., those who do not improve despite receiving large amounts of practice (Bernhardt et al., 2017; Jeffers et al., 2018; Smith, Ackerley, Barber, Byblow, & Stinear, 2019; Stinear et al., 2017). For a systematic review to examine the effect of extra practice, dose-response trials are required. This means that there has to be not only a dose, but also a response, i.e., the control group has to improve in order to be sure that a response was possible by the participants included in the trial. Re-examining the trials that were included in Study 1, all of them report an improvement in upper or lower limb activity in the control group (Cooke, Tallis, et al., 2010; Donaldson et al., 2009; English et al., 2015; GAPS, 2004; Han et al., 2013; Kim et al., 2014; Kowalczewski et al., 2007; Kwakkel et al., 1999b; Page et al., 2012; Ross et al., 2009)

except Partridge et al. (2000) who did not report baseline data. Therefore, the trials included in the review may be considered true dose-response studies. Rehabilitation is resource intensive (Dewey et al., 2001) and given three times the amount of usual rehabilitation is required to guarantee an improvement above usual care (Schneider et al., 2016), being able to identify which people after stroke are more likely to gain the most benefit is vital.

In Study 2, while close to half of the patients scored zero on the Box and Block Test and the Nine Hole Peg Test, this did reflect their upper limb activity in real life. Although half of the patients were unable to complete either test, over 90% of the patients recorded some grip strength, suggesting variation across the included sample. For some patients, this amount of grip strength was not necessarily able to translate into upper limb activity in real life, i.e., picking up a cup and grasping it.

In Study 3, the increase in the intensity of practice undertaken during an inpatient, upper limb rehabilitation class was studied. Intensity of practice was measured as repetitions over time. This produces some problems of interpretation, given that the time to complete one repetition must be considered. For example, a patient with minimal upper limb activity may practice a task continuously but only complete a small number of repetitions if the level of challenge is very high. The effort required to complete the repetition may be significant and while the proportion of practice time per class may remain high, the number of repetitions per practice time may be low (as it may take some time to complete one repetition). Furthermore, cyclic electrical stimulation may deliver an increase in the repetitions per practice time compared to a task completed with active movement (e.g., reach and grasp), since the time required to complete one repetition for the person with upper limb activity impairment may be greater than the time required to complete the electrical stimulation repetition. This may explain the observed decrease in the repetition rate between 12 months and 18 months in Study 3.

In Study 4, the increase in the duration of practice undertaken during inpatient, upper limb rehabilitation was studied. This study provided evidence that extra practice was feasible, however this was not able to be provided within the usual resources available within the inpatient rehabilitation unit. The participants were often unavailable during usual working hours, either completing usual daily activities (shower, dress, eat), engaged in usual rehabilitation, resting, or with family/ visitors. Therefore, the extra

upper limb practice was often undertaken after usual rehabilitation and before dinner (4.30-5.30pm) and within the common space in the ward to reduce transportation and where nursing staff could ensure the safety of the participants during self-directed practice. Seventy-two percent of the self-directed practice was undertaken in a group in the ward. Findings suggest that in the context of inpatient rehabilitation delivering extra upper limb practice may best be done using a group format outside normal hours.

COMPARISON OF THE FINDINGS TO PREVIOUS RESEARCH

In Study 1, the results of the review are in line with previous meta-analyses which suggest a beneficial effect of extra rehabilitation after stroke (Kwakkel, van Peppen, et al., 2004; Lohse et al., 2014; Veerbeek et al., 2011). The finding from the meta-analysis with all studies included produced an effect size of 0.39, which is similar to the small effect sizes ranging from 0.13 to 0.35 previously reported (Kwakkel, van Peppen, et al., 2004; Lohse et al., 2014; Veerbeek et al., 2011). However, when excluding studies which delivered only a small increase in rehabilitation, the larger effect size of 0.59 was found. Extra rehabilitation was defined as additional practice of exactly the same activity provided in usual practice. Because of this tight definition of 'extra', some studies which had been included in the previous reviews (Kwakkel, van Peppen, et al., 2004; Lohse et al., 2014; Veerbeek et al., 2011) were excluded which may account for the finding of a larger effect size in Study 1 than found previously. There has been only one systematic review examining amount of rehabilitation (Galloway et al., 2019) published since Study 1. This recent review, however, was designed to determine the effect of different amounts of exercise on cardiorespiratory fitness in adults more than six months after stroke (Galloway et al., 2019) rather than on activity performance. Similar to Study 1, the authors were limited by the number of well designed trials to make comparisons. While only five included trials directly compared different doses of exercise intensity, no trials compared different doses of exercise session duration (Galloway et al., 2019). Galloway and colleagues (2019) were, therefore, limited in drawing their conclusion but found a dose-response relationship between exercise at higher intensities (e.g., > 70% heart rate reserve) and improving cardiorespiratory fitness, but that these cardiorespiratory improvements might not translate to improvements in walking capacity (Galloway et al., 2019). They report that future trials must be designed to change only one aspect of amount of practice at one time to examine the dose-response effect (Galloway et al., 2019). There are two other protocols registered with the Prospective

Register of Systematic Reviews (PROSPERO) which may shed light in the future on this important issue (Ibrahim, Lawal, & Joseph, 2020; Michaelsen, Parizotto, de Souza, & da Silva, 2019).

Given that the search for systematic review presented in Study 1 was performed only up to October 2015, I have now updated the search to June 2020. There is only one new randomised trial that fits the Study 1 inclusion criteria. In this trial investigating different amounts of the same intervention, they found a small beneficial effect from additional practice, however participants in the experimental group only completed a 140% increase in the number of sit to stand repetitions compared with the control group (de Sousa et al., 2019). Unlike some of the papers included in the systematic review, the 140% increase in the amount of usual practice was calculated from actual sit to stand repetitions and not the intended session duration. This may account for the small beneficial effect despite providing a smaller increased than the 240% increase recommended. Furthermore, the overall, effect sizes were small, indicating uncertainty as to whether the treatment effect was clinically worthwhile (de Sousa et al., 2019). Even though this trial was published three years after the review, the amount of extra practice is well below the 240% increase in the amount of usual rehabilitation recommended in the review, demonstrating the ongoing challenge of translating research findings into practice.

In Study 2, there were many participants with significant upper limb activity limitations who were unable to register a score on either the Box and Block Test (43%) nor the Nine-Hole Peg Test (60%), i.e., both tests demonstrated a floor effect. However, the floor effect of the Nine-Hole Peg Test was larger. This finding is consistent with previous research which has found that at least some degree of upper limb activity is required to complete the Nine-Hole Peg Test (Jacob-Lloyd et al., 2005), and that the Box and Block Test is more responsive for detecting change in upper limb activity after stroke since more of adults after stroke can complete the test (Jacob-Lloyd et al., 2005; Lin et al., 2010). While Lin and colleagues (2010) concluded that the Box and Block Test is the preferred measure of upper limb activity in adults after stroke, the findings from Study 2 are more consistent with those of Thompson-Buteland colleagues (2004). These authours concluded that the suitability of different tests will depend on the activity level of the person completing the test (Thompson-Butel et al., 2014).

In Study 3, after the professional development program, the proportion of practice time

per class more than doubled (32 to 84%) and the repetitions per practice time more than tripled (2.2 min to 7.2 reps/min). This finding is consistent with a Cochrane review that synthesised 81 studies investigating professional development programs, which suggested that educational meetings (alone or combined with other interventions) can improve professional practice (Forsetlund et al., 2009) and supports previous research that has identified the successful use of specific models or frameworks for changing health professional behaviours (French et al., 2012; McCluskey et al., 2013; Michie et al., 2005; Novak & McIntyre, 2010; Petzold et al., 2012). However, the positive finding from Study 3 is in conflict with the research into professional development in rehabilitation, which has reported that professional development alone does not change clinical practice (McCluskey et al., 2016; McCluskey & Lovarini, 2005; Stevenson, Lewis, & Hay, 2006). The differences in method between the studies may account for the conflicting findings. Consistent with the Cochrane systematic review, the program in Study 3 provided staff education followed by staff meetings whereby staff themselves worked out how to integrate the training (i.e., staff were responsible for generating the solutions themselves). In this way, there are aspects of the professional development program which align with knowledge translation programs, and this may have influenced staff behaviour. As such, a program where one component is education, rather than education alone, was associated with an increases in the intensity of practice during an upper limb rehabilitation class. Implementation strategies and knowledge translation methods are now more defined and have been applied to increase adherence to clinical practice guidelines (Connell, Klassen, Janssen, Thetford, & Eng, 2018; Jolliffe, Hoffmann, & Lannin, 2019; Jolliffe, Morarty, et al., 2019). For example, the application of an audit and feedback model increased staff adherence to stroke guidelines in an inpatient acquired brain injury rehabilitation setting from 39% (95% CI 34 to 44) to 84% (95% CI 82 to 89) (Jolliffe, Morarty, et al., 2019).

In Study 4, adults undergoing inpatient rehabilitation were able to undertake 57 minutes of extra upper limb practice during a 73-minute session, on top of 37 minutes of usual upper limb rehabilitation per day. These results are comparable to the average amount of practice that the trials in Study 1 delivered; 37 minutes of usual upper limb rehabilitation per day to both groups and an extra 73 minutes of extra upper limb rehabilitation per day to the experimental group. In Study 4, this equates to a 200% increase in the amount of usual rehabilitation, only slightly less than the 240% increase suggested in Study 1. Furthermore, reports of fatigue, illness, or muscle soreness was low (12%) and consistent

with other studies in similar settings for adults after stroke (Bower, Clark, McGinley, Martin, & Miller, 2014; Stanton, Ada, Dean, & Preston, 2016). It has now been shown that most rehabilitation can be delivered without one-on-one supervision without resulting in a reduction in outcome for adults after stroke (Dorsch, Weeks, King, & Polman, 2019; Renner et al., 2016). A systematic review of efficacy of upper limb rehabilitation that will include the dose of therapy (minutes, weeks, repetitions) is currently underway (Hayward et al., 2019) and should provide key information.

STRENGTHS AND LIMITATIONS OF THE FINDINGS

In Study 1, the meta-analyses are likely to be affected by small study bias, with an average number of 35 participants each study. Also, the number of comparisons included in the meta-analysis was reduced by the reporting of medians in clinical trials where there were highly skewed data which could not be converted to means (SD). However, the mean PEDro score (>7 out of 10) shows that the included studies were of high quality and findings therefore are robust. The strengths of this review are that using studies of high quality, the estimate of the effect of extra rehabilitation after stroke is unconfounded by type of practice, and this has led to the estimation of the amount of extra practice needed to improve outcome over that achieved by usual care after stroke.

In Study 2, the main limitation is that the findings are relevant to a select group of adults after stroke who experience significant activity limitations but without moderate or severe cognitive or sensory impairments. The sample was drawn from a clinical population and included large numbers of people who were unable to register a score on either of the Box and Block Test nor the Nine Hole Peg Test. The mean rate attained by the sample on the Box and Block Test was 0.17 blocks/s which is substantially lower than the mean values reported in the literature >0.3 blocks/s. Together these may limit the generalisability of the study's findings. A further limitation was that the occupational therapy assessors were not blind to the aims of the study which may, in turn, have biased the findings (Anastasi & Urbina, 1997). And finally, self-reported ability to pick up a cup was used and not actual observed performance; that said, previous research suggests that there is a strong relationship between observed and self-reported physical ability after stroke (Teixeira-Salmela, Devaraj, & Olney, 2007).

In Study 3, the design does not allow the authors to be sure that the professional

development program was the cause of the increase in the intensity of practice undertaken in the upper limb class. First, the design did not control for the diagnosis of patients attending the upper limb classes, as participants were not the same at each of the three time periods. Specifically, the number of patients diagnosed with a stroke or stroke-like condition reduced over the data collection periods and may have contributed to the increase in intensity of practice at each time point. The potential for this increase to translate to patients with a stroke or stroke-like condition is therefore unknown. Second, our method did not control for potential observational errors associated with the observer reporting time and repetition data, particularly given that the observer was monitoring two variables for several people within the group at the one time. Third, the design did not control for the education of the staff who facilitated the classes at each of the three time periods. Staff differed in whether they had attended a professional development session across time periods and this may have had an impact on the intensity of practice. However, the staff to patient ratios were similar across time periods. Fourth, our method did not include the use of a behaviour change theory or framework (such as the Theoretical Domains Framework (Cane, O'Connor, & Michie, 2012) or the Capability, Opportunity, Motivation, Behaviour (COM-B) model (Michie, Atkins, & West, 2014)) to inform and guide design of the professional development program. Using an implementation science method, rather than one of ongoing professional development, may have led to a different set of unique strategies being employed to address the needs of the staff participants in Study 3.

In Study 4, access to one AbleX device limited the number of adults who could complete the extra upper limb practice program at one time and in some circumstances, recruitment was stopped to ensure delivery of the intervention. While the enrollment of 48% of the eligible participants is comparable to other studies (Lannin et al., 2018), access to more than one AbleX program, or use of the GRASP program alone, may improve the recruitment of future studies. Second, there was a high rate of early discharge; participants completed the extra upper limb practice program for a mean of three weeks, delivered over a mean of 20 session. This suggests that future trials either need to continue the program after discharge or reduce the duration from four to three weeks. Third, while the clinical outcomes suggest a promising improvement in upper limb activity and grip strength, it must be noted that all participants had some movement at the time of recruitment, which suggests they were capable of recovery due to having

had an intact corticospinal tract (Stinear et al., 2017). Fourth, the use of assessors who were aware of the study aims may have led to bias estimates of clinical outcomes.

IMPLICATIONS OF THE FINDINGS FOR RESEARCH

Findings of Study 1 have significant implications for research investigating substantial increases in practice. The review presented in Study 1 suggests that the provision of extra rehabilitation is feasible, and that programs need to provide a substantial amount of rehabilitation to guarantee an improvement in activity above that achieved by usual care. Future randomised trials investigating substantial increases in practice (i.e., more than 240% extra rehabilitation) are needed to further clarify the relationship between increasing the amount of rehabilitation and activity after stroke. However, in the only randomised trial that fits the inclusion criteria published since 2016, participants in the experimental group completed only 140% increase in the number of sit to stand repetitions compared with the control group (de Sousa et al., 2019). There are several other things learnt from this systematic review. Recently it was reported that only 36% randomised controlled trials report the amount and intensity of stroke rehabilitation intervention where two or more intervention doses were studied (Borschmann et al., 2018). This makes it difficult to work out the effect of amount of practice on outcome. Also, additional strategies to exclude patients who are known to not benefit from an increase in the amount of usual rehabilitation are needed (Bernhardt et al., 2017; Jeffers et al., 2018; Smith et al, 2019; Stinear et al., 2017). As noted in Chapter 2, there is a definite group of adults after stroke who do not demonstrate real recovery despite undertaking stroke rehabilitation (Bernhardt et al., 2017; Connell, Smith, Byblow, & Stinear, 2018; Jeffers et al., 2018; Smith et al., 2019; Stinear et al., 2017). There is a growing need for stroke research to be able to characterise and predict which people after stroke are more likely than others to respond to a given intervention (Bernhardt et al., 2017; Boyd et al., 2017; Jeffers et al., 2018; Smith et al., 2019; Stinear et al., 2017). Further, the lack of consistent outcome measures does not aid clarity of outcome of systematic reviews. This lack of consistent outcome measures for pooled analysis is a common problem facing systematic reviews of motor stroke recovery trials (Kwakkel et al., 2017). A core set of outcome measures and measurement time points has been proposed to address this issue (Bernhardt et al., 2017; Kwakkel et al., 2017; Kwakkel et al., 2019). When larger trials that use consistent outcome measures are completed, this

systematic review will be able to repeated in a way that will furnish more specific information.

In Study 2, a sample of convenience was used and this resulted in a cohort of adults after stroke of whom close to half were unable to register a score on either of the Box and Block Test nor the Nine Hole Peg Test. Although this may be representative of a usual stroke population, it would be useful to repeat this study with a sample of adults after stroke that was stratified in order to cover the whole range of possible levels of upper limb activity. Furthermore, while this study has established the relationship between self-reported picking up a cup and performance on the Box and Block Test and the Nine-Hole Peg Test, further investigation into how the test scores reflect observed upper limb activity for a range of different tasks (such as using cutlery, doing up buttons, etc.) is warranted.

Studies 3 and 4 were both pre- post-test studies investigating the potential of a professional development program (Study 3) and self-directed practice (Study 4) to increase the intensity (Study 3) and duration (Study 4) of practice during inpatient rehabilitation. Both studies show promise for the interventions studied. In Study 3, the increase in the intensity of practice at the site was maintained for 6 months after the cessation of the program. In Study 4, clinical outcomes suggest a promising improvement in upper limb activity and grip strength. However, these interventions are not ready for implementation in the clinic. Further investigation is warranted in the form of Phase II randomised trials.

IMPLICATIONS OF THE FINDINGS FOR CLINICAL PRACTICE

The main finding from Study 1 is the large increase in the amount of practice required to guarantee improvement in upper limb activity over usual care for adults after stroke. The impact of this systematic review has been large. It has made a novel contribution to the Australian Clinical Guidelines for Stroke Management (Figure 7.1) (Stroke Foundation, 2017) which means that it has significant implications for clinical practice. Not only does the 2017 version recommend "as much scheduled therapy (occupational therapy and physiotherapy) as possible" (Stroke Foundation, 2017, Chapter 5 of 8: Rehabilitation) but it also goes on to specify "a minimum of three hours a day of scheduled therapy (occupational therapy and physiotherapy) is recommended, ensuring at least two hours of

active task practice occurs during this time" (Stroke Foundation, 2017, Chapter 5 of 8: Rehabilitation). These are significantly important recommendations and provide clear justification for therapists to argue for increased resources in order to deliver more rehabilitation. In fact, both of these recommendations cite the systematic review presented in Study 1. Furthermore, a recent editorial examining the current state of play of the dose-response relationship between practice and outcome and strategies to increase the amount of practice undertaken by people with stroke also references this systematic review (Dorsch & Elkins, 2020). To date, 64 publications cite the systematic review presented in Study 1, demonstrating the importance of the research presented in this thesis to clinical practice.

(Australian) Stroke Foundation Clinical Guidelines for Stroke Management, 2010 **Section 2: Rehabilitation; amount and intensity of rehabilitation**		**Grade**
a)	Rehabilitation should be structured to provide as much practice as possible within the first six months after stroke.	A[470]
b)	For patients undergoing active rehabilitation, as much physical therapy (physiotherapy and occupational therapy) should be provided as possible with a minimum of one hour of active practice per day at least five days a week.	GPP
c)	Task-specific circuit class training or video self-monitoring should be used to increase the amount of practice in rehabilitation.	B[471, 472]
d)	For patients undergoing active rehabilitation, as much therapy for dysphagia or communication difficulties should be provided as they can tolerate.	C[476, 477-479]
e)	Patients should be encouraged by staff members, with the help of their family and/or friends if appropriate, to continue to practice skills they learn in therapy sessions throughout the remainder of the day.	GCP

(Australian) Clinical Guidelines for Stroke Management 2017 (v5.4 published on 21/11/2019) **Chapter 5 of 8: Rehabilitation; amount of rehabilitation**
Strong recommendation • For stroke survivors, rehabilitation should be structured to provide as much scheduled therapy (occupational therapy and physiotherapy) as possible. (Lohse et al. 2014; Schneider et al. 2016; Veerbeek et al. 2014) • For stroke survivors, group circuit class therapy should be used to increase scheduled therapy time. (English et al. 2015)

Practice statement
• Stroke survivors should be encouraged to continue with active task practice outside of scheduled therapy sessions. This could include strategies such as:
  ○ self-directed, independent practice;
  ○ semi-supervised and assisted practice involving family/friends, as appropriate.

Weak recommendation • A minimum of three hours a day of scheduled therapy (occupational therapy and physiotherapy) is recommended, ensuring at least two hours of active task practice occurs during this time. (Lohse et al. 2014; Schneider et al. 2016)

Figure 7.1. *Comparison of the summarised evidence for the amount of rehabilitation taken from the 2010 and 2017 Australian Stroke Foundation Guidelines (Stroke Foundation, 2010, 2017).*

The effect size of 0.59 from the systematic review presented in Study 1 is encouraging. In order to compare the amount of extra rehabilitation across studies, the extra was presented as a percentage increase. This method, while accurate, produces high numbers. For example, if usual rehabilitation involved 15 minutes of walking practice, and the extra amount of walking delivered was 30 minutes, then the increase was 200%. Also, these calculations used 'intended' increase in rehabilitation since this was consistently reported across the studies. It is possible that the 'intended' increase in rehabilitation did not match the 'actual' amount delivered. However, in those studies that reported both (intended and actual), 93% of the intended amount was actually delivered. Of the studies that delivered a substantial increase in rehabilitation amount, the average dose of usual rehabilitation was approximately 25 minutes per day in the control group and the average dose of extra therapy provided was 260% (i.e., a total of 90 minutes per day) in the experimental group. These numbers align well with the findings from the ROC curve analysis, suggesting that at least a 240% increase in rehabilitation is necessary to result in an improvement in activity. Clinically, for example, if a therapy service usually provides 30 minutes of reach and grasp rehabilitation per day, in order to ensure a better outcome, approximately 100 minutes of reach and grasp rehabilitation per day would be required. The challenge now is to determine how to increase the amount of rehabilitation. Implementation will demand a change in clinical practice that is far-reaching involving models of delivery, patient expectations, and therapist beliefs. Clinicians will need to apply novel methods to deliver around three times the amount of usual upper limb rehabilitation (Study 1). To deliver this increased amount of usual upper limb rehabilitation, clinicians will need to employ strategies to deliver upper limb practice of higher intensity and of longer duration, explored in both Study 3 and Study 4.

The findings of Study 2 suggest that while both the Box and Block Test and the Nine-Hole Peg Test measure upper limb activity in adults after stroke, the two tests are not interchangeable. Although the Nine-Hole Peg Test is a more difficult test to complete, the test result may be more accurate reflection of the amount of upper limb activity required for everyday life. If the purpose of the test is to reflect real upper limb activity, then the Nine-Hole Peg Test may in fact be more appropriate since the amount of upper limb activity required to move a peg is likely more consistent with the upper limb activity required to perform meaningful tasks in real life. The selection of which test to use may depend more on the purpose of measurement. If the purpose is for the test

scores to reflect the upper limb activity in real life, then the Nine-Hole Peg Test may provide a more accurate estimate than the Box and Block Test. If, on the other hand, the purpose is to detect small amounts of improvement at a sub-clinical level (i.e., minimal upper limb activity), then the Box and Block Test will be more responsive than the Nine-Hole Peg Test.

CONCLUSIONS

The studies presented in this thesis examined whether an increase in the amount of usual rehabilitation improves upper limb activity, the clinical utility of two common measures of upper limb activity, and two methods of delivering this extra practice to adults after stroke during inpatient rehabilitation. This thesis has made a valuable contribution to the body of knowledge about the amount of practice designed to target upper limb activity limitations in adults after stroke. It has provided clear evidence that an increase in the amount of usual rehabilitation by a significant amount (at least three times the amount of usual rehabilitation) needs to be provided to improve upper limb activity over the outcome achieved with usual rehabilitation. This thesis also presents preliminary investigations of two methods that inpatient rehabilitation services can deliver this extra practice. First, increasing the intensity of practice through the application of staff education programs. Second, increasing the duration of practice through extra practice sessions. Finally, a study has identified that while the Nine-Hole Peg Test is a more difficult test to complete than the Box and Block Test, it may be a more accurate reflection of upper limb activity in real life. Together these studies provide promising results. It is recommended that a phase II randomised trial now be conducted to evaluate the benefit of a large dose of extra practice, and that health service research also be conducted to better understand how to deliver these amounts of practice on a large scale.

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- Schneider EJ, Lannin NA, Ada L (2019). A professional development program increased the intensity of practice undertaken in an inpatient, upper limb rehabilitation class: a pre-post study. *Australian Occupational Therapy Journal*, 66 (3):362-368. doi: 10.1111/1440-1630.12562
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- Schneider EJ, Lannin NA, Ada L (2014). Increasing the intensity of rehabilitation to improve activity after stroke: a systematic review protocol. *Journal of Clinical Trials* 4:195. doi: 10.4172/2167-0870.1000195
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- Schneider EJ, Lannin NA, Ada L, Schmidt J (2016). Increasing the amount of usual rehabilitation improves activity after stroke: a systematic review. *Journal of Physiotherapy, 62(4):182-187.* doi:10.1016/j.jphys.2016.08.006
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  Date materials were obtained: May 6th 2020

- Schneider EJ, Ada L, Lannin NA (2019). Extra upper limb practice after stroke: a feasibility study. *Pilot and Feasibility Studies*, 5,156.
  doi: 10.1186/s40814-019-0531-5
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  Date materials were obtained: May 6th 2020

Appendix B: Ethics

The ethics approval and the participant information and consent forms for the collection of data used in study 2, along with the ethics approval, participant information and consent forms for Studies 2 and 4 are presented.

Study 2

- Ethics approval, Alfred Health
- Ethics approval, La Trobe University
- Participant information and consent forms

Study 3

- Ethics approval, Alfred Health
- Ethics approval, La Trobe University

Study 4

- Ethics approval certificate, Alfred Health
- Ethics approval certificate, La Trobe University
- Participant information and consent form

ETHICS COMMITTEE CERTIFICATE OF APPROVAL

This is to certify that

Project No: 367/17

Project Title: How do results on the Box and Block Test relate to other measurements of upper limb function?

Principal Researcher: A/Professor Natasha Lannin

Project Proposal Version 1.4 **dated:** 28-Aug-2017

Participant Information and Consent Form Version 1.2 **dated:** 15-Aug-2017
Person Responsible Information and Consent Form Version 1.2 **dated:** 15-Aug-2017

*was considered by the Ethics Committee on **24-Aug-2017**, meets the requirements of the National Statement on Ethical Conduct in Human Research (2007) and was **APPROVED** on **18-Sep-2017**.*

It is the Principal Researcher's responsibility to ensure that all researchers associated with this project are aware of the conditions of approval and which documents have been approved.

The Principal Researcher is required to notify the Secretary of the Ethics Committee, via amendment or progress report, of

- Any significant change to the project and the reason for that change, including an indication of ethical implications (if any);
- Serious adverse effects on participants and the action taken to address those effects;
- Any other unforeseen events or unexpected developments that merit notification;
- The inability of the Principal Researcher to continue in that role, or any other change in research personnel involved in the project;
- Any expiry of the insurance coverage provided with respect to sponsored clinical trials and proof of re-insurance;
- A delay of more than 12 months in the commencement of the project; and,
- Termination or closure of the project.

Additionally, the Principal Researcher is required to submit

- A Progress Report on the anniversary of approval and on completion of the project *(forms to be provided)*;

The Ethics Committee may conduct an audit at any time.

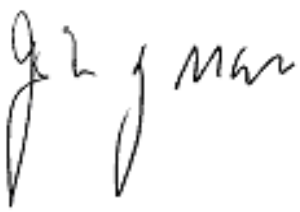
All research subject to the Alfred Hospital Ethics Committee review must be conducted in accordance with the National Statement on Ethical Conduct in Human Research (2007).

The Alfred Hospital Ethics Committee is a properly constituted Human Research Ethics Committee in accordance with the National Statement on Ethical Conduct in Human Research (2007).

SPECIAL CONDITIONS

None

SIGNED:



Professor John J. McNeil
Chair, Ethics Committee

Please quote project number and title in all correspondence

ETHICS COMMITTEE CERTIFICATE OF APPROVAL

This is to certify that

Project No: 442/14

Project Title: The InTENSE trial: optimising upper limb recovery following stroke

Principal Researcher: A/Prof Natasha Lannin

Protocol, Version 1.2, dated: 18/Nov/2014

Participant Information and Consent Form, Version 3, dated: 03/Dec/2014

*was considered by the Ethics Committee on **27/Nov/2014**, meets the requirements of the National Statement on Ethical Conduct in Human Research (2007) and was **APPROVED** on **11/Dec/2014***

It is the Principal Researcher's responsibility to ensure that all researchers associated with this project are aware of the conditions of approval and which documents have been approved.

The Principal Researcher is required to notify the Secretary of the Ethics Committee, via amendment or progress report, of

- Any significant change to the project and the reason for that change, including an indication of ethical implications (if any);
- Serious adverse effects on participants and the action taken to address those effects;
- Any other unforeseen events or unexpected developments that merit notification;
- The inability of the Principal Researcher to continue in that role, or any other change in research personnel involved in the project;
- Any expiry of the insurance coverage provided with respect to sponsored clinical trials and proof of re-insurance;
- A delay of more than 12 months in the commencement of the project; and,
- Termination or closure of the project.

Additionally, the Principal Researcher is required to submit

- A Progress Report on the anniversary of approval and on completion of the project *(forms to be provided)*;

The Ethics Committee may conduct an audit at any time.

All research subject to the Alfred Hospital Ethics Committee review must be conducted in accordance with the National Statement on Ethical Conduct in Human Research (2007).

The Alfred Hospital Ethics Committee is a properly constituted Human Research Ethics Committee in accordance with the National Statement on Ethical Conduct in Human Research (2007).

SPECIAL CONDITIONS

Provision of clinical trial registration details before commencing the study.

SIGNED:

Professor John J. McNeil
Chair, Ethics Committee

Please quote project number and title in all correspondence

LA TROBE UNIVERSITY

University Human Ethics Committee

RESEARCH OFFICE

MEMORANDUM

To: **Dr Natasha Lannin, School of Allied Health, College of SHE**

From: **Senior Human Ethics Officer, Ethics and Integrity**

Subject: **UHEC acceptance of The Alfred HREC approved project – 367/17**

Title: **How do results on the Box and Block Test relate to other measurements of upper limb function?**

Date: **31 October, 2017**

Thank you for submitting the above protocol to the University Human Ethics Committee (UHEC). Your material was forwarded to the UHEC Chair for consideration. Following evidence of a full review and subsequent final approval by the **The Alfred HREC**, the UHEC Chair agrees that the protocol complies with the National Health and Medical Research Council's *National Statement on Ethical Conduct in Human Research* and is in accordance with La Trobe University's *Human Research Ethics Guidelines*.

Endorsement is given for you to take part in this study in line with the conditions of final approval outlined by **The Alfred HREC.**

Limit of Approval. La Trobe UHEC endorsement is limited strictly to the research protocol as approved by **The Alfred HREC**.

Variation to Project. As a consequence of the previous condition, any subsequent modifications approved by **The Alfred HREC** for the project should be notified formally to the UHEC.

Annual Progress Reports. Copies of all progress reports submitted to **The Alfred HREC** must be forwarded to the UHEC. Failure to submit a progress report will mean that endorsement for your involvement this project will be rescinded. An audit related to your involvement in the study may be conducted by the UHEC at any time.

Final Report. A copy of the final report is to be forwarded to the UHEC within one month of it being submitted to **The Alfred HREC.**

If you have any queries on the information above please e-mail: **humanethics@latrobe.edu.au** or

contact me by phone.

On behalf of the La Trobe University Human Ethics Committee, best wishes with your research!

Kind regards,

Sara Paradowski
Senior Human Ethics Officer
Executive Officer – University Human Ethics Committee
Ethics and Integrity / Research Office
La Trobe University Bundoora, Victoria 3086
P: (03) 9479 – 1443 / F: (03) 9479 - 1464
http://www.latrobe.edu.au/researchers/ethics/human-ethics

LA TROBE UNIVERSITY

University Human Ethics Committee

RESEARCH OFFICE

MEMORANDUM

To: **A/Prof Natasha Lannin, Allied Health, College of SHE**

From: **Executive Officer, La Trobe University Human Ethics Committee**

Subject: **UHEC acceptance of The Alfred HREC approved project – 442/14**

Title: **The InTENSE trial: optimising upper limb recovery following stroke**

Date: **5 February 2015**

Thank you for submitting the above protocol to the University Human Ethics Committee (UHEC). Your material was forwarded to the UHEC Chair for consideration. Following evidence of a full review and subsequent final approval by the **The Alfred HREC**, the UHEC Chair agrees that the protocol complies with the National Health and Medical Research Council's *National Statement on Ethical Conduct in Human Research* and is in accordance with La Trobe University's *Human Research Ethics Guidelines*.

Endorsement is given for you to take part in this study in line with the conditions of final approval outlined by **The Alfred HREC.**

Limit of Approval. La Trobe UHEC endorsement is limited strictly to the research protocol as approved by **The Alfred HREC**.

Variation to Project. As a consequence of the previous condition, any subsequent modifications approved by **The Alfred HREC** for the project should be notified formally to the UHEC.

Annual Progress Reports. Copies of all progress reports submitted to **The Alfred HREC** must be forwarded to the UHEC. Failure to submit a progress report will mean that endorsement for your involvement this project will be rescinded. An audit related to your involvement in the study may be conducted by the UHEC at any time.

Final Report. A copy of the final report is to be forwarded to the UHEC within one month of it being submitted to **The Alfred HREC.**

If you have any queries on the information above please e-mail: **humanethics@latrobe.edu.au** or contact me by phone.

On behalf of the La Trobe University Human Ethics Committee, best wishes with your research!

Kind regards,

Sara Paradowski
Senior Human Ethics Officer
Executive Officer – University Human Ethics Committee
Ethics and Integrity / Research Office
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http://www.latrobe.edu.au/researchers/ethics/human-ethics

AlfredHealth

Participant Information and Consent Form- Adult providing own consent

Title: How do results on the Box and Block Test relate to other measurements of upper limb function?

Coordinating Principal Investigator: A/Professor Natasha Lannin

Associate Investigators: Megan White

Dr Kate Laver

Location: Alfred Health

Part 1 What does participation involve?

1. Introduction

You are invited to take part in this research project. This is because you have difficulties using one of your arms after a stroke. This research project provides us with information about assessment tools used to measure arm function after stroke.

This Participant Information Sheet/ Consent Form tells you about the research project. It explains the process involved. Knowing what is involved will help you decide if you want to take part in this research. Please read this information carefully and ask questions about anything that you don't understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative or friend.

Participation in this research is voluntary- if you do not wish to take part you don't have to. You will receive the best possible care whether or not you take part in this study. If you decide you want to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:

- Understand what you have read
- Consent to take part in the research project
- Consent to participate in the tests that are described
- Consent to the use of your personal and health information as described

You will be given a copy of this Participant Information and Consent Form to keep.

2. What is the purpose of this research?

One of the most common difficulties experienced after a stroke is a loss of movement or strength in one arm, limiting the ability to perform everyday activities. Therapists have a number of specific assessments that they do to measure function. For example, therapists may test how strongly you can grip something, or how easily you can pick up items. However, while these assessments are a routine component of therapy, we need to learn more about which are the most appropriate assessments to use and what information they provide.

3. What does participation in this research involve?

You will be asked to participate in arm and hand measurements as well as a short questionnaire. An occupational therapist will visit you to complete these measures. The measures will involve testing the strength in your arm as well as how quickly you can pick up and transport objects (such as small blocks and pegs). You will also be asked to rate how much you can use your arm in a range of everyday common tasks. It is expected that the therapist will spend approximately 20 minutes with you performing these assessments.

There are no additional costs associated with participating in this research project, nor will you be paid.

4. Other relevant information about the research project

This study is being conducted across all of Alfred Health. This includes all three sites including Alfred Hospital, Sandringham Hospital and Caulfield Hospital.

5. Do I have to take part in this research project?

Participation in any research project is voluntary. If you do not wish to take part, you do not have to. If you decide to take part and later change your mind, you are free to withdraw from the project at any time. Your decision whether you should take part or not take part, or to take part and then withdraw, will not affect your usual treatment, nor your relationship with the staff that treat you, nor your relationship with Alfred Health or with members of the research team.

6. What are the potential benefits of taking part?

While you may not receive any direct benefit from participating in this research, your participation will assist therapists to broaden their knowledge and provide the best care to future stroke patients.

7. What are the possible risks and disadvantages of taking part?

There are no known risks associated with participating in this study. Assessments used in this study are considered usual practice. The risk of discomfort or distress from being involved in this study is no greater than that associated with a routine rehabilitation program.

If you become upset or distressed as a result of participating in the research, a qualified person who is not a member of the research project, will be made available to provide counselling or support.

8. Can I have other treatments during this research project?

Yes, there will be no change to your usual care or therapy received while participating in this project.

9. What if I withdraw from this research project?

If you decide to take part and then later change your mind, you are free to withdraw for a period of up to two months after participation. After this date, your data will have been de-

identified and analysed along with other participants. If you do want to withdraw, please complete the attached Withdrawal of Participation Form.

10. Could this research project be stopped unexpectedly?

While unlikely, this research project would be stopped unexpectedly because of natural disaster or staff turnover.

11. What happens when the research project ends?

All non-identifiable data (electronic and hard copy) will be kept at the Alfred for 7 years in a secure environment. The information will be kept confidential and destroyed privately afterwards. The results of the study will be presented at conferences and published in health journals.

Part 2- How is the research project being conducted?

12. What will happen to information about me?

By signing the consent form you consent to the Occupational Therapist and relevant research staff collecting and using information about you for the research project. Any information obtained in connection with this research project will not identify you once collected. Information recorded on paper will be stored in a locked storage facility in the office of Associate Professor Natasha Lannin at Alfred Health. Electronic databases will be password protected. Your information will only be used for the purpose of this research project. Information will be securely stored for 7 years and then destroyed in line with Alfred Health procedures. Information about your involvement in this research project will be recorded in your progress notes at Alfred Health.

Information about you may be obtained from your health records held at Alfred Health for the purpose of this research. It is anticipated that results of this research project will be published and/or presented in a variety of forums. Your name and personal information will not be used in any publication or presentation.

In accordance with relevant Australian and/or Victorian privacy and other relevant laws, you have the right to request access to your own information collected and stored by the research team. You also have the right to request that any information with which you disagree be corrected. Please contact Megan White on 9076 7423 if you would like to access your information.

13. Complaints

If you are unhappy about any aspect of the study and wish to make a complaint, please contact the Research Governance Officer, Office of Ethics & Research Governance, Alfred Health. Please refer to the section **'Further Information and who to contact'** for these contact details.

14. What happens if I am injured as a result of participating in this research project?

If you suffer an injury as a result of your participation in this research project, please contact the research staff. Hospital care and treatment will be provided by the public health care system (Medicare) at no cost to you if you are eligible for Medicare benefits and elect to be treated as a public patient.

15. Who is organising and funding the research?

This research project is being conducted by Megan White (Occupational Therapist), Associate Professor Natasha Lannin (Alfred Health and LaTrobe University) and Dr Kate Laver (Flinders University). There is no commercial sponsorship and no financial reward is being obtained.

16. Who has reviewed the research project?

This study has been reviewed by the National Health and Medical Research Council. All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethics aspects of this research project have been approved by the HREC of Alfred Health.

This project will be carried out according to the National Statement on Ethical Conduct in Human Research (2007). This statement has been developed to protect the interests of people who agree to participate in human research studies.

17. Further information and who to contact

The person who you may need to contact will depend on the nature of your query. All contacts listed below are available during working hours.

Name	Megan White
Position	Occupational Therapist
Telephone	9076 7423
Email	m.white@cgmc.org.au

For matters relating to research at the site at which you are participating, the details of the local site complaints person are:

Complaints contact person

Name	Complaints Officer
Position	Office of Ethics & Research Governance, Alfred Health
Telephone	9076 3619
Email	research@alfred.org.au

Consent Form- Adult providing own consent

Title: How do results on the Box and Block Test relate to other measurements of upper limb function?

Protocol Number:

Coordinating Principal Investigator/
Principal Investigator: A/Professor Natasha Lannin
Associate Investigator(s): Megan White
Dr Kate Laver

Location: Alfred Health

Declaration by Participant

I have read the Participant Information Sheet or someone has read it to me in a language that I can understand.

I understand the purposes, procedures and risks of the research described in this project.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to participate in this research project as described and understand that I am free to withdraw at any time during the project without affecting my future care.

I understand that I will be given a signed copy of this document to keep.

Name of Participant (please print) _____

Signature _____ Date _____

Declaration by Researcher*

I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.

Name of Researcher† (please print) _____

Signature _____ Date _____

*An appropriately qualified member of the research team must provide the explanation of, and information concerning the research project.

AlfredHealth

LA TROBE UNIVERSITY

Participant Information and Consent Form: Interventional Project

Title: The InTENSE trial: optimising upper limb recovery following stroke (442-14)

Coordinating Principal Investigator	A/Professor Natasha Lannin, PhD, Alfred Health & La Trobe University, Melbourne
Associate Investigators	Dr Mithu Palit Caulfield Hospital, Melbourne
Locations of Study	Caulfield Hospital, Melbourne

Part 1 What does participation involve?

1. Introduction

You are invited to take part in this research project. This is because you have difficulties using one of your arms after a stroke and have been referred for injection with Botulinum Toxin A. The research project is testing whether intense therapy given after botulinum toxin injections into the arm is more helpful than just the injections alone.

This Participant Information Sheet/Consent Form tells you about the research project. It explains the tests and treatments involved. Knowing what is involved will help you decide if you want to take part in the research. Please read this information carefully and ask questions about anything that you don't understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend or your local doctor.

Participation in this research is voluntary- if you don't wish to take part, you don't have to; will receive the best possible care whether or not you take part in this study. If you decide you want to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:

- Understand what you have read
- Consent to take part in the research project
- Consent to having the tests and treatments that are described
- Consent to the use of your personal and health information as described.

You will be given a copy of this Participant Information and Consent Form to keep.

2. What is the purpose of this research?

One of the most common difficulties people experience following stroke is a loss of function in an arm limiting their ability to perform everyday activities. This change is partly caused by tightness in some muscles (spasticity) and weakness in other muscles. Botulinum Toxin A Injections are now routinely used to treat spasticity: the drug Botulinum Toxin relaxes the muscles to help reduce the effects of spasticity and this usually lasts for approximately 5 months.

Intensive therapy programs have been shown to be effective in improving arm function in people post stroke. However, people with spasticity often experience difficulty participating in such programs as the spasticity limits their movement. The impact of therapy used in conjunction with Botulinum Toxin to address the problems of spasticity is not known. This research aims to investigate whether implementing an intensive program of therapy after treatment with Botulinum Toxin is more effective in improving arm use after stroke than receiving the injection of Botulinum Toxin without therapy (which is standard practice).

This research has been initiated by Dr Natasha Lannin (Associate Professor of Occupational Therapy) from Alfred Health and La Trobe University.

3. What does participation in this research involve?

You will be involved in a randomised controlled research project. Sometimes we do not know which treatment is best for treating a condition and to find out we need to compare different treatments. We put people into groups and give each group a different treatment. The results are then compared to see if one is better. To try to make sure the groups are the same, each participant is put into a group by chance (random). This study involves two different participant groups:

Group 1: Usual Care Botulinum Toxin Injection. This group will receive botulinum toxin injection as planned already by their rehabilitation specialist.

Group 2: Therapy after Usual Care Botulinum Toxin Injection. This group will receive an intensive, evidence based therapy program for eight weeks following their botulinum toxin A injections.

You have a 50% chance of being selected into Group 1 (usual care botulinum toxin) and a 50% chance of being selected into Group 2 (therapy after usual care botulinum toxin).

This research project has been designed to make sure the researchers interpret the results in a fair and appropriate way and avoids researchers or participants jumping to conclusions.

Some of the tests or treatments used alongside this study may be part of standard care used to maintain your health even if you did not take part in this study. You may be responsible for the co-payment for botulinum toxin as part of your standard care. Your doctor will discuss this with you.

There are no additional costs associated with participating in this research project, nor will you be paid. All medication, tests and medical care required as part of the research project will be provided to you free of charge. You may be reimbursed for any reasonable travel or parking expenses associated with the research visit.

4. What do I have to do?

If you are assigned to the group receiving therapy after Botulinum Toxin, you will be required to attend sessions at the same hospital where you received your injections plus will also be asked to complete homework which consists of exercises for your hand and/or arm. The therapy that is prescribed may involve the use of casting, electrical stimulation and repetitive practice of activities and exercises using the arm; all therapy is designed to help get more movement in your arm and will be asking you to do a lot of repetition (ie. It will be considered to be intensive practice).

You will also be asked to participate in arm and hand measurements at the start of the study, after 3 months, and again at 12 months. A qualified physiotherapist or occupational therapist will visit you in your own home or the hospital to complete these assessments.

5. Other relevant information about the research project

This study is being conducted in four different hospitals across 3 states, including Caulfield Hospital in Melbourne, Epworth Healthcare in Melbourne, Repatriation General Hospital in Adelaide and Sacred Heart Rehabilitation in Sydney. There will be a total of 180 participants in the study recruited across all of the sites. Everyone who takes part in this study will have difficulties using their arm after a stroke and everyone will have received botulinum toxin injections to their arm and/or hand.

There are a number of different researchers working together on this study representing different hospitals and universities. This research is being coordinated by Associate Professor Natasha Lannin from Alfred Health and La Trobe University.

6. Does I have to take part in this research project?

Participation in any research project is voluntary. If you do not wish to take part, you do not have to. If you decide to take part and later change your mind, you are free to withdraw from the project at any stage.

Your decision whether you should take part or not take part, or to take part and then withdraw, will not affect your usual treatment, nor your relationship with the staff who treat you, nor your relationship with Alfred Health or with members of the research team. Should you decide to withdraw from this study, we will ask to keep the measurement information that has already been collected in the database. This will be kept without your name, so that you will remain unidentified.

7. What are the alternatives to participation?

You do not have to take part in this research project to receive treatment at this hospital. If you decide not to take part in the study you may still receive an injection of Botulinum Toxin at the Spasticity Clinic. The researcher will discuss these options with you before you decide whether or not you should take part in this research project. You can also discuss the options with your local doctor.

8. What are the possible benefits of taking part?

As this is a research study, we cannot hold that you will have any direct benefit from taking part. The potential benefits to you may include a decrease in the spasticity in your arm or hand, and an increase in the amount of movement you may have in their arm or hand. The long-term benefits to the community is the possible development of new treatment options for spasticity.

9. What are the possible risks and disadvantages of taking part?

There are no known risks associated with participating in the study. Therapy for the arm after stroke is considered usual practice, however in this case, we do not have the evidence to show it is effective in conjunction with Botulinum Toxin A injection. The risk of discomfort or distress

from being involved in this study is no greater that that associated with a routine rehabilitation program.

If you become upset or distressed as a result of taking part in the research, your study doctor will be able to arrange for counselling or other appropriate support. Any counselling or support will be provided by qualified staff who are not members of the research project team. This counselling will be provided free of charge to all participants who hold a Medicare card.

10. What if new information arises during this research project?

Sometimes during the course of a research project, new information becomes available about the intervention that is being studied. If this happens, your Physiotherapist or Occupational Therapist will tell you about it and discuss with you whether you want to continue in the research project. If you decide to withdraw, your Physiotherapist or Occupational Therapist will make arrangements for regular rehabilitation to continue at no cost through Community Health if you hold a Medicare card. If you decide to continue in the research project you will be asked to sign an updated consent form.

Also, on receiving new information, your Physiotherapist or Occupational Therapist might consider it to be in your best interests to withdraw from the research project. If this happens, the therapist will explain the reasons and arrange for regular rehabilitation to continue to continue at no cost through Community Health if you hold a Medicare card.

11. Can I have other treatments during this research project?

While you are taking part in this research project, you may not be able to have some treatments you have been taking for your stroke or for other reasons. It is important to tell the study doctor and the study staff about any treatments or medications that you may be taking, including over-the-counter medications, vitamins or herbal remedies, acupuncture or other alternative treatments. You should also tell the study doctor about any changes to these during participation in the research project. The study doctor should also explain to you which treatments or medications need to be stopped for the time that you are involved in the research project.

12. What if I withdraw from this research project?

If you decide to withdraw from the project, please notify a member of the research team before you withdraw. This notice will allow that person or the research supervisor to discuss any special requirements linked to withdrawing.

If you do withdraw your consent during the research project, the researchers will not collect additional personal information from you, although personal information already collected will be retained to ensure that the results of the research project can be measured properly and to comply with law. You should be aware that data collected by the research team up to the time you withdraw will form part of the research project results. If you do not want them to do this, you must tell them when you withdraw from the research project.

13. Could this research project be stopped unexpectedly?

It is highly unlikely that this project would be stopped unexpectedly. Possible reasons for discontinuing the study include:

- Unacceptable side effects
- The therapy being shown not to be effective
- The therapy being shown to work and not need further testing.

14. What happens when the research project ends?

At the end of the research project you will not receive further therapy sessions. You will receive verbal feedback about your progress from your Occupational Therapist or Physiotherapist as the therapy progresses.

Should you wish, you have the opportunity to be informed about the outcome of the study after the results have been analysed; if you wish to hear about the results of the study, you will need to provide an address to send the results to in late 2018.

Part 2 How is the research project being conducted?

15. What will happen to information about me?

By signing the consent form you consent to the Occupational Therapist or Physiotherapist and relevant research staff collecting and using personal information about you for the research project. Any information obtained in connection with this research project that can identify who you are will remain confidential. Any information obtained in connection with this research project, either paper or electronic, will be stored in a coded format so that your identifying details are not stored with your assessment results. Information recorded on paper will be stored in a locked storage facility in the office of Associate Professor Natasha Lannin at Alfred Health. Electronic databases will be password protected. Your information will only be used for the purpose of this research project and it will only be disclosed with your permission, or in compliance with the law. Information will be securely stored for 7 years and then destroyed in line with Alfred Health procedures. Information about your involvement in this research project will be recorded in your progress notes at Alfred Health.

Information about you may be obtained from your health records held at Alfred Health for the purpose of this research. Details of your medications prescribed and visits to you general practitioner may also be accessed via the Medicare database. You will be asked to fill out an additional consent form authorising the study access to your complete Medicare and Pharmaceutical Benefits Scheme (PBS) data. Medicare collects information on your doctor visits and the associated costs, while the PBS collects information on the prescription medications you have filled at pharmacies. The consent form is sent securely to the Department of Human Services who holds this information.It is anticipated that the results of this research project will be published and/or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that you cannot be identified, except with your permission. Your name and personal information will not be used in any publication or presentation.

In accordance with relevant Australian and/or Victorian privacy and other relevant laws, you have the right to request access to your own information collected and stored by the research team. You also have the right to request that any information with which you disagree be corrected. Please contact Associate Professor Natasha Lannin on telephone 0417 135 153 if you would like to access your information.

16 Complaints

If you are unhappy about any aspect of the study and wish to make a complaint, please contact the Research Governance Officer, Office of Ethics & Research Governance, Alfred Health. Please refer to section 21 '**Further information and who to contact**' for these contact details.

17 What happens if I am injured as a result of participating in this research project?

If you suffer an injury as a result of your participation in this research project, please contact the research staff. Hospital care and treatment will be provided by the public health care system (Medicare) at no cost to you if you are eligible for Medicare benefits and elect to be treated as a public patient.

18. Who is organising and funding the research?

This research project is being conducted by a team of researchers lead by Associate Professor Natasha Lannin (Alfred Health and La Trobe University). The project is being funded by a project grant from the National Health and Medical Research Council (NHMRC).

No member of the research team will receive a personal financial benefit from your involvement in this research project (other than their ordinary wages).

19. Who has reviewed the research project?

This study has been reviewed by the National Health and Medical Research Council. All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the HREC of Alfred Health.

This project will be carried out according to the *National Statement on Ethical Conduct in Human Research (2007)*. This statement has been developed to protect the interests of people who agree to participate in human research studies.

20 Further information and who to contact

The person who you may need to contact will depend on the nature of your query. All contacts listed below are available during working hours.

Name	Associate Professor Natasha Lannin
Position	Research Project Leader
Telephone	0417 135 153
Email	n.lannin@latrobe.edu.au

If you have any complaints about any aspect of the project and wish to talk to someone independent or ask any questions about being a research participant in general, then you may contact:

Complaints

Name	Emily Bingle
Position	Research Governance Officer, Office of Ethics & Research Governance, Alfred Health
Telephone	03 9076 3619
Email	research@alfred.org.au

You will need to tell Ms Bingle the following Alfred Health project number: 442/14

AlfredHealth

LA TROBE UNIVERSITY

Consent Form - *Adult providing own consent*

Title: The InTENSE trial: optimising upper limb recovery following stroke (442-14).

Coordinating Principal Investigator	A/Professor Natasha Lannin, PhD, Alfred Health & La Trobe University, Melbourne
Associate Investigators	Dr Mithu Palit, Caulfield Hospital, Melbourne
Locations of Study	Caulfield Hospital, Melbourne

Declaration by Participant

- I have read the Participant Information Sheet or someone has read it to me in a language that I understand.
- I understand the purposes, procedures and risks of the research described in the Participant Information Sheet.
- I give permission for my doctors, other health professionals, hospitals or laboratories to release information to Caulfield Hospital concerning my stroke for the purposes of this project. I understand that such information will remain confidential.
- I have had an opportunity to ask questions and I am satisfied with the answers I have received.
- I freely agree to participate in this research project as described and understand that I am free to withdraw at any time during the study without affecting my future health care.
- I understand that I will be given a signed copy of this document to keep.

Name of Participant (please print) _____

Signature _____ Date _____

Name of Witness* to Participant's Signature (please print) _____

Signature _____ Date _____

* Witness is not to be the investigator, a member of the study team or their delegate. In the event that an interpreter is used, the interpreter may not act as a witness to the consent process. Witness must be 18 years or older.

Declaration by Researcher

I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.

Name of Researcher (please print) _____

Signature _____ Date _____

† A member of the research team must provide the explanation of, and information concerning, the research project.

Note: All parties signing the consent section must date their own signature.

Participant ID:

PARTICIPANT CONSENT FORM

Consent to release of Medicare and/or Pharmaceutical Benefits Scheme (PBS) claims information for the purposes of InTENSE Study

Important Information

Complete this form to request the release of personal Medicare claims information and/or PBS claims information to InTENSE Study.

Any changes to this form must be initialled by the signatory. Incomplete forms may result in the study not being provided with your information.

By signing this form, I acknowledge that I have been fully informed and have been provided with information about this study. I have been given an opportunity to ask questions and understand the possibilities of disclosures of my personal information.

PARTICIPANT DETAILS

1. Mr ☐ Mrs ☐ Miss ☐ Ms ☐ Other ☐

Family name: _____ First given name: _____

Other given name (s): _____

Date of birth: _____

2. Medicare card number (including individual reference number)_____

3. Permanent address: _____

Postal address (if different to above): _____

AUTHORISATION

4. I authorise the Department of Human Services to provide my:

☐ Medicare claims history OR

☐ PBS claims history OR

☐ Medicare & PBS claims history

for the period* / /20 to: / /20 to the InTENSE Study.

*Note: The Department of Human Services can only extract 4.5 years of data (prior to the date of extraction), The consent period above may result in multiple extractions.

DECLARATION

I declare that the information on this form is true and correct.

5. Signed: _____ (participant's signature) Dated: ___/___/20___ **OR**

6. Signed by _____ (full name) _____ (signature) on behalf of participant

Dated: ___/___/201…

☐ Parent (where the participant is under the age of 14 years old*)

☐ Legal guardian** (where the participant is under the age of 14 years old*)

☐ Power of attorney** ☐ Guardianship order**

* Once a young person has turned 14 years old they must consent to their own information being released.
** Please attach supporting evidence

APP 5 – PRIVACY NOTICE

Your personal information is protected by law, including the Privacy Act 1988, and is collected by the Australian Government Department of Human Services. The collection of your personal information by the department is necessary for administering requests for statistical and other data.

Your information may be used by the department or given to other parties for the purposes of research, investigation or where you have agreed or it is required or authorised by law.

You can get more information about the way in which the Department of Human Services will manage your personal information, including our privacy policy at humanservices.gov.au/privacy or by requesting a copy from the department.

Power of attorney – A power of attorney is a document that appoints a person to act on behalf of another person who grants that power. In particular, an enduring power of attorney allows the appointed person to act on behalf of another person even when that person has become mentally incapacitated. The powers under a power of attorney may be unlimited or limited to specific acts.

Guardianship order – A Guardianship order is an order made by a Guardianship Board/Tribunal that appoints a guardian to make decisions for another person. A Guardianship order may be expressed broadly or limited to particular aspects of the care of another person.

A sample of the information that may be included in your Medicare claims history:

Date of service	Date of Processing	Item number	Item description	Provider charge	Schedule Fee	Benefit paid	Patient out of pocket	Bill type
20/04/09	03/05/09	00023	Level B consultation	$38.30	$34.30	$34.30	$4.00	Cash
22/06/09	23/06/09	11700	ECG	$29.50	$29.50	$29.50		Bulk Bill

Scrambled ordering Provider number*	Scrambled rendering Provider number*	Date of referral	Rendering Provider postcode	Ordering Provider postcode	Hospital indicator	Item category
	999999A		2300		N	1
999999A	999999A	20/04/09	2300	2302	N	2

* Scrambled Provider number refers to a unique scrambled provider number identifying the doctor who provided/referred the service. Generally, each individual provider number will be scrambled and the identity of that provider will not be disclosed.

A sample of the information that may be included in your PBS claims history:

Date of supply	Date of prescribing	PBS item code	Item description	Patient category	Patient contribution (this includes under copayment amounts**)	Net Benefit (this includes under copayment amounts**)	Scrambled Prescriber number*	Pharmacy postcode
06/03/09	01/03/09	03133X	Oxazepham Tablet 30 mg	Concessional Ordinary	$5.30	$25.55	9999999	2560
04/07/09	28/05/09	03161J	Diazepam Tablet 2 mg	General Ordinary	$30.85		9999999	2530

Form Category	ATC Code	ATC Name
Original	N05 B A 04	Oxazepam
Repeat	N05 B A 01	Diazepam

* Scrambled Prescriber number refers to a unique scrambled prescriber number identifying the doctor who prescribed the prescription. Generally, each individual prescriber number will be scrambled and the identity of that prescriber will not be disclosed.

** Under co-payments can now be provided for data after 1 June 2012

29-06-2015

Ms Emma Schneider
Occupational Therapy Dept
Caulfield Hospital

AlfredHealth

55 Commercial Road
PO Box 315 Prahran
Victoria 3181 Australia
Telephone 03 9076 2000
www.alfred.org.au

Dear Ms Schneider

Re: Project number *336/15*

Project Title: *Does the amount of upper limb practice provided to patients attending the Occupational Therapy Department upper limb group change after the provision of staff education?*

The activity which your application/paper describes has been considered and noted to be a quality assurance project that has already taken place.

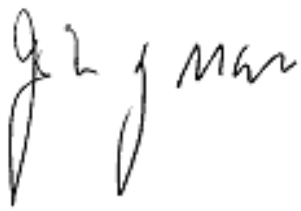
You have now requested some form of retrospective ethical approval to enable/support publication presentation of the project findings.

It is understood that sometimes there is a fine line between routine quality assurance/audit of departmental practice and low risk research. If results of the activity are likely to be disseminated outside the institution or may be written up and published at some stage, then a low risk ethics application should be made and approved, preferably before data collection commences.

The Ethics Committee does not normally grant retrospective approval for research (including audit) which has been conducted without going through a process of ethical review first. As required by the National Statement on Ethical Conduct in Human Research (2007), "(a) judgement that a human research proposal meets the requirements of this National Statement and is ethically acceptable must be made before research can begin…." (p.8) [Please note that anyone undertaking research should be familiar with this key document.]

In response to your request, the Ethics Committee is able to provide an acknowledgement that the activity was essentially an audit, is considered worthwhile and low risk, and the proposed publication/presentation raises no ethical issues.

Yours sincerely



Professor John J. McNeil
Chair, Ethics Committee

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t: 9076 3619
f: 9076 8841
e: research@alfred.org.au
w: www.alfredresearch.org

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Co-Manager
t: 9076 3848
e: r.frew@alfred.org.au

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Snr Research Governance Officer
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e: n.rosenow@alfred.org.au

Emily Bingle
Research Governance Officer /L Risk
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e: e.bingle@alfred.org.au

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Katja Loewe
Ethics Officer
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e: k.loewe@alfred.org.au

Kevin Mittelstaedt
Ethics Officer
t 9076 5308
e: k.mittelstaedt@alfred.org.au

Alfred Health incorporates
The Alfred
Caulfield General Medical Centre and
Sandringham & District Memorial Hospital
ABN 27 318 956 319

HEC16-094 (Finalised - Approved) - Application finalised as Approved

Inbox x

ResearchMasterEthics@latrobe.edu.au

to N.Lannin, ejschneider

Dear Natasha Lannin,

The following project has been assessed as complying with the National Statement on Ethical Conduct in Human Research. I am pleased to advise that your project has been granted ethics approval and you may commence the study.

Application ID: HEC16-094

Application Status/Committee: Finalised - Approved

Project Title: Staff education to increase the amount of upper limb practice completed by patients attending an upper limb group

Chief Investigator: Natasha Lannin
Other Investigators: Emma Schneider, Louise Ada

Date of Approval: 04/10/2016
Date of Ethics Approval Expiry: 23/12/2016

The following standard conditions apply to your project:

- Limit of Approval. Approval is limited strictly to the research proposal as submitted in your application.

- Variation to Project. Any subsequent variations or modifications you wish to make to your project must be formally notified for approval in advance of these modifications being introduced into the project.

- Adverse Events. If any unforeseen or adverse events occur the Chief Investigator must immediately notify the UHEC immediately. Any complaints about the project received by the researchers must also be referred immediately to the UHEC.

- Withdrawal of Project. If you decide to discontinue your research before its planned completion, you must inform the relevant committee and complete a Final Report form.

- Monitoring. All projects are subject to monitoring at any time by the University Human Ethics Committee.

- Annual Progress Reports. If your project continues for more than 12 months, you are required to submit a Progress Report annually, on or just prior to 12 February. The form is available on the Research Office website. Failure to submit a Progress Report will mean approval for this project will lapse.

- Auditing. An audit of the project may be conducted by members of the UHEC.

- Final Report. A Final Report (see above address) is required within six months of the completion of the project.

You may log in to ResearchMaster (https://rmenet.latrobe.edu.au) to view your application.

If you have any further questions, please contact the:
UHEC at humanethics@latrobe.edu.au
SHE College Human Ethics Sub-Committee at chesc.she@latrobe.edu.au
ASSC College Human Ethics Sub-Committee at chesc.assc@latrobe.edu.au

ETHICS COMMITTEE CERTIFICATE OF APPROVAL

This is to certify that

Project No: 94/15

Project Title: EXTRA Practice Study: Feasibility of an extra practice upper limb protocol for adults after stroke: a repeated-measures baseline-controlled phase 1 study.

Principal Researcher: A/Prof Natasha Lannin

Protocol Version 1.1 **dated:** 17-Mar-2015

Participant Information and Consent Form Version 1.1 **dated:** 17-Mar-2015

*was considered by the Ethics Committee on **26-Mar-2015**, meets the requirements of the National Statement on Ethical Conduct in Human Research (2007) and was **APPROVED** on **31-Mar-2015***

It is the Principal Researcher's responsibility to ensure that all researchers associated with this project are aware of the conditions of approval and which documents have been approved.

The Principal Researcher is required to notify the Secretary of the Ethics Committee, via amendment or progress report, of

- Any significant change to the project and the reason for that change, including an indication of ethical implications (if any);
- Serious adverse effects on participants and the action taken to address those effects;
- Any other unforeseen events or unexpected developments that merit notification;
- The inability of the Principal Researcher to continue in that role, or any other change in research personnel involved in the project;
- Any expiry of the insurance coverage provided with respect to sponsored clinical trials and proof of re-insurance;
- A delay of more than 12 months in the commencement of the project; and,
- Termination or closure of the project.

Additionally, the Principal Researcher is required to submit

- A Progress Report on the anniversary of approval and on completion of the project *(forms to be provided)*;

The Ethics Committee may conduct an audit at any time.

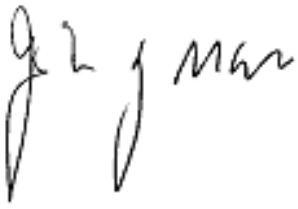
All research subject to the Alfred Hospital Ethics Committee review must be conducted in accordance with the National Statement on Ethical Conduct in Human Research (2007).

The Alfred Hospital Ethics Committee is a properly constituted Human Research Ethics Committee in accordance with the National Statement on Ethical Conduct in Human Research (2007).

SPECIAL CONDITIONS

None

SIGNED:



Professor John J. McNeil
Chair, Ethics Committee

Please quote project number and title in all correspondence

LA TROBE UNIVERSITY

University Human Ethics Committee

RESEARCH OFFICE

MEMORANDUM

To: **A/Prof Natasha Lannin, School of Allied Health, College of SHE**

From: **Executive Officer, La Trobe University Human Ethics Committee**

Subject: **UHEC acceptance of The Alfred HREC approved project – 94/15**

Title: **EXTRA Practice Study: Feasibility of an extra practice upper limb protocol for adults after stroke: a repeated-measures baseline-controlled phase 1 study**

Date: **1 May 2015**

Thank you for submitting the above protocol to the University Human Ethics Committee (UHEC). Your material was forwarded to the UHEC Chair for consideration. Following evidence of a full review and subsequent final approval by the **The Alfred HREC**, the UHEC Chair agrees that the protocol complies with the National Health and Medical Research Council's *National Statement on Ethical Conduct in Human Research* and is in accordance with La Trobe University's *Human Research Ethics Guidelines*.

Endorsement is given for you to take part in this study in line with the conditions of final approval outlined by **The Alfred HREC.**

Limit of Approval. La Trobe UHEC endorsement is limited strictly to the research protocol as approved by **The Alfred HREC**.

Variation to Project. As a consequence of the previous condition, any subsequent modifications approved by **The Alfred HREC** for the project should be notified formally to the UHEC.

Annual Progress Reports. Copies of all progress reports submitted to **The Alfred HREC** must be forwarded to the UHEC. Failure to submit a progress report will mean that endorsement for your involvement this project will be rescinded. An audit related to your involvement in the study may be conducted by the UHEC at any time.

Final Report. A copy of the final report is to be forwarded to the UHEC within one month of it being submitted to **The Alfred HREC.**

If you have any queries on the information above please e-mail: **humanethics@latrobe.edu.au** or

contact me by phone.

On behalf of the La Trobe University Human Ethics Committee, best wishes with your research!

Kind regards,

Sara Paradowski
Senior Human Ethics Officer
Executive Officer – University Human Ethics Committee
Ethics and Integrity / Research Office
La Trobe University Bundoora, Victoria 3086
P: (03) 9479 – 1443 / F: (03) 9479 - 1464
http://www.latrobe.edu.au/researchers/ethics/human-ethics

Participant Information Sheet/Consent Form

Interventional Study - *Adult providing own consent*

Title: The EXTRA Practice Study: the feasibility of an extra practice upper limb protocol for adults after stroke

Short Title	EXTRA
Coordinating Principal Investigator	A/Professor Natasha Lannin, PhD Alfred Health Occupational Therapy Department and La Trobe University School of Allied Health
Co-Investigator(s)	Emma Schneider, MOT, BBNSc Alfred Health Occupational Therapy Department
	Professor Louise Ada, The University of Sydney, Sydney
Location of Study	Caulfield Hospital, Melbourne

Part 1 What does my participation involve?

1 Introduction

You are invited to take part in this research project. This is because you have difficulties using one of your arms after having a stroke and you are participating in inpatient rehabilitation.

The research project is testing whether it is possible (feasible) for an inpatient to do 60 minutes of extra arm and hand practice in addition to your usual therapy. This Participant Information Sheet/Consent Form tells you about the research project. It explains the tests and treatments involved. Knowing what is involved will help you decide if you want to take part in the research.

Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend or your local doctor.

Participation in this study is voluntary. If you don't wish to take part, you don't have to. You will receive the best possible care whether or not you take part.

If you decide you want to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:
• Understand what you have read
• Consent to take part in the research project
• Consent to have the tests and treatments that are described
• Consent to the use of your personal and health information as described.

You will be given a copy of this Participant Information and Consent Form to keep.

2 What is the purpose of this research?

One of the most common difficulties people experience after stroke is an inability to use their arm and/or hand to perform everyday activities. This difficulty is because the muscles in the hand and arm are weak after stroke. Upper limb training aims to improve the amount a person can move, the control they have during the movement, and the strength of the muscles in the arm and hand. While in hospital, stroke patients are asked to do occupational therapy and physiotherapy exercises.
What remains unknown is whether it is possible (feasible) for an inpatient to practice for another 60 minutes every day on their own extra to their usual therapy exercises. This research aims to find out if receiving extra arm and hand practice in addition to usual therapy is feasible after stroke.

The results of this research will be used by Emma Schneider (Occupational Therapist at Caulfield Hospital) to obtain a Doctor of Philosophy degree from La Trobe University.

This research has been initiated by Dr Natasha Lannin (Associate Professor of Occupational Therapy) from Alfred Health.

3 What does participation in this research involve?

You will be participating in a phase 1 research project. Sometimes we do not know if interventions can effectively be provided and to find out we need to provide the extra therapy to a small number of people. We will ask 20 people to complete the semi-supervised EXTRA therapy package to see if the practice can be completed.

If you decide to take part, you will be asked to complete a semi-supervised EXTRA practice upper limb therapy package for one hour per day, six days a week for four weeks while an inpatient of Caulfield Hospital (or until discharged from hospital, whichever is first). These exercises are simple hand and arm movements and involves you following a set-out exercise program.

There are no additional costs associated with participating in this research project, nor will you be paid. All therapy and tests required as part of the research project will be provided to you free of charge.

There are no expected expenses associated with the research because you will be an inpatient at Caulfield Hospital for the duration of this study.

4 What do I have to do?

You will be required to complete extra arm and hand practice in addition to your usual rehabilitation program. You will be guided by an occupational therapist through these extra exercises. If you participate in this research you must complete 60 minutes of practice 6 days per week (Monday to Saturday). Please keep in mind that the practice sessions may take longer than 60 minutes as set-up time and rest breaks do not count toward your total actual practice time. The practice you complete by following this program will be in addition to your usual rehabilitation program and home exercise program (if you have one).

The EXTRA therapy package is designed to help get more strength of the muscles and control of the movement in your arm and will be asking you to do a lot of repetitions. It will be considered to be three times as much practice as what is considered usual. Each 60-minute practice session will involve 30 minutes of GRASP and 30 minutes of AbleX.

Graded Repetitive Arm Supplementary Program (GRASP) is an arm and hand exercise program developed for stroke patients. GRASP exercises include functional tasks, fine motor

skills and strengthening exercises. After initial training by a Research Occupational Therapist, you will be asked to work through the workbook and start the next day where you left off. The researcher will continue to monitor your performance and guide you to progress through the program when suitable.

AbleX is a computer based upper limb exercise system. AbleX runs through a laptop and has a handlebar that you hold with both hands. The system has a number of interactive games and provides you with immediate feedback on your performance. After initial training, the researcher will continue to monitor your performance and guide you to progress through the program when suitable. A researcher will help you to set-up the AbleX at each practice session.

You will be asked to track and record each session in a Participant Practice Log. Practice sessions may be completed in a group (where able).

You will also be asked to participate in arm and hand measurements at the start of the study, and weekly for 4 weeks. A qualified researcher and occupational therapist will administer these assessments.

5 Other relevant information about the research project

This study is being conducted at Caulfield Hospital. There will be a total of 20 participants in the study recruited across all of the inpatient rehabilitation and aged care wards of Caulfield Hospital.

6 Do I have to take part in this research project?

Participation in all research is voluntary. If you do not wish to take part, you do not have to. If you decide to take part and later change your mind, you are free to withdraw from the project at any stage.

If you do decide to take part, you will be given this Participant Information and Consent Form to sign and you will be given a copy to keep.

Your decision whether to take part or not to take part, or to take part and then withdraw, will not affect your routine treatment, your relationship with those treating you or your relationship with Alfred Health.

7 What are the alternatives to participation?

You do not have to take part in this research project to receive treatment at this hospital. If you decide not to take part in the study you will still receive the usual inpatient rehabilitation program. The researcher will discuss these options with you before you decide whether or not to take part in this research project. You can also discuss the options with your local doctor.

8 What are the possible benefits of taking part?

We cannot guarantee or promise that you will receive any benefits from this research; however, possible benefits may include an increase in the strength and amount of movement you may have in your arm or hand.

9 What are the possible risks and disadvantages of taking part?

There are no known risks associated with participating in the study. Therapy for the arm after stroke is considered usual practice. The risk of discomfort or distress from being involved in this study is no greater than that associated with a routine inpatient rehabilitation program.

10 What if new information arises during this research project?

Sometimes during the course of a research project, new information becomes available about the treatment that is being studied. If this happens, your researcher will tell you about it and discuss with you whether you want to continue in the research project. If you decide to withdraw, you will continue to participate in your regular inpatient rehabilitation program. If you decide to continue in the research project you will be asked to sign an updated consent form.

Also, on receiving new information, your researcher might consider it to be in your best interests to withdraw you from the research project. If this happens, he/ she will explain the reasons and arrange for your regular health care to continue.

11 Can I have other treatments during this research project?

This study is designed to better understand what happens if EXTRA therapy is added to usual care. Therefore, we do not anticipate any restrictions to other treatments while you are taking part in this research project. It is important to tell your study staff about all arm and hand exercises you are doing while at Caulfield Hospital, including acupuncture or other alternative treatments you may arrange outside of your usual care. You should also tell your study staff about any changes to these during your participation in the research project.

12 What if I withdraw from this research project?

If you decide to withdraw from the project, please notify a member of the research team before you withdraw. This notice will allow that person or the research supervisor to discuss any health risks or special requirements linked to withdrawing.

If you do withdraw your consent during the research project, the researchers will not collect additional personal information from you, although personal health information already collected will be retained to ensure that the results of the research project can be measured properly and to comply with law. You should be aware that data collected by the study staff up to the time you withdraw will form part of the research project results. If you do not want them to do this, you must tell them when you withdraw from the research project.

13 Could this research project be stopped unexpectedly?

It is highly unlikely that this project would be stopped unexpectedly. Possible reasons for discontinuing the study include:
• Unacceptable side effects
• Extra practice therapy is shown not to be feasible

14 What happens when the research project ends?

At the end of the research project you will not receive further therapy sessions from this research program. You will receive verbal feedback about your progress from the research Occupational Therapist as the therapy program progresses. At the end of this study you will continue to participate in the rehabilitation program as recommended by your treating team at Caulfield Hospital. If you are discharged from inpatient rehabilitation during the study period the study will be ceased.

Should you wish, you have the opportunity to be informed about the outcome of the study after the results have been analysed; if you wish to hear about the results of the study, you will need to provide an address to send the result to in late 2016.

Part 2 How is the research project being conducted?

15 What will happen to information about me?

By signing the consent form you consent to the Occupational Therapist and relevant research staff collecting and using personal information about you for the research project. Any information obtained in connection with this research project that can identify you will remain confidential. Any information obtained in connection with this research project, either paper or electronic, will be stored in a coded format so that your identifying details are not stored with your assessment results. Information recorded on paper will be stored in a locked filing cabinet at Caulfield Hospital and be the responsibility of Associate Professor Natasha Lannin. Electronic data will be password protected; only named investigators and employed research staff will have access to this information. Your information will only be used for the purpose of this research project and it will only be disclosed with your permission, except as required by law. Your information will be stored for 7 years and then destroyed in line with Alfred Health procedures. Information about your involvement in this research progress will be recorded in your progress notes at Alfred Health.

Information about you may be obtained from your health records held at Alfred Health for the purpose of this research. By signing the consent form you agree to the study team accessing health records if they are relevant to your participation in this research project.

It is anticipated that the results of this research project will be published and/or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that you cannot be identified, except with your permission. Your name and personal information will not be used in any publication or presentation.

In accordance with relevant Australian and/or Victorian privacy and other relevant laws, you have the right to request access to your information collected and stored by the research team. You also have the right to request that any information with which you disagree be corrected. Please contact Associate Professor Natasha Lannin 0417 135 153 if you would like to access your information.

16 Complaints and compensation

If you are unhappy about any aspect of the study and wish to make a complaint, please contact the Research Governance Officer, Office of Ethics and Research Governance, Alfred Health. Please refer to section 21 '**Further information and who to contact'** for these contact details.

If you suffer an injury as a result of your participation in this research project, please contact the research staff. Hospital care and treatment will be provided by the public health care system (Medicare) at no cost to you if you are eligible for Medicare benefits and elect to be treated as a public patient.

17 Who is organising and funding the research?

This research project is being conducted by a team of researchers led by Associate Professor Natasha Lannin (Alfred Health). We have not secured any funding for this project; the study is being conducted within our Occupational Therapy Department resources. No member of the research team will receive a personal financial benefit from your involvement in this research project (other than their ordinary wages).

18 Who has reviewed the research project?

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the HREC of Alfred Health and La Trobe University.

This project will be carried out according to the *National Statement on Ethical Conduct in Human Research (2007)*. This statement has been developed to protect the interests of people who agree to participate in human research studies.

19 Further information and who to contact

The person you may need to contact will depend on the nature of your query. All contacts listed below are available during work hours.

Clinical contact person

Name	Associate Professor Natasha Lannin
Position	Research Project Leader
Telephone	0417 135 153
Email	n.lannin@latrobe.edu.au

If you have any complaints about any aspect of the project, the way it is being conducted or any questions about being a research participant in general, then you may contact:

Complaints contact person

Name	Emily Bingle
Position	Research Governance Officer, Office of Ethics & Research Governance, Alfred Health.
Telephone	03 9076 3619
Email	research@alfred.org.au

You will need to reference the following Alfred Health project number: 94/15

Consent Form - *Adult providing own consent*

Title: The EXTRA Practice Study: the feasibility of an extra practice upper limb protocol for adults after stroke

Short Title	EXTRA
Coordinating Principal Investigator/ Principal Investigator	A/Professor Natasha Lannin, PhD Alfred Health Occupational Therapy Department
Associate Investigator(s)	Ms Emma Schneider Alfred Health Occupational Therapy Department Professor Louise Ada, The University of Sydney, Sydney
Location	Caulfield Hospital, Melbourne

Declaration by Participant

I have read the Participant Information Sheet or someone has read it to me in a language that I understand.

I understand the purposes, procedures and risks of the research described in the project.

I give permission for my doctors, other health professionals, hospitals or laboratories outside this hospital to release information to Caulfield Hospital concerning my disease and treatment for the purposes of this project. I understand that such information will remain confidential.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to participate in this research project as described and understand that I am free to withdraw at any time during the study without affecting my future health care.

I understand that I will be given a signed copy of this document to keep.

Name of Participant (please print) _____

Signature _____ Date _____

Declaration by Researcher†

I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.

Name of Researcher† (please print) _____

Signature _____ Date _____

† A senior member of the research team must provide the explanation of, and information concerning, the research project.

Note: All parties signing the consent section must date their own signature

Appendix C: Registration of studies

Study 1

- PROPERO registration

Study 4

- ANZCTR registration

STUDY 1 PROSPERO REGISTRATION

NIHR | National Institute for Health Research

PROSPERO
International prospective register of systematic reviews

Print | PDF

Increasing the amount of usual rehabilitation improves activity after stroke: a systematic review

Emma Schneider, Natasha Lannin, Louise Ada, Julia Schmidt

Citation

Emma Schneider, Natasha Lannin, Louise Ada, Julia Schmidt. Increasing the amount of usual rehabilitation improves activity after stroke: a systematic review. PROSPERO 2012 CRD42012003221 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42012003221

Review question

In people receiving rehabilitation timed at reducing activity limitations of the lower and/or upper limb after stroke, does adding extra rehabilitation (of the same content as usual rehabilitation) improve activity?
What is the amount of extra rehabilitation that needs to be provided to achieve a beneficial effect?

Searches

We will search the following electronic databases: MEDLINE, EMBASE, CINAHL, and the Cochrane Central Register of Controlled Trials (CENTRAL) from the earliest available until October 2015 for relevant articles available in English. The search strategy will include terms relating stroke, physical therapy, occupational therapy, rehabilitation and intensity (such as dose, frequency, quantity, duration, and amount). The search strategy for MEDLINE along with the adapted terms used with other databases will be available in the published systematic review.

Types of study to be included

Randomised or quasi-randomised trials.

Condition or domain being studied

Stroke resulting in activity limitations.

Participants/population

Inclusion: Adults aged 18 years or older (with 80% of participants having stroke and the remainder being stroke like conditions such as cerebral aneurysm).

Intervention(s), exposure(s)

Studies will be included if the experimental group received extra rehabilitation (of the same content as usual rehabilitation) on top of usual rehabilitation, aimed at improving lower limb activity or upper limb activity or both.

Comparator(s)/control

The control group received usual rehabilitation alone. The dose of usual rehabilitation will be calculated as the amount of time dedicated to rehabilitation of the activity included in the extra rehabilitation. For example, if the experimental group received 30 min of extra upper limb rehabilitation, and the control group received 60 min of rehabilitation consisting of 30 min upper limb and 30 min lower limb, the comparison of the same content would be 30 min extra upper limb rehabilitation with 30 min usual upper limb rehabilitation.

Context

Studies in hospital or rehabilitation settings will be included to capture a population post stroke. Intervention can be provided within the hospital, home or the community.

Main outcome(s)

Measures involving direct observation of upper or lower limb activity, regardless of whether they produce continuous data (eg, Box and Block Test, 10-m Walk Test) or ordinal data (eg, Action Research Arm Test, Functional Ambulation Category). The preferred assessments of lower limb ability will be the 10-m Walk Test (m/s) and the 6-minute Walk Test (m). The preferred assessments of upper limb ability will be the 9-Hole Peg Test (pegs/s) and the Box and Block Test (blocks/s).

Timing and effect measures

Immediately post intervention and up to 26 week post intervention.

Additional outcome(s)

None.

Data extraction (selection and coding)

Titles and abstracts will be displayed and screened by one reviewer to identify relevant studies. Full paper copies of relevant papers will be retrieved and the methods reviewed independently by two reviewers using predetermined criteria. Disagreements will be adjudicated by a third or fourth independent reviewer.
Information about the method (i.e., design, participants, chronicity, intervention, measures) and results (i.e., number of participants and mean (SD) of outcomes) will be extracted by a reviewer and crosschecked). Data will be converted where necessary using methods recommended by the Cochrane Handbook of Systematic Review Interventions. Missing data will be requested from study authors.

Risk of bias (quality) assessment

The methodological quality of studies will be assessed using the PEDro scale (www.pedro.prg.au). The scale produces a score out of 10 depending on whether the study controlled for the following scores of bias: random allocation; allocation concealment; similarity between groups at baseline; blinding of participants, personnel and outcome assessors; incomplete data and reporting of data. Wherever possible, PEDro scores recorded on the PEDro database will be used. If a study has not been rated by the PEDro team, two review authors will independently score the study and a third author will resolve any disagreements.

Strategy for data synthesis

We will describe the included studies in a table (design, number of participants, intervention, and measures). Meta-analysis will be performed. We will calculate 95% confidence intervals. Post intervention scores will be used to obtain the pooled estimate of the effect of extra rehabilitation using RevMan 5.1. Effect size will be reported as standardised mean difference and a random effects model will be used in the case of significant heterogeneity (I-squared > 50%). Statistical heterogeneity between the studies will be assessed using the I-squared statistic. We will also assess evidence of publication bias.
The relationship between percentage of extra rehabilitation provided and the effect size will be calculated using Pearson correlation coefficient. The amount of extra rehabilitation needed to provide a beneficial effect will be determined from an ROC curve. The percentage of extra practice provided in each study will be calculated and, using the SMD, we will calculate a Person correlation coefficient. A ROC curve calculation will be conducted using the positive or negative effect compared with the average weekly total volume of extra practice provided in each trial.

Analysis of subgroups or subsets

Subgroup analyses according to the time after stroke (acute versus chronic) and body part (upper versus lower limb) are planned where there are a sufficient number of comparable studies (4 or more).

Contact details for further information

Emma Schneider
eschneider.ot@gmail.com

Organisational affiliation of the review

La Trobe University
www.latrobe.edu.au

Review team members and their organisational affiliations

Ms Emma Schneider. La Trobe University, Alfred Heatlh
Dr Natasha Lannin. La Trobe University, Alfred Heatlh
Professor Louise Ada. The University of Sydney
Ms Julia Schmidt. University of British Columbia, Australian Catholic University

Type and method of review

Intervention, Systematic review

Anticipated or actual start date

05 May 2012

Anticipated completion date

01 June 2016

Funding sources/sponsors

Nil

Conflicts of interest

None known

Language

English

Country

Australia

Published protocol

http://www.omicsgroup.org/journals/increasing-the-intensity-of-rehabilitation-to-improve-activity-after-stroke-systematic-review-protocol-2167-0870.1000195.php?aid=35747

Stage of review

Review Completed not published

Subject index terms status

Subject indexing assigned by CRD

Subject index terms

Activities of Daily Living; Humans; Motor Activity; Physical Therapy Modalities; Recovery of Function; Stroke

Date of registration in PROSPERO

04 December 2012

Date of publication of this version

21 August 2016

Revision note for this version

The copy editor suggested different wording for the title and for the study questions. The new wording is clearer and more succinct. I have updated the PROSPERO registration to ensure that the systematic review registration matches the manuscript when it is published next month.

Details of any existing review of the same topic by the same authors

Stage of review at time of this submission

Stage	Started	Completed
Preliminary searches	Yes	Yes
Piloting of the study selection process	Yes	Yes
Formal screening of search results against eligibility criteria	Yes	Yes
Data extraction	Yes	Yes
Risk of bias (quality) assessment	Yes	Yes
Data analysis	Yes	Yes

Revision note

The copy editor suggested different wording for the title and for the study questions. The new wording is clearer and more succinct. I have updated the PROSPERO registration to ensure that the systematic review registration matches the manuscript when it is published next month.

Versions

04 December 2012
12 February 2016
01 April 2016
21 August 2016

STUDY 4 ANZCTR REGISTRATION

Trial registered on ANZCTR

Registration number	ACTRN12615000665538
Ethics application status	Approved
Date submitted	3/05/2015
Date registered	26/06/2015
Date last updated	11/07/2016
Type of registration	Prospectively registered

Titles & IDs

Public title	The EXTRA Practice Study: the feasibility of an extra practice upper limb protocol for adults after stroke
Scientific title	The EXTRA Practice Study: the feasibility of an extra practice upper limb protocol for adults after stroke
Secondary ID [1]	Nil known
Universal Trial Number (UTN)	U1111-1169-7070
Trial acronym	EXTRA
Linked study record	

Health condition

Health condition(s) or problem(s) studied:	
Stroke	
Hemiplegia	
Condition category	**Condition code**
Neurological	Other neurological disorders
Physical Medicine / Rehabilitation	Occupational therapy
Stroke	Ischaemic

Intervention/exposure

Study type	Interventional
Description of intervention(s) / exposure	Participants will be taught and supported to completed the EXTRA practice protocol for 60 minutes per day, six days per week for four weeks. Each 60 minute practice session will involve 30 minutes of Graded Repetitive Supplementary Program (GRASP) training and 30 minutes of the AbleX program. The EXTRA therapy program will be semi supervised by a qualified occupational therapist in a treatment room or in the patient's hospital room. The intervention period will extend for four weeks or until discharged from the rehabilitation unit (whichever is first; this study will not influence discharge dates which will be set by the treating rehabilitation team). GRASP is an arm and hand exercise program developed for stroke patients with upper extremity impairments and allows patients to undertake a self-directed arm and hand exercise program. GRASP exercises may include functional tasks, fine motor skills and strengthening exercises. Participants will be asked to start the next day where they left off. Every participant will be started at Level 1 and will go up to the next level when they can complete the program in one quarter of the time required (25 minutes). The AbleX is a computer based upper limb exercise system shown to be effective in providing repetitive, intense and engaging exercise that improves upper limb function. The AbleX runs thorough a Windows operating system on a laptop. Feedback on performance (accuracy), activity time (adherence) and exercise intensity is automatically captured with the exercise game. Participants will be asked to record the duration of each practice session. Should participants not complete the required amount of daily practice their reasons for not training will be recorded. Participants can choose for greater or less than the required daily minimum.
Intervention code [1]	Rehabilitation
Intervention code [2]	Treatment: Other
Comparator / control treatment	Not applicable
Control group	Uncontrolled

Outcomes

Primary outcome [1]	Upper limb activity measured by the Box and Block Test
Timepoint [1]	Baseline, week 1, week 2, week 3, week 4 after intervention commencement.
Primary outcome [2]	Upper limb activity measured by the 9-Hole Peg Test
Timepoint [2]	Baseline, week 1, week 2, week 3, week 4 after intervention commencement.
Primary outcome [3]	Grip strength measured by hand grip dynamometer (kg)
Timepoint [3]	Baseline, week 1, week 2, week 3, week 4 after intervention commencement.
Secondary outcome [1]	Recruitment and consent rates including number of patients admitted with a diagnosis of stroke (screened), number with hemiparesis (eligible), number of people who decline participation (refused) as well as the number of people who commenced the study but opted to stop (study dropouts).
Timepoint [1]	Six days per week, from first participant screened to finish of last participant.
Secondary outcome [2]	Participation will be recorded by recording the amount of practice completed/not completed during each individual participant's practice. A Participant Practice Log has been prepared to measure the type of practice, number of sessions, duration of each session, duration of active practice, number of repetitions completed, number of health professionals present at each therapy session, success of each session and any reason for why a practice session was missed pr shorter than the time required.
Timepoint [2]	Six days per week for 4 weeks from study commencement (repeated for each participant recruited).
Secondary outcome [3]	Satisfaction will be measured using the simple question "Would you recommend this program to a friend who had suffered a stroke and couldn't move their arm normally?". We will additionally ask for participant feedback using a qualitative survey that has been designed specifically for this study..
Timepoint [3]	4 weeks after intervention commencement (or the last session, if earlier)
Secondary outcome [4]	Adverse events will be tracked and recorded as per the NHMRC Position Statement. Any adverse event will be mandatorily reported to the Chief Investigator and Ethics Committee. Any adverse events will be recorded and classified according to whether they could be attributed to the therapy provided. There are no known/possible adverse events relating to this study.
Timepoint [4]	Daily, from start to end of intervention period.

Eligibility

Key inclusion criteria	- Medical diagnosis of stroke - Presence of hemiparesis/hemiplegia - Have a upper limb activity limitation (defined as <54 blocks on the Box and Block Test which is 20% reduction in the normative scores for adults aged 20-80 years) - Have at least grade 1 wrist extension and grade 3 shoulder elevation
Minimum age	18 Years
Maximum age	No limit
Gender	Both males and females
Can healthy volunteers participate?	No
Key exclusion criteria	- Have severe cognitive and/or language defects, which preclude them from following instructions in training sessions (score greater than or equal to 24 on the Mini Mental Status Examination) - Have any medical condition that precludes them participating in a rehabilitation program aimed at upper limb activity

Study design

Purpose of the study	Treatment
Allocation to intervention	Non-randomised trial
Procedure for enrolling a subject and allocating the treatment (allocation concealment procedures)	Potential participants will be identified by the investigators through the review of electronic inpatient ward lists and/or their medical record for confirmation of a diagnosis of stroke (screened) and the presence of hemiparesis/hemiplegia (eligible). Potential participants will be approached on the ward by a researcher who has no relationship with the potential participants to determine eligibility. If eligible, the researcher will then explain the study to potential participants and invite them to participate. Written information about the study will be provided to participants.
Methods used to generate the sequence in which subjects will be randomised (sequence generation)	
Masking / blinding	Open (masking not used)
Who is / are masked / blinded?	
Intervention assignment	Single group
Other design features	
Phase	Not Applicable
Type of endpoint(s)	Safety/efficacy

Statistical methods / analysis	Repeated measures analyses of variance will be used to compare the changes in outcome measure variables from baseline to Week four. Mean within-group differences (MD) (95%CI) will be calculated. Probabilities of less than 0.05 will be considered significant. Descriptive data will be reported as aggregated data; mea (range) and mean (sd) will both be reported to permit future sample size calculations. Feasibility will be analysed descriptively. Recruitment rates and proportions will be calculated. Counts for adverse events and an adverse event rate will be calculated. Sensitivity of outcome measures will also be evaluated and recommendations made about the outcome measures for future, larger, trials. Because sample sizes are small (typically less than 30 participants) Phase 1 trials are only able to detect the feasibility of the intervention. The number of participants needed to achieve this study objectives was determined by the study design.

Recruitment

Recruitment status	Completed

Date of first participant enrolment			
Anticipated	1/07/2015	**Actual**	27/07/2015

Date of last participant enrolment			
Anticipated	12/09/2016	**Actual**	4/06/2016

Date of last data collection			
Anticipated	11/09/2016	**Actual**	24/06/2016

Sample size					
Target	20	**Accrual to date**		**Final**	20

Recruitment in Australia	
Recruitment state(s)	VIC
Recruitment hospital [1]	Caulfield Hospital - Caulfield
Recruitment postcode(s) [1]	3162 - Caulfield

Funding & Sponsors

Funding source category [1]	Self funded/Unfunded
Name [1]	
Address [1]	
Country [1]	
Primary sponsor type	Hospital
Name	Alfred Health
Address	Caulfield Hospital, 260 Kooyong Road, Caulfield, Victoria 3162, Australia.
Country	Australia
Secondary sponsor category [1]	University
Name [1]	La Trobe University
Address [1]	Department of Occupational Therapy, Faculty of Health Sciences, La Trobe University, Plenty Road, Bundoora, Victoria 3086, Australia
Country [1]	Australia

Ethics approval

Ethics application status	Approved
Ethics committee name [1]	Alfred Health Ethics Committee
Ethics committee address [1]	260 Kooyong Road, Caulfield, Victoria 3162, Australia
Ethics committee country [1]	Australia
Date submitted for ethics approval [1]	
Approval date [1]	31/03/2015
Ethics approval number [1]	94/15

Summary

Brief summary	Arm and hand training is routinely provided within stroke rehabilitation programs around Australia. Arm and hand training for stroke survivors aims to improve the amount a person can move, the control they have during the movement, and the strength of the muscles in the arm and hand. Research has shown that hospitalised patients get between 30 to 60 minutes of hand and arm practice every day. Other research has shown that doing extra leg practice every day is not harmful and can lead to people being able to walk earlier than those who did not complete the extra practice. What remains unknown is whether it is feasible for an inpatient to do extra arm and hand practice than is currently offered in Australian hospitals, and if an inpatient completes extra arm and hand practice, does this also lead to a person being able to move more or earlier than those who only complete their usual therapy. This study aims to find out if receiving 60 minutes of extra arm and hand practice in addition to usual therapy is safe and feasible after stroke. Participants will be asked to complete a semi-supervised EXTRA practice upper limb therapy package for one hour per day, six days a week for four weeks while an inpatient of Caulfield Hospital.
Trial website	
Trial related presentations / publications	
Public notes	

Contacts

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Fax	
Email	e.schneider@alfred.org.au

No information has been provided regarding IPD availability

Summary results

Have study results been published in a peer-reviewed journal?	

Other publications

Have study results been made publicly available in another format?	

Results – basic reporting	
Results – plain English summary	

Appendix D: Supplementary material from Study 1

Study 1

- Search terms
- Papers excluded after evaluation of full text
- Supplementary figures

STUDY 1 SEARCH TERMS

Searches were conducted on each database on Thursday 15th October 2015.

MEDLINE, EMBASE

1. exp Cerebrovasular Disorders/
2. stroke$.tw.
3. cva$.tw.
4. cerebrovasuclar$.tw.
5. cerebral vascular$.tw.
6. (poststroke or post-stroke or cerebrovasc$ or brain vasc$ or cerebral vasc$ or apoplex$ or SAH).tw.
7. ((brain$ or cerebr$ or cerebell$ or intracran$ or intracerebral or vertebrovasilar) adj5 (isch?emi$ or infarct$ or thrombo$ or emboli$ or occlus$)).tw.
8. ((brain$ or cerebr$ or cerebell$ or intracerebral or intracranial or subarachnoid) adj5 (haemorrhage$ or hemorrhage$ or haematoma$ or hematoma$ or bleed$)).tw.
9. hemiplegia/ or exp paresis/
10. (hemipleg$ or hemipar$ or paresis or paretic).tw.
11. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12. exp Physical Therapy Modalities/
13. physical therapy.mp.
14. Physiotherapy.mp.
15. Occupational Therapy/
16. rehabilitat$.mp.
17. Rehabilitation/
18. motor relearn$.mp.
19. bobath.mp.
20. 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19
21. intensit$.mp.
22. frequen$.mp.
23. duration$.mp.
24. dos$.mp.
25. quantit$.mp.
26. total units$.mp.
27. amount$.mp.

28. 21 or 22 or 23 or 24 or 25 or 26 or 27
29. 11 and 20 and 28
30. limit 29 to humans and English

Cochrane Register of Controlled Trials (CENTRAL)
Stroke and Intensity (limit to trials)

CINAHL

1. MH Cerebrovascular Disorders
2. TI (stroke* OR CVA* OR cerebrovascular* OR cerebral vascular*) OR AB (stroke* OR CVA* OR cerebrovascular* OR cerebral vascular*)
3. TI (poststroke OT post-stroke OR cerebrovasc* OT brain vasc* OR cerebral vasc* OR apoplexy*) OR AB (poststroke OT post-stroke OR cerebrovasc* OT brain vasc* OR cerebral vasc* OR apoplexy*)
4. TI (brain OR cerebr* OR cerebell* OR intracranial* OR vertebrovasilar) n3 (isch?emi* OR infarct* OR thrombo OR emboli* OR occlus*) OR AB (brain OR cerebr* OR cerebell* OR intracranial* OR vertebrovasilar) n3 (isch?emi* OR infarct* OR thrombo OR emboli* OR occlus*)
5. TI (brain* OR cerebr* OR intracerebral OR intracranial OR subarachnoid) n3 (haemorrhage* OR haemorrhage* OR haematoma* OR hematoma* OR bleed) OR AB (brain* OR cerebr* OR intracerebral OR intracranial OR subarachnoid) n3 (haemorrhage* OR haemorrhage* OR haematoma* OR hematoma* OR bleed)
6. TI (hemiplegia OR paresis+) OR AB (hemiplegia OR paresis+)
7. TI (hemipleg* OR hemipar* OR paresis OR paretic) OR AB (hemipleg* OR hemipar* OR paresis OR paretic)
8. S1 OR S2 OR S3 OR S4 OR S5 OF S6 OR S7
9. MH ‘Physical Therapy’
10. TI physiotherapy* or AB physiotherapy*
11. MH ‘Occupational Therapy’
12. Rehabilitat*
13. TI (motor relearn*) OR AB (motor relearn*)
14. TI bobath OR AB bobath
15. S9 OR S10 OR S11 OR S12 OR S13 OR S14

16. TI (intensi* OR frequen* OR duration* OR dose* OR quantit* OR (total unit*) OR amount) OR AB (intensi* OR frequen* OR duration* OR dose* OR quantit* OR (total unit*) OR amount)
17. S15 AND S16
18. S8 AND S17
19. Limit to English, Human, exclude Medline records

STUDY 1 PAPERS EXCLUDED AFTER EVALUATION OF FULL TEXT

Appendix Table 1. *Papers excluded after evaluation of full text.*

Studies (n=74)	Reasons for exclusion							
	1	2	3	4	5	6	7	8
Abo et al., 2014			✓		✓			
Allison & Dennett, 2007			✓		✓			
Ang et al., 2014			✓		✓			
Askim et al., 2010			✓		✓			
Barreca, Sigouin, Lambert, & Ansley, 2004	✓							
Britton, Harris, & Turton, 2008	✓							
Byl, Pitsch, & Abrams, 2008			✓		✓			
Carmeli, Peleg, Bartur, Elbo, & Vatine, 2011			✓		✓			
Cauraugh, Naik, Lodha, Coombes, & Summers, 2011			✓		✓			
Chen et al., 2002			✓		✓			
Cha, Kim, Hwang, & Chung, 2014			✓		✓			
Chi, Yu, & Bi, 2013							✓	
Cozean, Pease, & Hubbell, 1988					✓			
de Jong, Dijkstra, Gerritsen, Geurts, & Postema, 2013			✓		✓			
Demetrios et al., 2014			✓		✓			
Di Lauro et al. 2003			✓		✓			
English et al., 2014								✓
Feys et al., 1999			✓		✓			
Globas et al., 2012			✓		✓			
Grasel, Biehler, Schmidt, & Schupp, 2005				✓	✓			
Hesse, Welz, Werner, Quentin, & Wiessel, 2011					✓			
Hillier et al., 2011	✓							
Howe, Taylor, Finn, & Jones, 2005			✓		✓			
Hsieh et al., 2011					✓			
Hsu et al., 2010				✓	✓			
Hunter et al., 2011			✓		✓			
Kalra, Dale, & Crome, 1993	✓							
Kalra, 1994	✓							
Khan, Oesch, Gamper, Kool, & Beer, 2011			✓		✓			
Kirk-Sanchez, et al., 2003						✓		
Kuys et al., 2011			✓		✓			
Kwakkel, 2001	✓							
Kwakkel, Wagenaar, Twisk, Lankhorst, & Koetsier, 1999	✓							
Kwakkel, Kollen, & Wagenaar, 2002								✓
Kwakkel & Wagenaar, 2002								✓
Langhammer, & Stanghelle, 2010					✓			
Lee, Kilbreath, Singh, Zeman, & Davis, 2010			✓	✓	✓			
Lee, Kim, & Lee 2014			✓		✓			
Macko et al., 2005					✓			
Martinsson, Eksborg, & Wahlgren, 2003			✓		✓			
Michielsen et al., 2011			✓		✓			
Mudie, Winzeler-Mercay, Radwan, & Lee, 2012			✓					
Nugent, Schurr, & Adams, 1994	✓							
Outermans, van Peppen, Wittink, Takken, & Kwakkel, 2010			✓		✓			
Page, Dunning, Hermann, Leonard, & Levine, 2011					✓			
Patten, Condliffe, Dairaghi, & Lum, 2013			✓		✓			

Studies	Reasons for exclusion							
	1	2	3	4	5	6	7	8
Pundik, Holcomb, McCabe, & Daly, 2012	✓							
Richards et al., 1993			✓					
Ryan, Enderby, & Rigby, 2006a		✓						
Ryan, Enderby, & Rigby, 2006b		✓						
Sahin, Ugurlu, & Albayrak, 2012			✓		✓			
Scianni, Teixeira-Salmela, & Ada, 2010	✓				✓			
Severinsen, Jakobsen, Pedersen, Overgaard,& Andersen, 2014			✓		✓			
Shendkar, Lenka, Biswas, Kumar, & Mahadevappa, 2015			✓		✓			
Shutter & Whyte, 1999	✓							
Sivenius, Pyorala, Heinonen, Salonen, & Riekkinen, 1985			✓			✓		
Slade et al.,, 2002		✓						
Smith et al, 1981				✓	✓			
Smith, Garraway, Smith, & Akhtar, 1982	✓							
Sunderland et al., 1992			✓		✓			
Swanton, Bower, & Gustafsson, 2012	✓							
Tankisheva, Bogaerts, Boonen, Feys, & Verschueren, 2014			✓		✓			
Tavernese et al., 2013			✓		✓			
Treger, Landesman, Tabacaru, & Kalichman, 2014					✓			
Tung, Yang, Lee, & Wang, 2010			✓		✓			
van Delden et al., 2013			✓		✓			
van Wijk, Cumming, Churilov, Donnan, & Bernhardt, 2012	✓		✓					
Wang, Yang, Tsai, Wang, & Chan, 2002			✓		✓	✓		
Wang, Lu, Xie, Yao, 2004							✓	
Wolf et al., 2006			✓		✓			
Wolf et al., 2007			✓		✓			
Yavuzer et al., 2006			✓		✓			
Young et al., 2015	✓				✓			
Zhu, Song, Q, & Liu, 2008							✓	

1 = Research design not RCT or QCT

2 = Participants not ≥80% with diagnosis of stroke, others being stroke-like

3 = Experimental intervention was not of the same content as control intervention

4 = Intervention not aimed at reducing limitations of lower and/or upper limb

5 = Not comparison of extra rehabilitation on top of usual rehabilitation versus usual rehabilitation

6 = Not enough information

7 = Not available in English

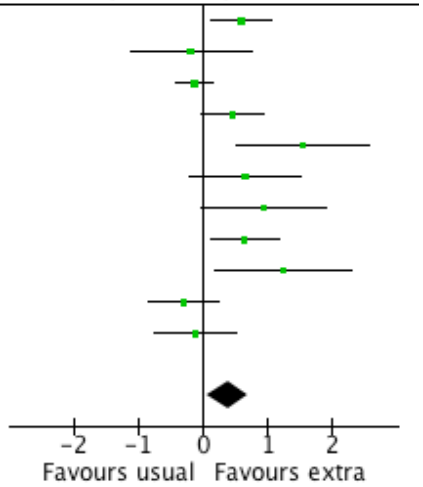
8 = Duplicate study or duplicate participants in previous study

STUDY 1 SUPPLEMENTARY FIGURES

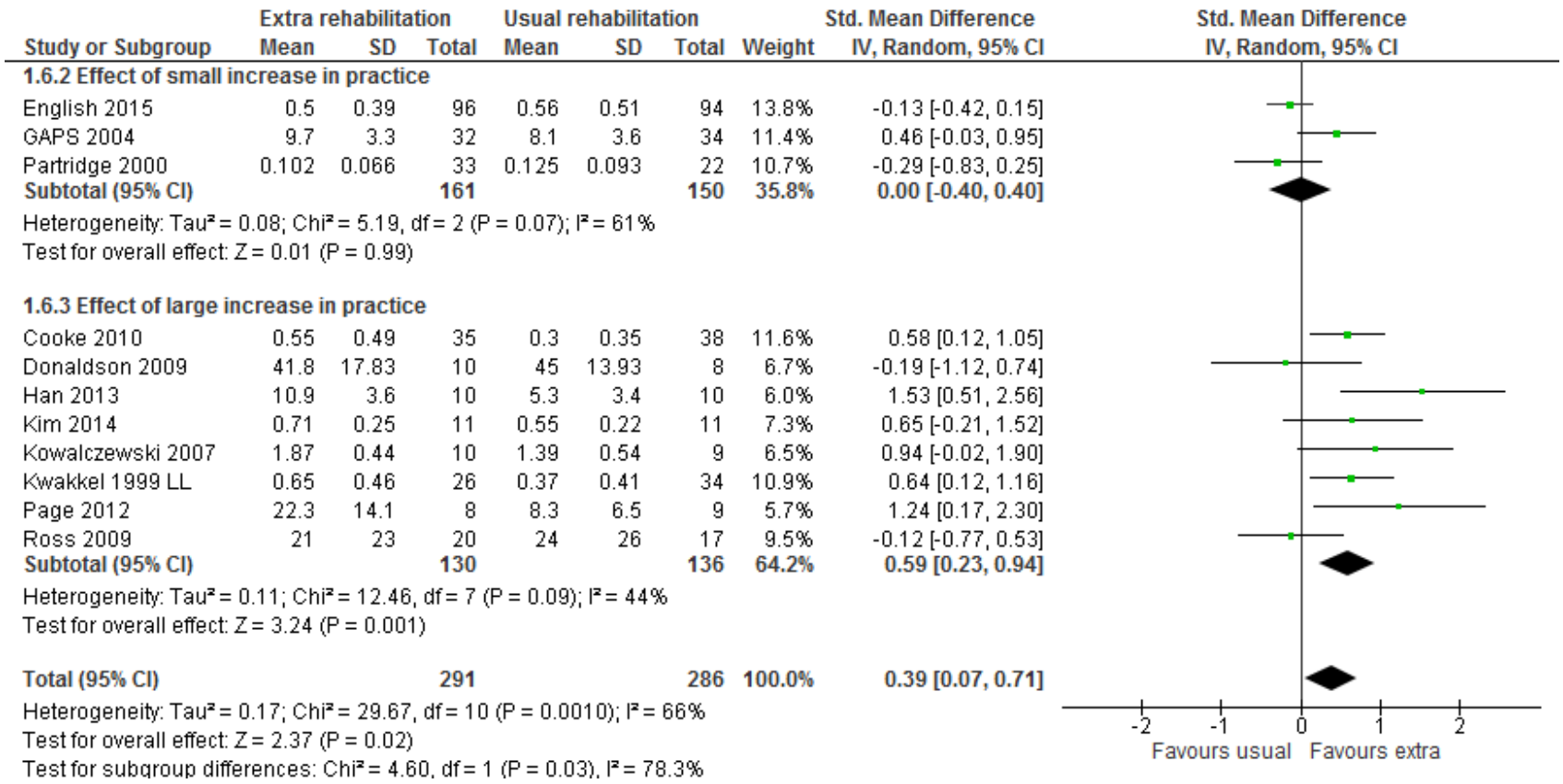
Study or Subgroup	Extra rehabilitation Mean	SD	Total	Usual rehabilitation Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Cooke 2010	0.55	0.49	35	0.3	0.35	38	11.6%	0.58 [0.12, 1.05]
Donaldson 2009	41.8	17.83	10	45	13.93	8	6.7%	-0.19 [-1.12, 0.74]
English 2015	0.5	0.39	96	0.56	0.51	94	13.8%	-0.13 [-0.42, 0.15]
GAPS 2004	9.7	3.3	32	8.1	3.6	34	11.4%	0.46 [-0.03, 0.95]
Han 2013	10.9	3.6	10	5.3	3.4	10	6.0%	1.53 [0.51, 2.56]
Kim 2014	0.71	0.25	11	0.55	0.22	11	7.3%	0.65 [-0.21, 1.52]
Kowalczewski 2007	1.87	0.44	10	1.39	0.54	9	6.5%	0.94 [-0.02, 1.90]
Kwakkel 1999 LL	0.65	0.46	26	0.37	0.41	34	10.9%	0.64 [0.12, 1.16]
Page 2012	22.3	14.1	8	8.3	6.5	9	5.7%	1.24 [0.17, 2.30]
Partridge 2000	0.102	0.066	33	0.125	0.093	22	10.7%	-0.29 [-0.83, 0.25]
Ross 2009	21	23	20	24	26	17	9.5%	-0.12 [-0.77, 0.53]
Total (95% CI)			**291**			**286**	**100.0%**	**0.39 [0.07, 0.71]**

Heterogeneity: $Tau^2 = 0.17$; $Chi^2 = 29.67$, df = 10 (P = 0.0010); $I^2 = 66\%$

Test for overall effect: Z = 2.37 (P = 0.02)



Appendix Figure 1. *Detailed forest plot of standardised mean difference (95% CI) of the effect of extra rehabilitation on top of usual rehabilitation compared with usual rehabilitation for activity immediately after the period of intervention (n=577 participants). LL=lower limb.*



Appendix Figure 2. *Detailed forest plot of standardised mean difference (95% CI) of the effect of the extra rehabilitation on top of usual rehabilitation compared with usual rehabilitation for activity, subgrouped by the relative amount of extra practice. LL=lower limb.*

Appendix E: Supplementary material from Study 2

Study 2

- Individual data

STUDY 2 INDIVIDUAL DATA

Appendix Table 2. *Individual data.*

ID	Age (years)	Gender (male, Y)	Time Since Stroke (months)	Right side hemiplegia (Yes/No)	Dominant UL (Y, Right)	Lives alone (Y/N)	Cognition number of errors	Education, attended University (Y/N)	Sensation (0=Normal; 1=Impaired; 2=Absent)	Walks unaided (Y/N)	Grip Strength Baseline (Kg)	BBT Baseline blocks/s	NHPT Baseline pegs/s	ROC Curve move peg in 60 seconds (1=Yes)	ROC Curve can pick up a cup (1=Yes)
1	83	Y	0.4	Y	Y	Y	3	Y	0	N	28	0.57	0.54	1	1
2	35	N	33	Y	Y	N	3	Y	0	N	4	0.23	0.29	1	1
3	33	Y	1	Y	Y	N	0	0	0	N	9	0	0.00	0	0
4	33	Y	0.1	Y	Y	N	2	Y	1	N	17	0.08	0.00	0	0
5	65	Y	0.23	Y	Y	Y	2	0	0	N	34	0.4	0.31	1	1
6	64	N	0.33	Y	Y	Y	5	Y	1	Y	10	0.8	0.37	1	1
7	54	Y	1.5	N	Y	N	6	0	0	N	8	0.33	0.21	1	1
8	77	Y	0.25	N	N	N	3	0	0	N	22	0.33	0.02	1	0
9	62	Y	0.4	Y	Y	N	1	0	0	Y	16	0.4	0.03	1	1
10	82	N	1	N	Y	Y	1	0	0	N	4	0.48	0.22	1	1
11	77	Y	0.22	N	Y	N	2	0	0	N	6	0.18	0.00	0	0
12	73	Y	0.22	Y	Y	Y	2	Y	0	N	29	0.67	0.44	1	1
13	72	N	0.2	N	Y	Y	3	Y	0	N	20	0.67	0.62	1	1
14	54	N	0.4	N	Y	N	2	0	0	N	13	0.3	0.34	1	1
15	46	N	0.5	Y	Y	N	0	Y	0	N	4	0	0.00	0	0
16	74	Y	1	Y	Y	Y	4	N	0	N	18	0.25	0.16	1	1
17	47	N	1.5	N	Y	N	2	N	0	N	1	0.08	0.00	0	0
18	49	Y	74	N	Y	Y	0	N	1	N	8	0	0.00	0	0
19	70	Y	22	N	Y	N	1	Y	2	N	2	0.02	0.00	0	0
20	35	Y	17	Y	Y	N	0	Y	1	Y	8	0.05	0.00	0	0
21	32	N	14	Y	Y	N	0	N	2	Y	4	0	0.00	0	0
22	52	Y	38	N	Y	N	3	N	1	N	1	0	0.00	0	0
23	68	Y	74	N	Y	Y	0	N	2	N	1	0	0.00	0	0
24	42	Y	68	Y	Y	N	1	Y	0	Y	12	0	0.00	0	0
25	46	N	73	Y	N	N	2	N	0	Y	2	0	0.00	0	0
26	59	N	30	Y	Y	N	1	N	1	N	4	0.28	0.00	0	0
27	60	Y	105	N	Y	Y	3	N	1	N	12	0.15	0.00	0	0
28	38	Y	44	N	Y	N	2	Y	1	N	10	0	0.00	0	0
29	69	Y	135	Y	Y	N	0	N	2	Y	30	0.28	0.00	0	0
30	31	Y	25	Y	Y	N	2	0	2	Y	4	0	0.00	0	0
31	57	Y	20	Y	Y	N	3	0	0	Y	8	0	0.00	0	0
32	50	Y	78	N	Y	N	0	Y	1	Y	1	0	0.00	0	0
33	33	Y	30	Y	Y	N	2	N	2	N	0	0	0.00	0	0
34	76	Y	45	Y	Y	N	3	N	0	Y	13	0	0.00	0	0
35	75	2	6	Y	Y	N	0	N	0	N	0	0	0.00	0	0
36	37	Y	63	Y	Y	N	0	Y	0	Y	18	0.3	0.01	1	1
37	75	N	30	N	Y	N	2	N	0	N	0	0.13	0.04	1	0

ID	Age (years)	Gender (male, Y)	Time Since Stroke (months)	Right side hemiplegia (Yes/No)	Dominant UL (Y, Right)	Lives alone (Y/N)	Cognition number of errors	Education, attended University (Y/N)	Sensation (0=Normal; 1=Impaired; 2=Absent)	Walks unaided (Y/N)	Grip Strength Baseline (Kg)	BBT Baseline blocks/s	NHPT Baseline pegs/s	ROC Curve move peg in 60 seconds (1=Yes)	ROC Curve can pick up a cup (1=Yes)
38	73	Y	24	Y	Y	N	2	N	0	N	10	0	0.00	0	0
39	80	N	40	N	Y	N	0	N	1	N	2	0	0.00	0	0
40	44	Y	43	N	Y	N	1	N	0	N	18	0.02	0.00	0	0
41	36	Y	11	Y	Y	N	1	Y	2	N	9	0.08	0.00	0	0
42	49	Y	21	N	Y	N	0	N	2	Y	4	0	0.00	0	0
43	49	Y	213	N	N	Y	0	Y	2	N	3	0	0.00	0	0
44	20	Y	26	Y	Y	N	2	N	1	N	4	0	0.00	0	0
45	68	Y	11	Y	Y	N	1	N	1	N	1	0	0.00	0	0
46	64	N	12	N	Y	N	2	N	1	N	0	0	0.00	0	0
47	71	Y	34	Y	Y	N	2	N	0	Y	20	0.2	0.03	1	0
48	56	N	24	Y	Y	N	4	N	1	N	0	0	0.00	0	0
49	56	N	9	N	Y	N	1	Y	1	N	6	0	0.00	0	0
50	54	Y	656	Y	Y	N	1	Y	0	Y	13	0	0.00	0	0
51	58	Y	65	N	Y	N	2	N	2	N	6	0	0.00	0	0
52	79	Y	1	N	Y	Y	3	N	0	N	8	0.47	0.43	1	1
53	32	N	1	N	Y	N	0	N	1	N	16	0.57	0.45	1	1
54	61	Y	1	N	Y	N	1	N	0	Y	26	0.3	0.14	1	1
55	49	N	4	Y	Y	Y	1	N	2	Y	10	0.35	0.14	1	1
56	48	N	5	Y	N	0	5	N	0	N	7	0.35	0.38	1	1
57	65	Y	12	Y	Y	1	0	Y	1	N	14	0.35	0.06	1	1
58	66	Y	5	N	Y	0	0	N	0	Y	32	0.6	0.51	1	1
59	69	Y	4	Y	Y	0	2	N	1	N	4	0.3	0.24	1	1
60	38	Y	23	Y	Y	0	0	N	0	Y	46	0.92	0.75	1	1

Appendix F: Supplementary material from Study 3

- Data collection form
- Individual data

STUDY 3 DATA COLLECTION FORM

Appendix Table 3. *Inpatient, upper limb rehabilitation class descriptive data collection form.*

Date of class:_____

Attendee	Upper limb activity Interventions							
	CIMT (minutes and reps)	Repetitive task-specific training (minutes and reps)	Mechanical assisted training (minutes and reps)	Mental practice (minutes and reps)	EMG Biofeedback (minutes and reps)	ES (minutes and reps)	FES (minutes and reps)	Mirror therapy (minutes and reps)
1	Start: End: Reps:	Start: End: Reps:	Start: End: Reps:	Start: End: Reps:	Start: End: Reps:	Start: End: Reps:	Start: End: Reps:	Start: End: Reps:
2	Start: End: Reps:	Start: End: Reps:	Start: End: Reps:	Start: End: Reps:	Start: End: Reps:	Start: End: Reps:	Start: End: Reps:	Start: End: Reps:
3	Start: End: Reps:	Start: End: Reps:	Start: End: Reps:	Start: End: Reps:	Start: End: Reps:	Start: End: Reps:	Start: End: Reps:	Start: End: Reps:
4	Start: End: Reps:	Start: End: Reps:	Start: End: Reps:	Start: End: Reps:	Start: End: Reps:	Start: End: Reps:	Start: End: Reps:	Start: End: Reps:
5	Start: End: Reps:	Start: End: Reps:	Start: End: Reps:	Start: End: Reps:	Start: End: Reps:	Start: End: Reps:	Start: End: Reps:	Start: End: Reps:
6	Start: End: Reps:	Start: End: Reps:	Start: End: Reps:	Start: End: Reps:	Start: End: Reps:	Start: End: Reps:	Start: End: Reps:	Start: End: Reps:

Staff Member	Attended Training	
1	Y	N
2	Y	N
3	Y	N
4	Y	N

STUDY 3 INDIVIDUAL DATA

Appendix Table 4. *Inpatient, upper limb rehabilitation class descriptive data.*

Class (month)	Number of staff facilitating (n)	Number of staff attended development program (n)	Number of patients attending (n)
0	3	0	7
0	1	0	0
0	2	0	4
0	3	0	6
0	0	0	0
12	3	2	6
12	2	2	4
12	3	2	3
12	3	2	6
12	1	1	2
18	3	2	3
18	3	1	5
18	3	0	6
18	3	1	7
18	3	2	4

Appendix Table 5. *Individual patient data.*

Patient (n)	Time (month)	Class duration (minutes)	Patient diagnosis (Stroke / Progressive/ Cord/ Other)	Practice time (minutes)	Repetitions (n)	Active time per session time (%)	Repetitions per active time (reps/min)
1	0	55	S	12	28	21.82	2.3
2	0	55	S	35	100	63.64	2.9
3	0	55	S	0	0	0.00	0.0
4	0	55	S	27	76	49.09	2.8
5	0	55	S	28	280	50.91	10.0
6	0	55	S	3	15	5.45	5.0
7	0	50	S	25	96	50.00	3.8
8	0	55	S	47	130	85.45	2.8
9	0	50	S	0	0	0.00	0.0
10	0	50	S	0	0	0.00	0.0
11	0	50	S	0	0	0.00	0.0
12	0	50	S	0	0	0.00	0.0
13	0	50	S	0	0	0.00	0.0
14	0	50	S	35	20	70.00	0.6
15	0	50	S	35	100	70.00	2.9
16	0	50	S	15	40	30.00	2.7
17	0	50	S	25	20	50.00	0.8
18	12	59	P	59	416	100.00	7.1
19	12	60	P	58	300	96.67	5.2
20	12	54	C	53	1590	98.15	30.0
21	12	56	O	43	238	76.79	5.5
22	12	54	C	50	399	92.59	8.0
23	12	59	C	59	180	100.00	3.1
24	12	57	C	30	180	52.63	6.0
25	12	56	O	43	238	76.79	5.5
26	12	65	O	45	119	69.23	2.6
27	12	60	C	45	270	75.00	6.0
28	12	60	P	60	380	100.00	6.3
29	12	60	P	60	274	100.00	4.6
30	12	54	C	50	248	92.59	5.0
31	12	54	C	46	795	85.19	17.3
32	12	46	C	40	240	86.96	6.0
33	12	47	C	47	670	100.00	14.3
34	12	40	P	40	213	100.00	5.3
35	12	56	S	0	0	0.00	0.0
36	12	48	S	34	140	70.83	4.1
37	12	45	S	45	206	100.00	4.6
38	12	52	S	47	215	90.38	4.6
39	18	58	P	38	204	65.52	5.4
40	18	60	P	53	800	88.33	15.1
41	18	47	O	37	430	78.72	11.3
42	18	47	P	43	390	91.49	9.1
43	18	45	C	40	160	88.89	4.0
44	18	53	O	45	540	84.91	12.0
45	18	60	P	42	418	70.00	10.0
46	18	46	P	29	215	63.04	7.4
47	18	35	C	31	105	88.57	3.4
48	18	55	P	51	248	92.73	4.9
49	18	41	C	30	180	73.17	6.0
50	18	56	P	56	506	100.00	9.0
51	18	60	O	57	182	95.00	3.2
52	18	51	P	46	301	90.20	6.5
53	18	5	S	5	34	100.00	6.8
54	18	55	S	44	317	80.00	7.2
55	18	43	S	43	121	100.00	2.8
56	18	53	S	49	161	92.45	3.3
57	18	47	S	42	117	89.36	2.8
58	18	55	S	47	110	85.45	2.3
59	18	55	S	50	172	90.91	3.4
60	18	6	S	4	5	66.67	1.3
61	18	50	S	44	151	88.00	3.4
62	18	53	S	37	290	69.81	7.8
63	18	41	S	35	105	85.37	3.0

Appendix G: Supplementary material from Study 4

Study 4

- Individual data

STUDY 4 INDIVIDUAL DATA

Appendix Table 6. *Individual data, demographics.*

ID	Age (years)	Sex (M/F)	Time since stroke (days)	Side of hemipleg ia (R/L)	Living situation (Alone / Others)	Education, attended university (Y/N)	Length of stay until discharge (days)	Cognition MMSE (0-30)	Unilateral spatial neglect (Y/N)	Loss of upper limb sensation (None, Some, Complete)	Spasticity (Y/N)	Contracture (Y/N)	Rehab complexit y scale (0-20)	Grasps unaided (Y/N)	Walks unaided (Y/N)
1	83	M	12	R	A	Y	21	27	N	N	N	Y	11	Y	N
2	35	F	402	R	O	Y	587	27	N	N	Y	Y	16	N	N
3	75	F	33	R	A	N	98	25	Y	N	Y	N	12	N	N
4	33	M	29	R	O	N	69	30	N	N	N	N	12	N	N
5	33	M	3	R	O	Y	35	28	N	S	N	N	14	N	N
6	65	F	7	R	A	N	16	28	N	N	Y	N	12	Y	N
7	64	F	10	R	A	Y	36	25	N	S	N	N	12	Y	Y
8	54	M	43	L	O	N	79	24	N	N	N	N	12	Y	N
9	77	M	8	L	O	N	42	27	Y	N	N	N	11	Y	N
10	62	F	14	R	O	N	12	29	N	N	N	N	11	Y	Y
11	82	F	33	L	A	N	48	29	N	N	Y	N	11	Y	N
12	77	M	7	L	O	N	20	28	N	N	N	N	12	N	N
13	73	M	7	R	A	Y	21	28	N	N	N	N	11	Y	N
14	72	F	6	L	A	Y	13	27	N	N	N	N	10	Y	N
15	54	F	13	L	O	N	41	28	N	N	N	N	15	Y	N
16	46	F	15	R	O	Y	43	30	N	N	N	N	16	N	N
17	83	F	14	R	A	Y	83	28	N	N	N	Y	13	N	N
18	74	M	31	R	A	N	48	26	N	N	N	N	10	N	N
19	68	M	28	L	O	Y	60	28	N	N	Y	N	13	N	N
20	47	F	43	L	O	N	56	28	N	N	Y	N	14	N	N

Appendix Table 7. *Individual data, feasibility of intervention.*

ID	Usual rehabilitation scheduled per day, mean (minutes)	Total practice time (minutes)	Sessions completed, 0-24 (number)	Sessions missed, 0-24 (number)	Session missed early discharge (number)	Sessions missed illness (number)	Sessions missed withdrawal (number)	Mean practice time per session (minutes)	Mean session duration (minutes)	Acceptability Recommend (Y/N)	Acceptability Amount (too Much / too Little / just Enough)	Acceptability Training make you tired (Y/N)	Acceptability if tired Yes, so tired you wanted to stop (Y/N)	Acceptability Satisfaction (1-6)
1	0	677	11	13	11	2	0	61.5	83	Y	E	N	x	5
2	0	1027	24	0	0	0	0	42.8	109	Y	E	N	x	5
3	36	1079	18	6	0	6	0	59.9	82	Y	E	N	x	5
4	48	1317	21	3	0	3	0	62.7	73	Y	L	Y	N	5
5	60	179	3	21	0	6	15	59.7	75	N	M	Y	N	3
6	0	600	10	14	12	2	0	60.0	69	Y	E	Y	N	5
7	12	1032	18	6	0	6	0	57.3	72	Y	E	N	x	5
8	24	885	17	6	0	6	0	52.1	63	Y	E	N	x	5
9	45	1428	24	0	0	0	0	59.5	76	Y	E	Y	N	4
10	60	130	6	19	14	5	0	21.7	62	Y	E	Y	Y	5
11	39	1135	20	4	0	4	0	56.8	67	Y	E	Y	Y	5
12	24	942	15	9	9	0	0	62.8	67	Y	E	Y	Y	5
13	88	932	15	9	9	0	0	62.1	67	Y	E	N	x	5
14	0	472	8	16	15	1	0	59.0	69	Y	E	N	x	5
15	30	1361	24	0	0	0	0	56.7	65	Y	E	N	x	5
16	45	1381	23	1	0	1	0	60.0	70	Y	E	Y	N	5
17	57	1347	24	0	0	0	0	56.1	73	Y	E	N	x	5
18	33	1443	24	0	0	0	0	60.1	71	Y	E	N	x	4
19	60	1029	21	3	0	3	0	49.0	65	Y	E	N	x	5
20	74	1044	17	7	7	0	0	61.4	73	Y	E	N	x	5

Appendix Table 8. *Individual data, clinical outcomes.*

ID	B&BT Baseline (blocks/s)	B&BT End (blocks/s)	NHPT-Baseline	NHPT – End	Grip strength Baseline (Kg)	Grip strength End (Kg)
1	0.57	0.87	0.54	0.69	28	32
2	0.23	0.35	0.29	0.32	4	6
3	0.00	0.00	0.00	0.00	0	1
4	0.00	0.67	0.00	0.07	9	12
5	0.08	0.25	0.00	0.02	17	22
6	0.40	0.62	0.31	0.39	34	36
7	0.80	1.05	0.37	0.72	10	13
8	0.33	0.62	0.21	0.32	8	12
9	0.33	0.63	0.02	0.39	22	24
10	0.40	0.58	0.03	0.46	16	24
11	0.48	0.77	0.22	0.58	4	8
12	0.18	0.45	0.00	0.06	6	12
13	0.67	1.02	0.44	0.72	29	36
14	0.67	0.93	0.62	0.75	20	22
15	0.30	1.18	0.34	1.20	13	20
16	0.00	0.62	0.00	0.46	4	19
17	0.00	0.18	0.00	0.00	0	4
18	0.25	0.35	0.16	0.30	18	22
19	0.00	0.05	0.00	0.00	0	4
20	0.08	0.40	0.00	0.05	1	2

Appendix H: Published manuscripts

Study 1

Schneider EJ, Lannin NA, Ada L (2014). Increasing the intensity of rehabilitation to improve activity after stroke: a systematic review protocol. *Journal of Clinical Trials* 4:195. doi: 10.4172/2167-0870.1000195

Schneider EJ, Lannin NA, Ada L, Schmidt J (2016). Increasing the amount of usual rehabilitation improves activity after stroke: a systematic review. *Journal of Physiotherapy, 62 (4):182-187.* doi: 10.1016/j.jphys.2016.08.006

Study 3

Schneider EJ, Lannin NA, Ada L (2019). A professional development program increased the intensity of practice undertaken in an inpatient, upper limb rehabilitation class: a pre-post study. *Australian Occupational Therapy Journal*, 66 (3):362-368. doi: 10.1111/1440-1630.12562

Study 4

Schneider EJ, Ada L, Lannin NA (2019). Extra upper limb practice after stroke: a feasibility study. *Pilot and Feasibility Studies, 5,156.* doi: 10.1186/s40814-019-0531-5

Schneider et al., J Clin Trials 2014, 4:6
http://dx.doi.org/10.4172/2167-0870.1000195

Clinical Trials

Protocol Open Access

Increasing the Intensity of Rehabilitation to Improve Activity after Stroke: Systematic Review Protocol

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Abstract

Question: Repetitive practice facilitates motor learning after stroke but the effect of a rehabilitation program which provides an extra amount of the same, repetitive practice per week remains unknown. This protocol paper describes the methods to address the questions of a planned systematic review:

(1) Does extra practice per week of the same rehabilitation lead to improved activity in stroke survivors? and

(2) What is the amount of extra rehabilitation that needs to be provided to achieve an effect?

Method: A systematic review will be conducted, commencing with a search of Medline, EMBASE, CINAHL, and CENTRAL databases. Randomised and non-randomized controlled trials that compare stroke rehabilitation programs involving similar content but different duration (recorded as therapy time per day or week) will be included. The outcome of interest will be activity, represented by walking ability or upper limb ability. The methodological quality of included studies will be assessed independently by two reviewers using the PEDro scale. Data will be extracted by two reviewers and will be pooled in a meta-analysis where there is sufficient homogeneity. We will calculate mean differences (MD) or standardized mean differences (SMD) and 95% CI for continuous outcomes as appropriate. We will calculate a Pearson correlation coefficient and ROC calculation to define the amount (in hours) of extra rehabilitation that needs to be provided to achieve improved activity in stroke survivors.

Discussion: Findings will explore the relationship between increasing intensity of rehabilitation and improved activity in stroke survivors, and provide guidance to rehabilitation clinicians, inform policy and provide future directions for research.

Systematic review registration: PROSPERO CRD42012003221.

Keywords: Stroke; Rehabilitation; Occupational therapy; Physical therapy; Review systematic; Meta-analysis; Intensity; Dose-response

Background

Stroke is a leading cause of disability among adults worldwide; approximately 80% of stroke survivors are left with impairments affecting activity and participation [1,2]. Repetitive practice promotes motor learning in stroke survivors and prior investigations have shown that an increase in the amount of practice can improve motor outcomes for stroke survivors [3-8]. Despite this overarching finding, confounding factors have been identified when investigating the relationship between increased rehabilitation intensity and patient-level outcomes [5,6,9]. While more practice is considered best, there is uncertainty regarding the sensitivity of the relationship between rehabilitation intensity and improved activity performance after stroke.

Motor learning occurs through active engagement of the participant in repetitive practice of specific tasks that are challenging, progressive and skill-based [6]. It is generally accepted that therapists should encourage the person with stroke to complete high numbers of repetitions [10-12]. Since 1996 previous systematic reviews have explored the effect of increased amounts of practice in rehabilitation programs; each review has included between 7 and up to 30 randomized and non-randomized controlled trials, and all have consistently generated findings that suggest an overall trend of a positive effect [4-9], i.e. that providing more therapy leads to better outcomes. Earlier reviews found a small to medium positive effect on walking ability from additional walking practice (summary effect size of 0.32, SD 0.11-0.52) [8], and significant improvement in ADL from an additional 16 hours of exercise therapy stroke (summary effect size of 0.22, SD 0.07-0.37) [7]. However, more recent investigations exposed conflicting factors that were overlooked during investigations into the complex relationship between a rehabilitation program providing intensive practice and improved outcome [6,9].

More recent systematic reviews modified their inclusion criteria in an attempt to address the criticism made of earlier reviews; that studies provided different therapy interventions across trial arms which would understandably result in different outcomes [5]. An intensive program would provide extra practice of the same task per day or per week, yet some previously included trials were not designed to measure the effect of different doses of the same therapy, rather they studied different types of therapy delivered in different doses, or they studied therapy compared to no therapy [9]. When controlling for therapy type, there was no evidence for an effect of intensity [9] demonstrating that earlier investigations of the relationship may have been inflated.

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Furthermore, earlier reviews did not distinguish between the types of activity practiced, simply grouping all types of practice together to represent a generalized practice incorporating the duration of the entire rehabilitation program. They defined an intensive rehabilitation program as 'more time in rehabilitation', thus, actually investigating the effect of an accumulated duration of therapy not the effect of an intensive rehabilitation program [3,7-9]. While the number of repetitions completed over a specific time period is the most sensitive measure of intensity, the duration of rehabilitation sessions is the most commonly reported measure in trials investigating the effect of intensity on outcome [4-9]. When the total duration of practice is matched there is strong evidence of a positive non-linear relationship between dose and response, suggesting a small overall benefit of augmented intervention time in therapy (g=0.35; 95% CI (0.26-0.45); Z_{obs}=7.21) [6]. However a more sensitive approach is to calculate the 'dose' of extra practice by comparing the difference of 'time in rehabilitation per day or per week' provided to the control group compared to the experimental group.

The planned systematic review aims to build on this knowledge by searching for recent randomized trials designed to measure the effect of more practice of the same rehabilitation. It will identify and synthesize evidence of the association between increasing the intensity of rehabilitation and improving activity in stroke survivors and determine the strength of the effect. A meta-analysis will be completed along with further investigation into the relationship between an intensive rehabilitation program and improved activity after stroke. We aim to determine the sensitivity of an intensive rehabilitation program on improving activity as well as explore the issue of how much more practice is necessary. We also aim to determine if a threshold exists to determine the strength of the effect. The information sought in this review will provide unique information relative to previous systematic reviews. Therefore, the specific questions that the methods of this review will address are:

1. Does extra practice per week of the same rehabilitation lead to improved activity in stroke survivors?
2. What is the amount of extra rehabilitation that needs to be provided to achieve an effect?

Method

A systematic review will be carried out (Figure 1) and reporting will adhere to the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement [13]. The protocol for the review was registered with the International Prospective Register of Systematic Reviews (PROSPERO) and has the registration number CRD42012003221.

Identification and selection of studies

Searching: The following electronic databases will be searched: Medline, EMBASE, CINAHL, and the Cochrane Central Register of Controlled Trials (CENTRAL). Medical Subject Headings (MeSH) relating to *stroke, hemiplegia, physical therapy, occupational therapy, rehabilitation* and *intensity* will be combined with text words in search strategies. An additional documentation file details the search strategy. The MEDLINE search strategy will be adapted for other databases with the assistance of an informed specialist (a medical librarian). One reviewer (ES) will review titles and abstracts of the records identified from the electronic searches and exclude irrelevant studies. Full text versions of the remaining studies will be obtained and two reviewers (ES and NL) will select studies for inclusion based on the pre-specified inclusion criteria (Table 1). Disagreements will be adjudicated by a third reviewer (LA). Trial authors will be contacted for missing study details when required, and reasons for exclusion of full text papers will be documented. Eligible papers will be published in peer-reviewed journals and available in English. No date restrictions will be set. Conference proceedings will not be included.

Characteristics of studies

Design: Randomized and non-randomized controlled trials will be included in this review. For three armed trials and multiple-armed trials comparing different intensities of rehabilitation, we will enter the sample size for the group receiving the most minutes of rehabilitation per week compared to the group receiving the least minutes of rehabilitation per week.

Participants and settings: Participants will be aged 18 years or older. Studies will be included where 80% or more of participants have a diagnosis of stroke (diagnosed using any recognized diagnostic criteria) and loss at the level of activity [14]. Studies will be included if the participants are at any stage of recovery (acute, sub-acute, or chronic) and receiving occupational therapy and/or physical therapy in hospital, rehabilitation or community settings. Study details will be recorded, including the number of participants, age, gender, diagnosis, time since onset of stroke, and type of rehabilitation service (acute,

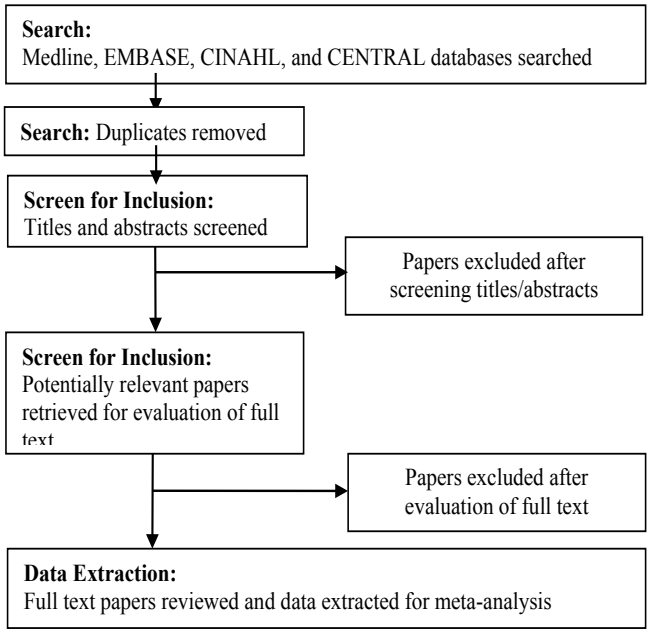

Figure 1: Flow of studies through the review.

Design	• Randomized controlled trials and/or controlled trials.
Participants	• Adult age ≥18 years old with a diagnosis of stroke (as diagnosed using any recognized diagnostic criteria) (≥ 80%, others being stroke-like). • Activity limitations affecting walking and/or upper limb ability.
Intervention	• Activity limitations affecting walking and/or upper limb ability.
Outcome measures	• Performance of activity measured by walking or upper limb ability.

Table 1: Inclusion criteria.

sub-acute or chronic). The number of people recruited to the study, randomized and number of withdrawals will be noted.

Intervention: Interventions must involve active engagement of the participant to promote motor learning. Interventions will be classified as involving active engagement if at least half of the total interventions are targeted at the level of activity, as defined by the International Classification of Function (ICF) [14], and if at least one aim of the intervention is to improve walking ability, upper limb ability and/or both. Activity-specific interventions, such as additional sit-to-stand practice, will be included for comparison as long as both groups received interventions that would result in a similar outcome. Interventions provided to the experimental and control group will be matched at the activity level so that both groups received rehabilitation to practice the same activity in different durations (minutes per day or per week). The minutes of practice received by the control group will be calculated specific to the activity completed during the extra practice they received. Differences in the minutes of practice will be used to calculate percentages of practice provided to both groups. As this review is investigating the effect of extra minutes of rehabilitation per week, a group that does not receive any therapy will not be included. A greater contrast in the duration of intervention time per day/week between the experimental and control groups would most accurately represent the effect of an intensive rehabilitation program.

Outcome measures: The primary outcome of interest is activity. Included outcome measures will assess at the ICF level of activity performance in walking ability and upper limb activity. Assessments of walking ability may include assessment of gait speed (10-m Walk Test in s) and distance (6-min Walk Test in m). Assessments of upper limb activities may include the Nine Hole Peg Test and the Box and Block Test. To check the similarities of the studies we will record the outcome measures used and time points when they were administered. All review authors will assign outcome measures to the domain assessed (walking ability and/or upper limb activities). If data are skewed or more than one outcome measure is used in the same domain from the same study, we will include timed performance tests and the outcome measure most frequently used across included studies. There are no secondary objectives; however, all other outcome measures will be noted.

Data Extraction

Two review authors will independently extract study data and record information on a pre-designed data extraction form. Information about the method (design, participants, intervention, outcome measures) and outcome data (number of participants exposed to intensive rehabilitation, mean (SD), walking ability and upper limb ability) will be extracted. Data will be crosschecked and differences resolved by discussion or a third review author as necessary.

Assessment of methodological quality

The methodological quality of studies will be assessed using the PEDro scale [15]. The scale produces a score out of 10 depending on whether the study controlled for the following sources of bias: random allocation; allocation concealment; similarity between groups at baseline, blinding of participants, personnel and outcome assessors; incomplete outcome data and reporting of data. Wherever possible, PEDro scores recorded on the PEDro database will be used. If a study has not been rated by the PEDro team, two review authors will independently score the study and a third review author will resolve any disagreements.

Data analysis

Where there is sufficient homogeneity between studies we will conduct a meta-analysis to determine if more practice per week of the same rehabilitation leads to improved activity after stroke. We will only pool outcome measures in meta-analysis if they are timed performance outcome measures. For continuous outcomes we will calculate Standardized Mean Differences (SMD) using RevMan 5.1 [16]. The immediate post-intervention scores will be used to first conduct a fixed-effects meta-analysis. Heterogeneity will be assessed via visual inspection of the forest plot and consideration of both the chi-squared test and the I-squared statistic. We will apply a random-effects meta-analysis and conduct a sub-group analysis to assess the impact of heterogeneity on the SMD. In the case of significant statistical heterogeneity (I-squared over 50%) we will conduct a sensitivity analysis and apply a random-effects meta-analysis. We will not pool data if there is considerable variation in the results (I-squared statistic >75%).

We will calculate the percentage of extra practice provided in each trial and, using the SMD, we will calculate a Pearson correlation coefficient to explore the relationship between an increasing intensity of rehabilitation and improved walking and upper limb ability.

The positive or negative effect of increasing the amount of practice will be compared with the total volume of extra practice provided in each trial to conduct a ROC curve calculation. We will conduct a ROC curve calculation to determine the amount of extra rehabilitation that needs to be provided to achieve improved activity in stroke survivors. If there are a sufficient number of comparable studies (four or more), we will perform subgroup analysis to determine if the benefit of extra practice per week is dependent on the type of activity practiced (walking or upper limb activity) or the rehabilitation approach used.

A narrative synthesis summarizing the main findings of all included studies will be provided. It will be structured around the type and duration of rehabilitation, target population characteristics, type of outcome and intervention content. The description of studies will include a measure of stroke severity where available, such as the NIH Stroke Scale. In addition, we will summarize the time since stroke and the amount of rehabilitation stroke patients received compared to the amount planned across the experimental and control conditions, noting any recorded barriers to intervention. We will comment on the format of intervention provided, for example whether it was provided one-to-one or in a group setting.

Dealing with missing data: We will contact trial authors for missing data and convert available data where possible, as recommended by the Cochrane Handbook of Systematic Reviews of Interventions [17].

Unit of analysis issues: The unit of randomization in these trials is the individual patient. The number of participants in the intensive rehabilitation and usual care groups will reflect the two selected experimental groups; the mean and standard deviations will remain unchanged.

Discussion

This review will explore the complexity that exists between the relationship of an intensive rehabilitation program and improved activity in stroke survivors.

The results of this systematic review will be compared to previous findings with differences and similarities explained. We will additionally compare our findings to data from studies which provide

information on actual amounts of therapy provided and to current recommendations regarding the amount of therapy that should be provided in rehabilitation. While this review will provide information on the sensitivity of the optimal dose of therapy, there may be challenges in implementation: workforce shortages, current models of delivery (typically 1:1), patient expectations and motivation, therapist expectations and access to resources.

Findings will thus provide guidance to occupational therapists and physical therapists, inform policy decisions and provide future directions for research. Findings may lead to the development of a rehabilitation program that delivers the ideal opportunity for practice and will help clinicians identify how much extra practice stroke survivors have to do in a rehabilitation program to achieve improved outcomes.

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Research

Increasing the amount of usual rehabilitation improves activity after stroke: a systematic review

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KEY WORDS

Stroke
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ABSTRACT

Questions: In people receiving rehabilitation aimed at reducing activity limitations of the lower and/or upper limb after stroke, does adding extra rehabilitation (of the same content as the usual rehabilitation) improve activity? What is the amount of extra rehabilitation that needs to be provided to achieve a beneficial effect? **Design:** Systematic review with meta-analysis of randomised trials. **Participants:** Adults aged 18 years or older that had a diagnosis of stroke. **Intervention:** Extra rehabilitation with the same content as usual rehabilitation aimed at reducing activity limitations of the lower and/or upper limb. **Outcome measures:** Activity measured as lower or upper limb ability. **Results:** A total of 14 studies, comprising 15 comparisons, met the inclusion criteria. Pooling data from all the included studies showed that extra rehabilitation improved activity immediately after the intervention period (SMD = 0.39, 95% CI 0.07 to 0.71, I^2 = 66%). When only studies with a large increase in rehabilitation (> 100%) were included, the effect was greater (SMD 0.59, 95% CI 0.23 to 0.94, I^2 = 44%). There was a trend towards a positive relationship (r = 0.53, p = 0.09) between extra rehabilitation and improved activity. The turning point on the ROC curve of false versus true benefit (AUC = 0.88, p = 0.04) indicated that at least an extra 240% of rehabilitation was needed for significant likelihood that extra rehabilitation would improve activity. **Conclusion:** Increasing the amount of usual rehabilitation aimed at reducing activity limitations improves activity in people after stroke. The amount of extra rehabilitation that needs to be provided to achieve a beneficial effect is large. **Trial registration:** PROSPERO CRD42012003221. **[Schneider EJ, Lannin NA, Ada L, Schmidt J (2016) Increasing the amount of usual rehabilitation improves activity after stroke: a systematic review. *Journal of Physiotherapy* 62: 182–187]**

Introduction

Stroke is the leading cause of disability worldwide.[1] Difficulty walking and using the arm to complete self-care tasks are the most common activity limitations reported by stroke survivors.[2,3] Practice is essential for motor learning and needs to be structured to offer a progressive challenge to reduce activity limitations.[4–7] Consequently, clinical practice guidelines for stroke rehabilitation worldwide recommend that programs deliver a large amount of practice in order to maximise outcome after stroke.[8–10]

Several systematic reviews have explored the effect of the amount of practice on outcome after stroke.[5–7,11–14] Three systematic reviews with meta-analyses have specifically investigated the effect of extra practice on motor outcomes after stroke. Kwakkel et al[11] found that extra rehabilitation improved activities of daily living (SMD 0.13, 95% CI 0.03 to 0.23, 24 randomised trials). Verbeek et al[6] found that extra lower limb rehabilitation within 6 months of stroke improved walking ability (SMD 0.32, 95% CI 0.11 to 0.52, 11 randomised trials) and walking speed (SMD 0.22, 95% CI 0.01 to 0.43, eight randomised trials). Most recently, Lohse et al[5] found that extra rehabilitation improved outcome (SMD 0.35, 95% CI 0.26 to 0.45, 34 randomised trials). Furthermore, previous reviews have suggested that there is a dose-response relationship, where the greater the extra rehabilitation, the greater the benefit,[5–7,11,12,14] regardless of time after stroke.[5]

Importantly, however, these previous systematic reviews included trials that did not investigate different doses of the same content of rehabilitation. For example, some of the included trials compared the effect of rehabilitation with no rehabilitation. Other included trials provided extra rehabilitation that was of different content to the usual rehabilitation, thereby confounding the analysis of amount of rehabilitation with type of rehabilitation. Cooke et al[12] recognised these limitations and examined seven trials where the extra rehabilitation was delivered on top of usual rehabilitation and was of the same content. A meta-analysis of the seven studies was not performed, but the effect sizes of several trials with the same outcomes suggested that there was some evidence supporting the hypothesis that extra rehabilitation on top of usual rehabilitation improves outcomes after stroke.[12]

Rehabilitation is resource intensive, both on the part of the patient and the healthcare system. It is therefore important to

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determine the effect of increasing the amount of usual rehabilitation after stroke, and to ensure that this estimate is not confounded by the effect of extra rehabilitation of different content. Therefore, the aim of this review was to examine the effect of extra rehabilitation of the same content on top of usual rehabilitation.

Therefore, the research questions for this systematic review were:

1. In people receiving rehabilitation aimed at reducing activity limitations of the lower and/or upper limb after stroke, does adding extra rehabilitation (of the same content as the usual rehabilitation) improve activity?
2. What is the amount of extra rehabilitation that needs to be provided to achieve a beneficial effect?

Box 1. Inclusion criteria.

Design
- Randomised or quasi-randomised trial

Participants
- Adults (≥ 18 years old)
- Diagnosis of stroke (≥ 80% participants with stroke, others being stroke-like)

Intervention
- Extra rehabilitation (of the same content as usual rehabilitation) aimed at reducing activity limitations (of lower and/or upper limb)

Outcome measures
- Measures of activity

Comparisons
- Extra rehabilitation on top of usual rehabilitation versus usual rehabilitation

Method

Identification and selection of studies

A systematic review of randomised or quasi-randomised trials was undertaken so that guidelines could be based on the highest level of evidence. Searches were conducted of Medline, EMBASE, CINAHL, and the Cochrane Register of Controlled Trials (CENTRAL) databases, from the earliest date available until October 2015, for relevant articles available in English. Search terms included words related to *stroke*, *physical therapy*, *occupational therapy*, *rehabilitation* and *intensity* (such as dose, frequency, quantity, duration and amount) (see Appendix 1 on the eAddenda for full search strategy). Titles and abstracts were displayed and screened by one reviewer to identify potentially relevant studies. Full paper copies of potentially relevant papers were retrieved. Reference lists of articles included in this review and of similar systematic reviews were screened to determine any additional studies meeting the inclusion criteria. The methods of retrieved papers were reviewed independently by two reviewers (ES and JS) using predetermined criteria (Box 1). An independent reviewer (NL or LA) adjudicated any disagreements.

Assessment of characteristics of studies

Quality

The quality of the included studies was assessed by extracting PEDro scores from the Physiotherapy Evidence Database (www.pedro.org.au). The PEDro scale generates a score out of 10 depending on whether the quality of each study meets each item of the tool.[15] Where a study was not included on the database, two review authors independently scored the study (ES and JS), and a third review author resolved any disagreements (NL).

Participants

Studies were included if ≥ 80% participants were adults with stroke (with the remainder being stroke-like conditions such as cerebral aneurysm). Characteristics of participants, such as age, gender, time since stroke and type of rehabilitation service, were examined to assess the similarity of the studies.

Intervention

Studies were included if they examined the effect of an increased dose of rehabilitation. That is, the experimental group received extra rehabilitation (of the same content as usual rehabilitation) on top of usual rehabilitation aimed at improving lower limb activity or upper limb activity or both. The control group received usual rehabilitation alone. The dose of usual rehabilitation was calculated as the amount of time dedicated to rehabilitation of the activity included in the extra rehabilitation. For example, if the experimental group received 30 minutes of extra upper limb rehabilitation, and the control group received 60 minutes of rehabilitation consisting of 30 minutes upper limb and 30 minutes lower limb, the comparison of the same content would be 30 minutes extra upper limb rehabilitation plus 30 minutes usual upper limb rehabilitation (60 minutes) versus 30 minutes usual upper limb rehabilitation.

Outcome measures

Measures involving direct observation of upper or lower limb activity were used, regardless of whether they produced continuous data (eg, Box and Block Test, 10-m Walk Test) or ordinal data (eg, Action Research Arm Test, Functional Ambulation Category).

Data analysis

Information about the method (ie, design, participants, intervention, measures) and results (ie, number of participants and mean (SD) of outcomes) were extracted by one reviewer and crosschecked by another reviewer. Data were converted, where necessary, using methods recommended by the *Cochrane Handbook of Systematic Reviews*.[16] Authors were contacted where information was unavailable.

Post-intervention scores were used to obtain the pooled estimate of the effect of extra rehabilitation using RevMan 5.1 software.[17] Since different outcome measures were used, the effect size was reported as Cohen's standardised mean difference (SMD) with a 95% CI. A random-effects model was used and in the case of significant heterogeneity ($I^2 > 50\%$), a sensitivity analysis was carried out to confirm the source of heterogeneity. Sub-group analyses according to the time after stroke (acute versus chronic) and body part (upper versus lower limb) were planned *a priori* where there were a sufficient number of comparable studies. The relationship between percentage of extra rehabilitation provided and the effect size was calculated using Pearson correlation coefficient. The amount of extra rehabilitation needed to provide a beneficial effect was determined from a receiver-operator characteristic (ROC) curve.

Results

Flow of studies through the review

The electronic search strategy identified 5141 studies, of which 284 were duplicates. After screening titles, abstracts and reference lists, 89 potentially relevant papers were retrieved. Among these, 74 papers failed to meet the inclusion criteria (see Appendix 2 on the eAddenda for a summary of excluded papers), and therefore 15 papers reporting 14 studies were included in the review (Figure 1).

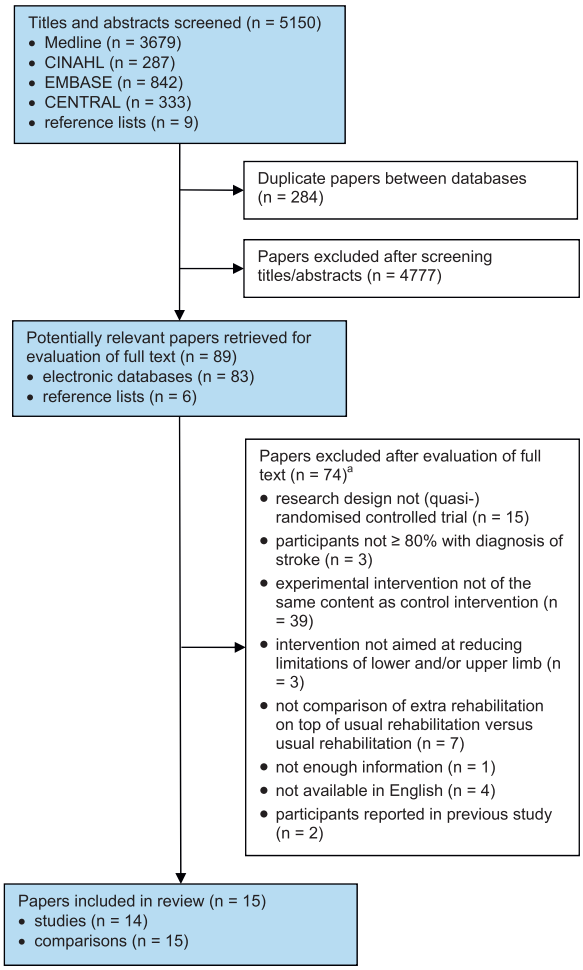

Figure 1. Flow of studies through the review.
[a] Papers may have been excluded for failing to meet more than one inclusion criterion.

Characteristics of included studies

The 14 studies included in this review involved 954 participants in 15 comparisons investigating the effect of extra rehabilitation on top of usual rehabilitation for improving activity (Table 1).[18–32] Additional information was requested from the authors of four studies.[21,28,29,31]

Quality

The mean PEDro score of included papers was 6.9 out of 10, with individual study scores ranging from 5 to 8 (Table 2). All of the papers reported random allocation, baseline similarity, between-group difference, and point estimate variability. The majority of papers reported concealed allocation (80%), assessor blinding (87%), and < 15% loss to follow-up (87%). No papers reported participants or therapist blinding and 40% reported performing an intention-to-treat analysis.

Participants

Across the studies, the mean age ranged from 49 to 75 years. Time after stroke ranged from a few weeks to > 6 months, with 86% of the studies carried out within 6 months after stroke.

Intervention

All the studies involved the experimental group receiving extra rehabilitation on top of usual rehabilitation, and the control group receiving usual rehabilitation. Furthermore, the extra rehabilitation was the same content as usual (or a component of usual) rehabilitation. Extra rehabilitation included upper limb activity (nine comparisons), lower limb activity (four comparisons), or both upper and lower limb activity (two comparisons). One included study involved three trial arms; only the experimental group receiving therapy 7 days per week and the control group receiving usual care were included.[19]

Outcome measures

Upper limb activity was measured using the Wolf Motor Function Test (two comparisons) or the Action Research Arm Test (seven comparisons). Lower limb activity was measured using timed tests of walking speed (five comparisons) and the Rivermead Mobility Index (one comparison).

Effect of extra rehabilitation on top of usual rehabilitation

The immediate effect of extra rehabilitation on top of usual rehabilitation was examined by pooling post-intervention data using a random effects model from 11 comparisons that measured activity immediately after the intervention period. These comparisons were from studies of good quality (PEDro score 7.2 out of 10) and comprised 577 participants. Extra rehabilitation improved activity immediately after the intervention period (SMD = 0.39, 95% CI 0.07 to 0.71) (Figure 2); see Figure 3 on the eAddenda for a detailed forest plot. Four comparisons could not be included in the analysis: one because there was no immediate data,[31] one because there was no post-intervention data,[18] and two because the data were too skewed to enable conversion from non-parametric data to parametric data.[26,28](upper limb) There was substantial statistical heterogeneity (I^2 = 66%), indicating that the variation between the results of the trials was above the variation expected by chance. A sensitivity analysis revealed that the heterogeneity was not explained by the quality of the trials (PEDro score > 6/10), assessor blinding (yes or no), sample size (> 20 participants per trial), severity of participants (> 20% normal activity), chronicity of participants (> 6 months post stroke) or limb rehabilitated (upper versus lower). However, heterogeneity was partially explained by the amount of extra practice. In order to standardise extra rehabilitation across the comparisons, it was expressed as percentage increase per week. When re-analysed, separating trials into small (≤ 100%) or large (> 100%) increases in amount of

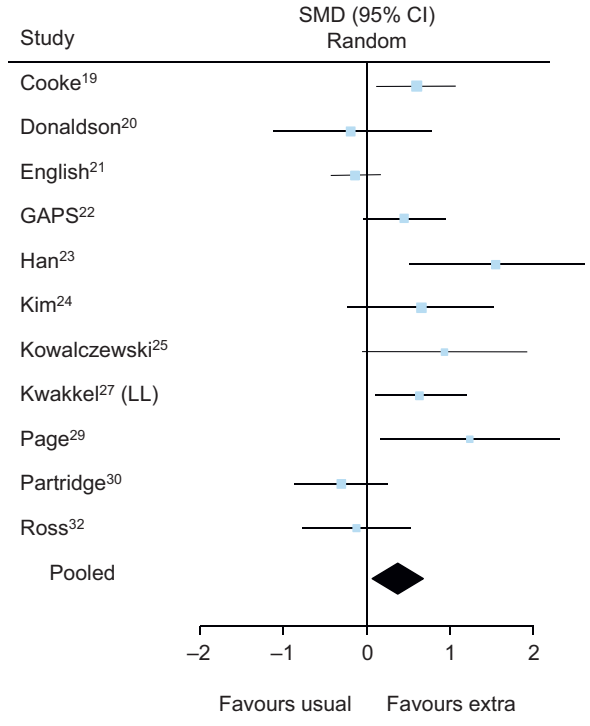

Figure 2. Standardised mean difference (95% CI) of the effect of extra rehabilitation on top of usual rehabilitation compared with usual rehabilitation for activity immediately after the period of intervention (n = 577 participants). LL = lower limb.

Table 1
Summary of included studies (n = 14).

Study	Design	Participants	Intervention	Outcome measures [a]
Burgar[18]	QRCT	n = 36 Age (*yr*) = 61 (SD n/s) Gender = n/s Time since stroke < 6 mth	Extra = UL rehabilitation 60 min x 5/wk x 3 wk (↑ 100%) Usual = UL rehabilitation 60 min x 5/wk x 3 wk	• UL activity = Wolf Motor Function Test (ability, 0 to 5) • Timing = 0, 3, 26 wk
Cooke[19]	RCT	n = 73 Age (*yr*) = 67 (SD 13) Gender = 59% male Time since stroke < 6 mth	Extra = LL rehabilitation 60 min x 4/wk x 6 wk (↑ 240%) Usual = LL rehabilitation 20 min x 5/wk x 6 wk	• LL activity = 10-m Walking Test (comfortable speed, m/s) • Timing = 0, 6, 12 wk
Donaldson[20]	RCT	n = 20 Age (*yr*) = range 44 to 90 Gender = 50% male Time since stroke < 6 mth	Extra = UL rehabilitation 60 min x 4/wk x 6 wk (↑ 240%) Usual = UL rehabilitation 20 min x 5/wk x 6 wk	• UL activity = Action Research Arm Test (0 to 57) • Timing = 0, 6, 12 wk
English[21]	RCT	n = 190 Age (yr) = 69 (SD 13) Gender = 58% male Time since stroke < 6 mth	Extra = LL rehabilitation 12 min x 2/wk x 4 wk (↑ 40%) Usual = LL rehabilitation 12 min x 5/wk x 4 wk	• LL activity = 6-min Walking Test (m/s) • Timing = 0, 4, 26 wk
GAPS[22]	RCT	n = 70 Age (*yr*) = 68 (SD 11) Gender = 59% male Time since stroke < 6 mth	Extra = UL + LL rehabilitation 30 to 40 min x 5/wk x 10 wk (↑ 100%) Usual = UL + LL rehabilitation 30 to 40 min x 5/wk x 10 wk	• LL activity = Rivermead Mobility Index (0 to 15) • Timing = 0, 12, 26 wk
Han[23]	RCT	n = 20 Age (*yr*) = 49 (SD 6) Gender = 75% male Time since stroke < 6 mth	Extra = UL rehabilitation 120 min x 5/wk x 6 wk (↑ 200%) Usual = UL rehabilitation 60 min x 5/wk x 6 wk	• UL activity = Action Research Arm Test (0 to 57) • Timing = 0, 6 wk
Kim[24]	RCT	n = 22 Age (*yr*) = 51 (SD 9) Gender = 59% male Time since stroke > 6 mth	Extra = LL rehabilitation 30 min x 5/wk x 4 wk (↑ 300%) Usual = LL rehabilitation 10 min x 5/wk x 4 wk	• LL activity = 10-m Walking Test (comfortable speed, m/s) • Timing = 0, 4 wk
Kowalczewski[25]	RCT	n = 19 Age (*yr*) = 61 (SD 16) Gender = 53% male Time since stroke < 6 mth	Extra = UL rehabilitation 60 min x 4/wk x 3 to 4 wk (↑ 400%) Usual = UL rehabilitation 60 min x 1/wk x 3 to 4 wk	• UL activity = Wolf Motor Function Test (ability, 0 to 5) • Timing = 0, 4, 26 wk
Kwakkel[26,27]	RCT	n = 101 Age (*yr*) = 66 (SD 12) Gender = 43% male Time since stroke < 6 mth	Extra 1 = UL rehabilitation 30 min x 5/wk x 20 wk (↑ 200%) Extra 2 = LL rehabilitation 30 min x 5/wk x 20 wk (↑ 200%) Usual = LL rehabilitation 15 min x 5/wk x 20 wk UL rehabilitation 15 min x 5/wk x 20 wk	• UL activity = Action Research Arm Test (0 to 57) • LL activity = 10-m Walking Test (comfortable speed, m/s) • Timing = 0, 20, 26 wk
Lincoln[28]	RCT	n = 189 Age (*yr*) = 73 (SD n/s) Gender = 51% male Time since stroke < 6 mth	Extra = UL rehabilitation 24 min x 5/wk x 5 wk (↑ ?%) Usual = UL + LL rehabilitation 30 to 45 min x 5/wk x 5 wk	• UL activity = Action Research Arm Test (0 to 57) • Timing = 0, 6, 26 wk
Page[29]	RCT	n = 17 Age (*yr*) = range 38 to 75 Gender = 59% male Time since stroke > 6 mth	Extra = UL rehabilitation 90 min x 5/wk x 8 wk (↑ 300%) Usual = UL rehabilitation 30 min x 5/wk x 8 wk	• UL activity = Action Research Arm Test (0 to 57) • Timing = −1, 9 wk
Partridge[30]	RCT	n = 55 Age (*yr*) = range 60 to 94 Gender = n/s Time since stroke = n/s	Extra = UL + LL rehabilitation 30 min x 5/wk x 6 wk (↑ 100%) Usual = UL + LL rehabilitation 30 min x 5/wk x 6 wk	• LL activity = 5-m Walking Test (comfortable speed, m/s) • Timing = 0, 6, 26 wk
Rodgers[31]	RCT	n = 105 Age (*yr*) = 75 (SD n/s) Gender = 55% male Time since stroke < 6 mth	Extra = UL rehabilitation 30 min x 5/wk x 6 wk (↑ ?%) Usual = UL + LL rehabilitation 45 min x 5/wk x 6 wk	• UL activity = Action Research Arm Test (0 to 57) • Follow up = 0, 26 wk
Ross[32]	RCT	n = 37 Age (*yr*) = 59 (SD 19) Gender = 57% male Time since stroke < 6 mth	Extra = UL rehabilitation 60 min x 5/wk x 6 wk (↑ 200%) Usual [b] = UL rehabilitation 30 min x 5/wk x 6 wk	• UL activity = Action Research Arm Test (0 to 57) • Timing = 0, 6 wk

LL = lower limb, n/s = not stated, QRCT = quasi-randomised controlled trial, RCT = randomised controlled trial, UL = upper limb, ? = unknown.
[a] Outcome measures and their timing listed are those analysed in the review. There may have been other measures reported in the paper.
[b] Information was provided by authors.

practice, the large increase in rehabilitation improved activity (SMD 0.59, 95% CI 0.23 to 0.94, I^2 = 44%) (Figure 4); see Figure 5 on the eAddenda for a detailed forest plot.

Amount of extra rehabilitation needed to achieve a beneficial effect

There was a trend towards a positive relationship (r = 0.53, p = 0.09) between the amount of extra rehabilitation and improved activity when examining the 11 comparisons with data available immediately after the intervention period. Extra rehabilitation was expressed as percentage increase per week and deemed beneficial when the SMD was 0.5 in favour of the experimental group. The turning point on the ROC curve of false versus true benefit (AUC = 0.88, p = 0.04) indicated that at least an extra 240% rehabilitation is needed for significant likelihood that the amount of rehabilitation will improve activity in stroke survivors (Figure 6). That is, the amount of practice required would need to be more than tripled from what is usually provided.

Discussion

This review provides evidence that extra rehabilitation aimed at reducing activity limitations in either the upper or lower limb, added to usual rehabilitation, improves activity in people after stroke. Furthermore, given that the extra practice was of the same

Table 2
PEDro criteria and scores for included papers (n = 15).

Study	Random allocation	Concealed allocation	Groups similar at baseline	Participant blinding	Therapist blinding	Assessor blinding	<15% dropouts	Intention-to-treat analysis	Between-group difference reported	Point estimate and variability reported	Total (0 to 10)
Burgar[18]	Y	N	Y	N	N	Y	Y	N	Y	Y	6
Cooke[19]	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8
Donaldson[20]	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8
English[21]	Y	Y	Y	N	N	Y	Y	N	Y	Y	7
GAPS[22]	Y	Y	Y	N	N	N	Y	Y	Y	Y	7
Han[23]	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8
Kim[24]	Y	Y	Y	N	N	Y	N	N	Y	Y	6
Kowalczewski[25]	Y	N	Y	N	N	Y	Y	N	Y	Y	6
Kwakkel[27]	Y	N	Y	N	N	N	Y	N	Y	Y	5
Kwakkel[26]	Y	Y	Y	N	N	Y	Y	N	Y	Y	7
Lincoln[28]	Y	Y	Y	N	N	Y	N	N	Y	Y	6
Page[29]	Y	Y	Y	N	N	Y	Y	N	Y	Y	7
Partridge[30]	Y	Y	Y	N	N	Y	Y	N	Y	Y	7
Rodgers[31]	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8
Ross[32]	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8

N = no, Y = yes.

content as usual rehabilitation, the effect was purely a result of an increase in the amount of rehabilitation. The amount of extra rehabilitation that needs to be provided to achieve a beneficial effect is large – in the order of 240%.

The effect size of 0.59 for a large (> 100%) increase in extra rehabilitation is encouraging. In order to compare the amount of extra rehabilitation across studies, the extra was presented as a percentage increase. This method, while accurate, produces high numbers. For example, if usual rehabilitation involved 15 minutes of walking practice, and the extra amount of walking delivered was 30 minutes, then the increase was 200%. Also, these calculations used 'intended' increase in rehabilitation, because this was consistently reported across the studies. It is possible that the 'intended' increase in rehabilitation did not match the 'actual' amount delivered. However, in those studies that reported both (intended and actual), 93% of the intended amount was actually delivered. Of the studies that delivered a large increase in rehabilitation amount, the average dose of usual rehabilitation was approximately 25 minutes per day in the control group and the average dose of extra rehabilitation provided was 260% (ie, 90 minutes per day) in the experimental group. These numbers align well with the findings from the ROC curve analysis, suggesting that at least a 240% increase in rehabilitation is necessary to result in an improvement in activity. Clinically, for example, if a therapy service usually provides 30 minutes of reach and grasp rehabilitation per day, in order to ensure a better outcome, approximately 100 minutes of reach and grasp rehabilitation per day would be required.

Overall, the results of this review are in line with previous meta-analyses that investigated 'dose', which suggest a beneficial effect of extra rehabilitation after stroke.[5,6,11] The finding from our meta-analysis, with all studies included, produced an effect size of 0.39, which is similar to the small effect sizes ranging from 0.13 to 0.35 found previously. However, when

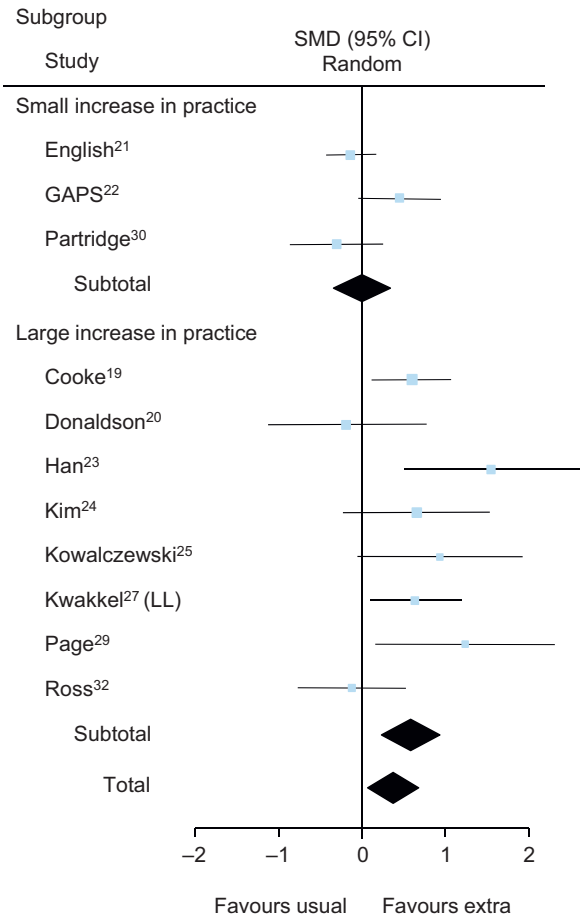

Figure 4. Standardised mean difference (95% CI) of the effect of the extra rehabilitation on top of usual rehabilitation compared with usual rehabilitation for activity, subgrouped by the relative amount of extra practice into small (≤100%) or large (>100%) increase.
LL = lower limb.

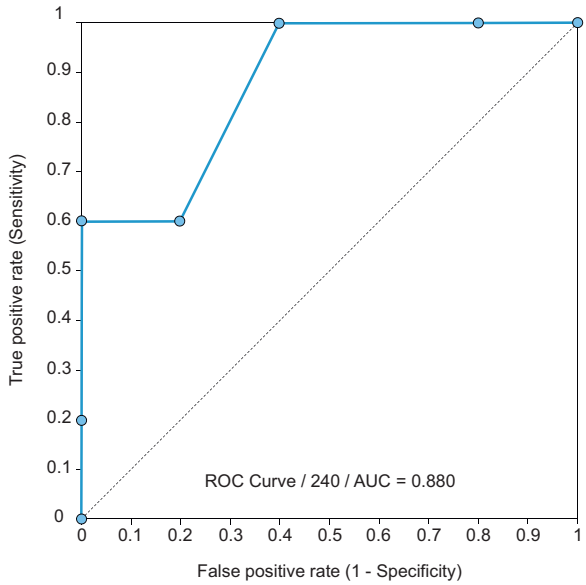

Figure 6. ROC curve of the true versus false benefit for amount of extra rehabilitation per week immediately after the period of intervention (n = 11 comparisons).

excluding studies that delivered only a small increase in rehabilitation, we found a larger effect size of 0.59. We used specific criteria to define 'extra rehabilitation' to mean additional practice of exactly the same activity provided in usual practice. Because of this tight definition of 'extra' rehabilitation, we excluded some studies that had been included in previous reviews;[5,6,11] this may account for our finding of a larger effect size than the previous reviews.

Our meta-analyses may have been affected by small study bias, with an average number of 35 participants per study. Also, the number of comparisons included in the meta-analysis was reduced by the reporting of medians in clinical trials where there were highly skewed data that could not be converted to means (SD). However, the mean PEDro score (> 7/10) showed that the included studies were of high quality and the findings therefore were robust. The strengths of this review were that by using these high-quality studies, we have estimated the effect of extra rehabilitation after stroke unconfounded by type of practice, and used this to estimate a threshold amount of extra practice needed to improve activity after stroke.

This review suggests that the provision of extra rehabilitation is feasible, and that programs need to provide a substantial amount of rehabilitation to guarantee an improvement in activity. Future randomised trials investigating substantial increases in practice (ie, more than 240% extra rehabilitation) would further clarify the relationship between increasing the amount of rehabilitation and activity after stroke. The challenge now is to determine how to increase the amount of rehabilitation. Implementation will demand a change in clinical practice that is far-reaching; models of delivery, patient expectations, and therapist beliefs should be guided by our findings.

What is already known on this topic: After stroke, difficulties with walking and using the arm for self-care are common, but rehabilitation can reduce these activity limitations. Previous systematic reviews have not distinguished the effect of increasing the amount of the same type of rehabilitation from the effect of adding extra rehabilitation of a different type.
What this study adds: Increasing the amount of rehabilitation after stroke improves activity, but a large amount of extra rehabilitation needs to be provided to achieve a beneficial effect.

eAddenda: Figures 3 and 5, and Appendices 1 and 2 can be found online at doi:10.1016/j.jphys.2016.08.006

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Competing interests: Nil.

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Pilot and Feasibility Studies

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Extra upper limb practice after stroke: a feasibility study

Emma J. Schneider[1,2*], Louise Ada[3] and Natasha A. Lannin[1,2,4]

Abstract

Background: There is a need to provide a large amount of extra practice on top of usual rehabilitation to adults after stroke. The purpose of this study was to determine if it is feasible to add extra upper limb practice to usual inpatient rehabilitation and whether it is likely to improve upper limb activity and grip strength.

Method: A prospective, single-group, pre- and post-test study was carried out. Twenty adults with upper limb activity limitations who had some movement in the upper limb completed an extra hour of upper limb practice, 6 days per week for 4 weeks. Feasibility was measured by examining recruitment, intervention (adherence, efficiency, acceptability, safety) and measurement. Clinical outcomes were upper limb activity (Box and Block Test, Nine-Hole Peg Test) and grip strength (dynamometry) measured at baseline (week 0) and end of intervention (week 4).

Results: Of the 212 people who were screened, 42 (20%) were eligible and 20 (9%) were enrolled. Of the 20 participants, 12 (60%) completed the 4-week program; 7 (35%) were discharged early, and 1 (5%) withdrew. Participants attended 342 (85%) of the possible 403 sessions and practiced for 324 (95%) of the total 342 h. In terms of safety, there were no study-related adverse events. Participants increased 0.29 blocks/s (95% CI 0.19 to 0.39) on the Box and Block Test, 0.20 pegs/s (95% CI 0.10 to 0.30) on the Nine-Hole Peg Test, and 4.4 kg (95% CI 2.9 to 5.9) in grip strength, from baseline to end of intervention.

Conclusions: It appears feasible for adults who are undergoing inpatient rehabilitation and have some upper limb movement after stroke to undertake an hour of extra upper limb practice. The magnitude of the clinical outcomes suggests that further investigation is warranted and this study provides useful information for the design of a phase II randomized trial.

Trial registration: Australian and New Zealand Clinical Trial Registry (ACTRN12615000665538).

Keywords: Rehabilitation, Occupational therapy, Physical therapy, Task-specific motor training

Background

Upper limb activity is necessary for participation in activities of daily living [1]. More than 80% of stroke survivors have motor impairments that can include changes to muscle strength as well as difficulty in controlling movement [2]. This decrease in muscle strength and control results in a person needing assistance to complete basic daily activities [1]. Upper limb rehabilitation, therefore, aims to improve both muscle strength and movement control [3] and is structured to provide repetitive upper limb practice of specific tasks that are challenging, progressive and skill-based [4, 5]. Yet the recovery of upper limb activity after stroke is often poor [6] and stroke survivors perceive that their time spent in upper limb rehabilitation was not sufficient [7].

There is high-level evidence that an increase in the amount of supervised rehabilitation improves motor outcome for stroke survivors [4, 8–10], with four systematic reviews finding small to moderate effect sizes [8–10]. One review investigated how much extra rehabilitation was required to produce a benefit and found that a 240% increase in the amount of usual rehabilitation was needed to ensure that the extra rehabilitation improved activity [10]. For example, if 25 min of upper limb rehabilitation per day is usual, an extra 60

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min (a total of 85 min per day) would need to be provided to result in an improvement in upper limb activity. This is almost three times the amount of usual rehabilitation and a large amount of extra practice.

The challenge now is to determine a feasible way to provide a large amount of extra practice taking into account staff and resource constraints. Most studies to date have delivered extra rehabilitation in one-on-one sessions outside the usual rehabilitation service [11–21]. This model of delivery, however, is not an efficient way to increase the amount of usual rehabilitation in an inpatient rehabilitation service. The potential to provide extra rehabilitation without using one-on-one supervised sessions has been explored using various strategies such as gaming, group practice or homework [22–26]. We propose to investigate using largely self-directed practice within inpatient rehabilitation as a way of increasing the amount of upper limb practice in the subacute phase after stroke. In preparation for a large, fully-powered randomized trial, it is important to understand the feasibility of recruitment, delivering the intervention and collecting the outcome measures. Therefore, the primary questions of this study were:

1. Is it feasible (in terms of recruitment, intervention and measurement) for people who are undergoing inpatient rehabilitation and have some movement in the upper limb after stroke to undertake an extra hour of upper limb practice, 6 days per week for 4 weeks?
2. Is the extra practice likely to improve upper limb activity and grip strength?

Method

Design

A prospective, single-group, pre- and post-test study was conducted at a metropolitan inpatient rehabilitation hospital in Melbourne, Australia. The participants received extra upper limb practice for 4 weeks. Outcomes were measured at baseline (week 0) and at the end of intervention (week 4). The design of the study is presented in Fig. 1. Outcome measures were collected by occupational therapists trained in the procedures who were not blinded to the aims of the study. University and hospital human research ethics committees approved this study. All participants gave written informed consent before data collection began.

Setting

The study was conducted in one sub-acute rehabilitation hospital that has > 25 beds dedicated to multidisciplinary inpatient rehabilitation after stroke.

Participants and therapists

Consecutive patients admitted for inpatient rehabilitation with stroke between July 2015 and June 2016 were screened for eligibility by a researcher within 72 h of admission. Patients were eligible if they had a medical diagnosis of stroke, were aged over 18 years, had an upper limb activity limitation (defined as < 54 blocks on the Box and Block Test which is a 20% reduction in the normal scores of adults aged 20–80 years) [27], and had some upper limb activity (> Grade 1 wrist extension and > Grade 3 shoulder elevation on manual muscle testing) in order to be able to carry out the practice [28]. Patients were excluded if they had severe cognitive and/or language defects (Mini Mental Status Examination score ≤ 24) [29], had any medical condition that precluded them participating in a rehabilitation program aimed at upper limb activity, or had a discharge date that precluded them completing the 4-week program. For patients who were initially ineligible (no upper limb activity), screening was repeated weekly to establish if they became eligible. Age (year), sex (number male), time since stroke (days), side of hemiplegia (number right), living situation (lives alone), education (attended university), cognition (Mini Mental Status Examination, 0–30) [29], unilateral special neglect (Albert's Line Cancellation Test, number of lines left uncrossed) [30], loss of light touch sensation (none/some/complete), spasticity (Tardieu Scale Quality of Muscle Reaction, 0–5) [31], contracture (range of motion at the wrist and elbow), complexity of rehabilitation needs (Rehabilitation Complexity Scale-Extended, 0–20) [32], and ability to pick up a cup unaided (number) and walk unaided (number) were collected at baseline to describe the sample.

Occupational therapists overseeing the extra upper limb practice all had experience in neurological rehabilitation and were trained in task-specific motor training and the trial intervention prior to study commencement. One therapist was involved in overseeing the extra upper limb practice, with incidental support from two additional therapists.

Intervention

Participants undertook an extra hour of upper limb practice, 6 days a week (Monday to Saturday) for 4 weeks, consisting of two self-directed programs designed to be used by adults with stroke: the Graded Repetitive Arm Supplementary Program (GRASP) and the AbleX [22, 23]. GRASP is a self-directed arm and hand program that incorporates strengthening exercises, part practice and practice of whole upper limb activities [22]. GRASP has three levels of difficulty. The level of difficulty prescribed was determined by participant performance on weekly clinical outcome measures and ability to complete half of the tasks at the maximum number of set repetitions [22]. The therapist provided the participant with one of six GRASP kits (manual and equipment) at the start of each session. AbleX is a computer-based upper limb program that was set up by the therapist on a laptop. Participants hold a

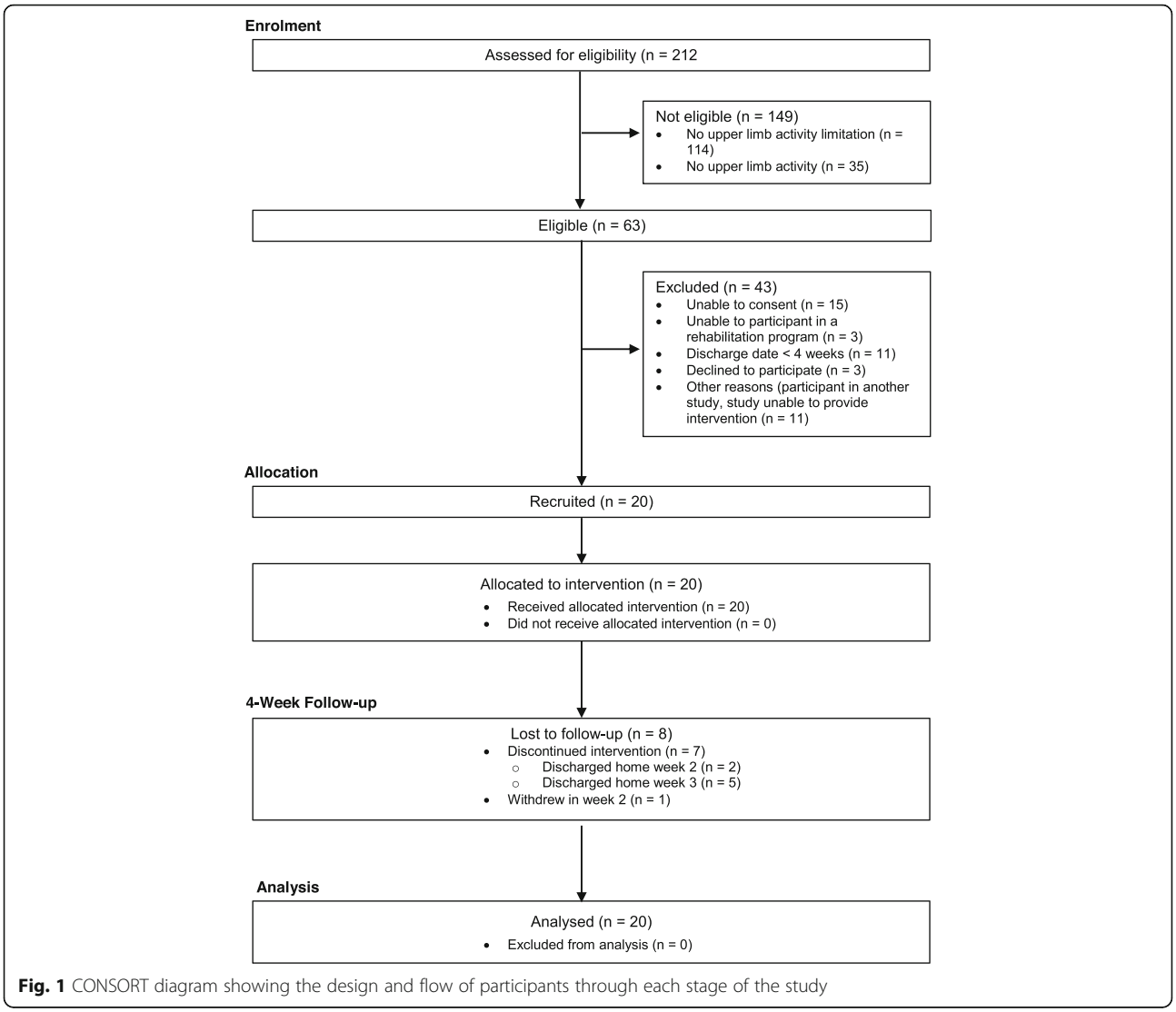

Fig. 1 CONSORT diagram showing the design and flow of participants through each stage of the study

controller in their affected hand or bilaterally to play a range of computer games designed to promote target-hitting [23]. The computer system provides participants with immediate feedback on their performance (accuracy), activity time (adherence) and exercise intensity [23].

Therapists provided direction and encouragement to practice, set-up the equipment, checked the quality of the practice, and progressed the difficulty of practice to ensure the level of challenge was always high. The amount of support was gradually reduced once the participant could follow the self-directed programs. To set up the equipment, the therapist provided the participant with a pre-packed GRASP kit or laptop. The extra practice could be undertaken at any time during usual rehabilitation hours (8 a.m. to 5 p.m.), individually or in a group, in the therapy area or a common space in the ward. The time of the extra practice session was scheduled on the participant's timetable to ensure the participant was ready for each session. Participants were encouraged to complete the required amount of daily practice but could choose to practice for greater or less than 60 min per session. The amount of practice and session duration was tracked and recorded by the participant with assistance from the therapist using a stopwatch and paper diary.

No other aspects of the multidisciplinary rehabilitation were changed. The amount of usual upper limb rehabilitation that was scheduled on the participant's timetable by the multidisciplinary rehabilitation team was collected. Usual upper limb rehabilitation could include a combination of individual and group sessions provided by occupational therapists and/or physiotherapists targeting task-specific motor training of the affected upper limb.

Outcome measures

Feasibility

The feasibility of the study involved examining recruitment, intervention (adherence, efficiency, acceptability, and safety)

and measurement. The feasibility of recruitment was determined by calculating the proportion of enrolled patients from the population who were screened for eligibility. Feasibility of the intervention was determined by examining adherence (the number of sessions attended as a proportion of the number of possible sessions), efficiency (the amount of practice as a proportion of total minutes), acceptability (participants yes/no responses to 5 statements about the training and rating of their acceptability from 0 to 5, Table 2), and safety (the number of adverse events such as fatigue, illness, muscle soreness, or injuries as a proportion of the number of sessions attended). If required, an interpreter or non-verbal communication assisted the participant. The feasibility of measurement involved examining how many participants could be measured for all outcomes.

Clinical

Clinical outcomes were upper limb activity and grip strength. Upper limb activity was measured using the Box and Block Test (number of blocks) and the Nine-Hole Peg Test (s). Grip strength (kg) was measured using dynamometry. The Box and Block Test is a timed test of the ability to grasp and release. The instructions for the test were standardized according to Mathiowetz et al. [27]. Participants were asked to pick up and move one block at a time over a barrier to the other side of the box as quickly as possible. The ability to grasp and release was transferred to a rate of performance by dividing the number of blocks moved by 60 s (number of blocks/s).

The Nine-Hole Peg Test is a timed test of the ability to grasp, manipulate and place small objects with one hand. The instructions for the test were modified to incorporate additional stopping points [33, 34]. Participants were asked to pick up the 9 pegs one at a time and place them in the holes until all nine holes were filled; then remove the 9 pegs one at a time and return them to the tray. The participants were told not to continue the test if they had placed zero pegs into the holes at 60 s [33]. The participants were told not to continue the test if they had not completed the test (placed and removed all 9 pegs) in 120 s [34]. The number of pegs moved was quantified as 0–18 pegs; either 0–9 pegs placed into the holes or 10–18 pegs returned to the tray. The score was then transferred to a rate of performance by dividing the number of pegs moved by the number of seconds to complete or stop the test (pegs/s).

Dynamometry of maximum voluntary contraction of grip measures the strength of muscles in the forearm and hand. The instructions for the test were standardized according to Horowitz [35]. Grip strength was quantified by the number of kilograms achieved. If the participant could register some strength but not enough to reach the first increment on the dynamometer (at 2 kg), the score was recorded as 1 kg.

Sample size

Due to the nature of a feasibility study, a formal sample size calculation was not performed [36]. We aimed to recruit 20 participants as this was considered an adequate number to assess the feasibility [37].

Data analysis

For participant characteristics and feasibility outcomes, descriptive statistics are presented as mean (SD) or number (%). For clinical outcomes, paired between-time differences (week 4 minus week 0) are presented as mean difference (95% CI). When a participant was discharged home or from the study before week 4, a measure was taken at this time.

Results

Characteristics of participants

Twenty participants aged 63 (SD 17) years, of which 11 (55%) were men, participated in the study. Characteristics of participants are presented in Table 1. Usual upper limb rehabilitation was scheduled for a mean of 37 (SD 26) min per day with 4 (20%) participants scheduled to receive no upper limb rehabilitation.

Feasibility

Recruitment

Over an 11-month period, 212 people were screened, 42 (20%) were eligible, and 20 (9%) were enrolled. In terms of retention, at week 4, 7 (35%) participants had already been discharged home and one (5%) had withdrawn (co-enrolled in another study and reported fatigue). Participants completed the extra upper limb practice program for a mean of 3 (SD 1) weeks. The flow of participants through the study is presented in Fig. 1.

Intervention

Removing the 77 sessions missed due to early discharge of seven participants from the study, there were a possible 403 sessions. Adherence to the intervention was 85% (i.e., 342 out of a possible 403 sessions). Forty-five (11%) sessions were missed because of non-attendance (illness, fatigue, visitors); and 15 (4%) sessions were missed because the participant withdrew. Efficiency of the intervention was 95%; i.e., participants completed 324 h of practice during a total of 342 h. Participants undertook a mean of 57 (SD 9) min of extra upper limb practice during a mean session of 73 (SD 10) min. Acceptability of the intervention is presented in Table 2. Overall, the participants were satisfied (4.8 out of 5.0) with their extra practice. In terms of safety, the incidence of fatigue, illness, or muscle soreness during the 342 intervention sessions was 40 (12%); 32 (9%) reports of fatigue; 4 (1%) reports of illness; 4 (1%) reports of localized muscle soreness in the affected arm.

Table 1 Baseline characteristics of participants

Characteristic	(*n* = 20)
Age (year), mean (SD)	63 (17)
Sex, *n* male (%)	11 (55)
Time since stroke (day), mean (SD)	38 (87)
Side of hemiplegia, *n* right (%)	12 (60)
Living situation, *n* lives alone (%)	9 (45)
Education, *n* attended university (%)	9 (45)
Cognition (MMSE, 0–30), mean (SD)	28 (2)
Neglect (Albert's Line Cancelation Test), *n* (%)	2 (10)
Loss of light touch sensation, *n* (%)	
None	18 (90)
Some	2 (10)
Complete	0 (0)
Spasticity (Tardieu Scale Quality of Muscle Reaction, 0–5), mean (SD)	
Wrist flexors	0.15 (0.38)
Biceps	0.2 (0.51)
Contracture upper limb, *n* (%)	3 (15)
Complexity of rehabilitation needs (RCS, 0–20), mean (SD)	12 (2)
Grasps unaided, *n* (%)	10 (50)
Walks unaided, *n* (%)	2 (10)

MMSE Mini-Mental Status Exam, *RCS* Rehabilitation Complexity Scale-Extended

There were no injuries or serious adverse events (study related or otherwise).

Measurement

Clinical outcomes were collected from all 20 (100%) participants at week 4 or prior to discharge home or withdrawal.

Clinical

The group clinical outcomes are presented in Table 3. There was a mean 0.29 blocks/s (95% CI 0.19 to 0.39) increase on the Box and Block Test from baseline to end of intervention. There was a mean 0.20 pegs/s (95% CI 0.10 to 0.30) increase on the Nine-Hole Peg Test from baseline to end of intervention. There was a mean 4.4 kg (95% CI 2.9 to 5.9) increase in grip strength from baseline to end of intervention.

Discussion

This study demonstrates that it appears feasible for people who are undergoing inpatient rehabilitation and have some movement in the upper limb after stroke to undertake an extra hour of upper limb practice, 6 days per week until discharge or for up to 4 weeks. Participants attended the majority of sessions, practiced for the majority of session duration, rated the acceptability of the intervention as high, and reported a low number of adverse events during the extra upper limb practice. The change observed in the clinical outcomes suggests a promising improvement in upper limb activity and grip strength above what might normally be expected [39]. For example, it has been suggested that time alone accounts for 16% improvement in impairments over 6–10 weeks [39] compared with our 42% improvement in grip strength and 100% improvement in upper limb activity over 4 weeks.

This study provided evidence that extra practice was feasible; however, this was not provided within the usual resources provided within the inpatient rehabilitation unit. The participants were often unavailable during usual working hours, either completing usual daily activities (shower, dress, eat), engaged in usual rehabilitation, resting, or with family/visitors. Therefore, the extra upper limb practice was often undertaken after usual rehabilitation and before dinner (4.30–5.30 p.m.) and within the common space in the ward to reduce transportation and where nursing staff could ensure the safety of the participants during self-directed practice. Seventy-two percent of the self-directed practice was undertaken in a group in the ward. We recommend that future trials designed to deliver extra upper limb practice to adults undergoing inpatient rehabilitation consider (i) using a group format and (ii) the timing of sessions.

Adults undergoing inpatient rehabilitation were able to undertake a mean of 57 min of extra upper limb

Table 2 Acceptability of the extra rehabilitation

Acceptability	(*n* = 20)
Would you recommend this program to a friend who had suffered a stroke and couldn't move their arm normally, number yes (%)	19 (95)
On average, was the program, number yes (%):	
Too much practice/exercise for your arm and hand?	1 (5)
Too little practice/exercise for your arm and hand?	1 (5)
Just enough practice/exercise for your arm and hand?	18 (90)
Did the practice make you tired, number yes (%)	8 (40)
Did the practice make you so tired that you wanted to stop, number yes (%)	3 (15)
How satisfied are you with the extra practice you received (0–5*), mean (SD)	4.8 (0.5)

*Where 0 is 'strongly not satisfied at all' and 5 is 'very satisfied'

Table 3 Mean (SD) for clinical outcomes at each time, mean (95% CI) difference between times and reference values for healthy adults

Clinical outcome	Reference value	Times		Difference between times
		Week 0	Week 4	Week 4 minus Week 0
Box and Block Test (blocks/s)	1.3 [27]	0.29 (0.25)	0.58 (0.33)	0.29 (0.19 to 0.39)
Nine-Hole Peg Test (pegs/s)	1.0 [34]	0.18 (0.20)	0.37 (0.33)	0.20 (0.10 to 0.30)
Grip strength (kg)	32 [38]	12 (11)	17 (11)	4 (3 to 6)

practice during a mean session of 73 min, on top of a mean of 37 min of usual upper limb rehabilitation per day. These results are comparable to the findings of the Schneider et al. [10] systematic review; 37 min of usual upper limb rehabilitation per day and an extra 73 min of extra upper limb rehabilitation per day. This equates to a 200% increase in the amount of usual rehabilitation, only slightly less than the suggested 240% increase [10]. Furthermore, reports of fatigue, illness, or muscle soreness was low (12%) and consistent with other studies in similar settings for adults after stroke [40, 41].

There are limitations to this study. First, the use of one AbleX device limited the number of adults who could complete the extra upper limb practice program at one time and in some circumstances, recruitment was stopped to ensure delivery of the intervention. While the enrollment of 48% of the eligible participants is comparable to other studies [42], access to more than one AbleX program, or use of the GRASP program alone, may improve the recruitment of future studies. Second, the high rate of early discharge; participants completed the extra upper limb practice program for a mean of 3 weeks, delivered over a mean of 20 sessions. This suggests that future trials either need to continue the program after discharge or reduce the duration from 4 to 3 weeks. Third, while the clinical outcomes suggest a promising improvement in upper limb activity and grip strength, it must be noted that all participants had some movement at the time of recruitment, which suggests they were capable of recovery due to having had an intact corticospinal tract [43]. Fourth, the use of assessors who were aware of the study aims may have led to bias estimates of clinical outcomes.

Conclusion

It appears feasible for adults who are undergoing inpatient rehabilitation and have some upper limb movement after stroke to undertake an extra 1 h of upper limb practice, 6 days per week until discharge or for up to 4 weeks. The extra upper limb practice program was feasible when delivered outside usual therapy time and in a group in the common space of the ward. Clinical outcomes suggest a promising improvement in upper limb activity and grip strength. Further investigation is warranted and this study provides useful information for the design of a phase II randomized trial.

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Authors' contributions
All authors contributed to the conception and design of the study. EJS led the study and drafted the manuscript. All authors analysed and interpreted the data for the study, and revised the manuscript for intellectual content. All authors approved the final manuscript and are accountable for all aspects of the work.

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Availability of data and materials
The datasets used and/analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate
This study was conducted in accordance with Alfred Health ethics committee as well as La Trobe University human ethics committee that gave approval (ethics number 94/15). All participants gave written informed consent before data collection began.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interest.

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