Beyond the RCT - understanding the relationship between interventions, individuals and outcome - the example of neurological rehabilitation

Paula Kersten ¹, Caroline Ellis-Hill ¹, Kath McPherson ², Rachel Harrington ³

¹ School of Health Sciences, University of Southampton, Southampton SO17 1BJ, United Kingdom
² Health and Rehabilitation Research Institute, AUT University, Auckland, New Zealand
³ Medical Directorate, NHS South East Coast, United Kingdom

Address for correspondence:
Paula Kersten
School of Health Sciences
University of Southampton
Southampton
SO17 1BJ
United Kingdom
Email: P.Kersten@soton.ac.uk
Phone: +44 2380595299
Fax: +44 2380595301

Word count: 3,357
Word count abstract 242
Abstract

Background
Rehabilitation is highly complex, involving multiple processes, outcomes, and stakeholders. The way we deliver our services and work with our clients and their families, should be informed by research approaches that produce the wide range of knowledge needed. This paper aims to explore the degree to which the dominant approach to ‘evidence’ (the randomised clinical trial or RCT) meets those needs and discuss alternate/additional ways of gaining evidence.

Methods
A critical review of the literature allowing exploration of problems encountered in rehabilitation RCTs and alternative approaches.

Findings
We discuss some problematic issues related to using RCTs in rehabilitation research (for example the large number of people excluded from trials, and the small numbers of people with some neurological conditions making RCTs non viable). Alternative approaches are discussed including Clinical Practice Improvement studies (sometimes called Practice Based Evidence or PBE), which provide data on patients treated in routine practice; qualitative research, which can provide an understanding of the users of health care services to ensure they are meeting their needs; and metasynthesis, which can be used to summarise several qualitative studies to enhance our understanding of the principles underlying service delivery. Finally we explore how clinicians and commissioners often use evidence generated by forms of research other than the RCT.

Conclusion
The best answers about how to enhance rehabilitation outcomes are likely to come from a combination and integration of the most appropriate methods. In conclusion, we urge for more joined up thinking, for learning from different fields so that we can develop more effective and appropriate health care and rehabilitation.
Introduction

The World Health Organisation defines rehabilitation as ‘a process aimed at enabling people experiencing disabilities to reach and maintain their optimal physical, sensory, intellectual, psychological and social functional levels. Rehabilitation services aim to provide disabled people with the tools they need to attain independence and self-determination’ (1). This definition demonstrates the complexities of rehabilitation with its multiple outcomes and multiple stakeholders including individuals experiencing disabilities, their families, clinicians and commissioners as well as the wider population. During the rehabilitation process an array of professionals, such as rehabilitation physicians, therapists, nurses, social workers and psychologists, work alongside people experiencing disabilities. Although the activities of many of these professionals overlap (2), they vary in terms of focus (e.g. ranging from physical activities to talking therapies) and the nature of therapeutic relationships. In this complex world, the way we deliver our services and work with our clients and their families, should be informed by changing knowledge at the cellular level (associated with pathology and disease processes), through to the individual and family level (of experience, recovery and adaptation), and indeed the social level (of contexts including but not limited to the ability – or choice - to resource what is needed). Ensuring approaches that produce the knowledge that is most needed is therefore at the very heart of considering what outcomes are most important and ensuring our services help these be achieved.

The randomised controlled trial (RCT) has long been held up to be the ‘gold standard’ of research evidence and, by some is regarded as the only gold standard in research
related to interventions. This paper aims to explore the perceived dominance of the RCT and highlight alternate/additional ways of gaining evidence, which will give us knowledge and understanding about the effectiveness of interventions. We will use the example of neurological rehabilitation to illustrate some of the tensions and contentions in a field where evidence is both necessary and rarer than desirable. We will begin by defining the RCT, outlining some of the difficulties in utilising this approach in rehabilitation research and explore the types of knowledge required and used by clinicians and commissioners, i.e. those who are responsible for providing and planning rehabilitation services.

Randomised controlled trials, as most are aware, are defined as experiments in which investigators allocate eligible people to a treatment or control group (the latter receiving exactly the same intervention, but without the ‘key’ active ingredient under consideration) on a random basis. They are considered to provide the most reliable form of scientific evidence for intervention studies in which we are particularly interested in explaining causal relationships (3). Many rehabilitation trials compare new interventions to standard care, since withholding rehabilitation altogether is often considered unethical under the Declaration of Helsinki (4). The confidence with which we can judge if any change in observed outcomes in individuals in the RCT is due to the intervention under investigation is dependent upon the internal validity of the study (including how ‘usual care’ is defined). Thus, it is important to rule out other possible explanations that might have caused the observed outcomes (confounding variables). Other threats to internal validity include, for example, selection bias, expectancy effects, the Hawthorne effect, measurement bias and regression to the mean (5-8) (Sim p99-102). Along with these, there are a number of
other issues that mean RCTs are particularly problematic in rehabilitation. In this paper we will explore such issues including the complexity of rehabilitation interventions, heterogeneity of populations, selective research samples and multiple understandings and perspectives of benefits.

**Problematic issues related to using RCTS in rehabilitation research**

The RCT is a particularly valuable methodology for evaluating discrete interventions where both the intervention and the context within which it is delivered can be strictly controlled and described. However, individual rehabilitation interventions can be made up of many, rather than individual components such as those specific to the intended intervention (e.g. an exercise programme) and active ingredients non-specific to the intended intervention (e.g. empathy, good communication). Rehabilitation interventions are also aimed at multiple levels, including those at the impairment, activity and participation level and these are not easy to measure especially those of higher order (i.e. participation and quality of life) (9). Thus, it is not an easy task to unpack what is happening within a rehabilitation programme and at what level it has most impact. Indeed, many reviews in neurological conditions conclude that interventions should be described in more detail in terms of their components, intensity, frequency, duration, professional background and experience of provider and setting (10-14).

External validity, referring to the inferences that can be made from the study findings beyond the actual study sample, is considered to be greater in trials than other forms of research. However, in order to achieve homogeneity of the sample, often a great
many people from the generally heterogeneous population have to be excluded. It has been suggested that this restrictive selection significantly reduces generalisability as research participants can be different from those who do not take part (e.g. in terms of level of intelligence or sociability) (9) and often only 10-15% of the total population with the condition are eligible for any one study (15). For example a Cochrane review of exercise therapy for multiple sclerosis found that three types of exclusion criteria were used (13). These criteria included, a) a history of cardiovascular, respiratory, orthopaedic and metabolic disorders or other medical conditions which would preclude participation; b) cognitive impairment, common in MS, was often an exclusion criterion; c) some studies excluded patients on immunosuppressants or interferons. The largest study (16) included 50 patients, but excluded 254 (84%). Thus, whilst it is recognised that a trial methodology is the most appropriate method to explore effectiveness, study results are often only generalisable to a very limited sub-group of patients. This leaves many researchers summarising that conclusions from traditional experimental designs are compromised by relatively small numbers in the face of marked heterogeneity in populations, interventions and the outcome measures that are most relevant to record (10;12;14;17-19).

For some neurological populations, which affect only small numbers of patients, RCTs may not be possible or appropriate. For example, in the UK motor neuron disease has been reported to affect around 6-8 people per 100,000 (20), spinal muscular atrophies 10 in 100,000 (21), and Guillain-Barré syndrome 0.5 to 4 in 100,000 (22). For these populations RCTs of rehabilitation interventions would be practically extremely difficult to achieve and we therefore need different methodologies for low prevalence health conditions. RCTs have also come under
criticism, for example, for being divorced from reality; they tend to take place in centres of excellence and/or recruit only motivated, cooperative, better educated and carefully selected patients who may be receiving more than the normal amount of medical attention (e.g. (23-26)).

**Additional (alternate) ways of understanding the effectiveness of interventions**

The complexity of rehabilitation was demonstrated in a recent Clinical Practice Improvement study (also known as Practice Based Evidence [PBE] studies) in which researchers described in detail the content of stroke rehabilitation (2) and developed a taxonomy of stroke rehabilitation activities and interventions. For physiotherapy alone the taxonomy included 10 activities (e.g. practicing mobility) and 63 interventions (e.g. muscle strengthening exercises) (2;27;28). Another example of a PBE study in spinal cord injury rehabilitation is given by Whiteneck et al. in this edition (reference Whiteneck paper in this special issue). A key strength of the PBE methodology is that it includes the measurement of patients treated in routine practice, rather than in specially controlled circumstances, and the inclusion of virtually every patient contributes to a more naturalistic view (29;30). It enables the study of the wide variation of human responses to illness and the variation in practice of health care providers in order to examine correlations between those patients, their experiences, and their outcomes (29). Thus, through exploring which variables are most associated with outcomes, researchers can unravel relations that might not otherwise become apparent (2). Although PBE studies to date have involved very large number of patients (as in thousands) there is a lack of knowledge regarding required sample size, currently reducing the applicability of this approach in many settings or in conditions
where large samples are not possible or available (rare conditions, certain geographic regions). In addition, the PBE methodology is really only suited to populations who currently receive rehabilitation (such as people with stroke or spinal cord injury). The methodology clearly cannot be applied where people whose rehabilitation needs remain largely unmet (such as muscular dystrophy) (31). Although the PBE methodology is very useful in developing theories, because it examines associations, it is not suited to theory testing and conclusions cannot be drawn regards causality (32). One data analysis approach, Structural Equation Modelling (SEM), has to date not been employed in PBE studies but could be considered as it allows the estimation and testing of causal relationships (33;34).

The RCT gives specific understanding, i.e. does a specific intervention produce a specific outcome (or not). Qualitative research is ideally placed to tease out less tangible, but no less important, questions in rehabilitation, often related to the process of the intervention. Qualitative studies are increasingly recognised as usefully carried out prior to, alongside, or after traditional experimental studies (35;36). They can help to illuminate treatment issues, for example, indicating why some patients respond in a particular way to treatment; its use in generating critique of current practice, indicating where standard practice may not be beneficial to one or more groups of people; provide evidence for or against public health or prevention programs and evidence relevant to the formulation of better health policy (37). Indeed qualitative research can be very useful to explore why clinicians do not always apply the methods of intervention as per the research protocol with their patients. For example, qualitative work alongside two recent of our own pilot RCTs in Traumatic Brain Injury and Multiple Sclerosis showed that clinicians were finding it hard to
commit to the protocol which was largely based on building a trusting therapeutic relationship and discussion to engage the patient in the rehabilitation process (38;39). Interview data in these studies indicated that to some extent, difficulties arose due to the time it takes to achieve these objectives and the notion that maybe health care professionals are not funded to ‘talk’ but to ‘do’. Such findings are particularly useful for highlighting steps needed to maintain treatment fidelity during a trial, but also when introducing new approaches if ‘proven benefit’ is to translate into the expected outcomes for the patients. Another example comes from a recent review of the effects of evidence based clinical practice guidelines (CPG) in the Netherlands, which found that they have a significant impact upon the structures and processes of care but only a moderate, and very variable effect upon patient health outcomes (40). Indeed, the authors recommended that further research should evaluate barriers to the recommendations and guidelines. It is possible that the guidelines’ impact on patient health outcomes was less significant as they had been based on findings from traditional systematic reviews only.

Although most texts would contend that you cannot generalise findings from qualitative studies, this could be disputed; if people describe participant recruitment, the methodology and researcher in sufficient detail, the reader can judge how relevant the knowledge created is to their own situation (41). Further, the metasynthesis is a comparatively new method to bring the diversity of qualitative research together. A recent metasynthesis, pulling together the experiences of living with a stroke, found remarkably similar findings in the nine included studies (42). Its findings suggested a sudden, overwhelming and fundamental life change for the stroke survivor, and that transition and transformation form a background for loss, uncertainty and social
isolation. Through adaptation and reconciliation of identity the stroke survivors were able to move forward towards meaningful recovery. Another paper in this special issue further illustrates the use of metasynthesis in TBI (refer to Levack et al in this special issue). Implementing findings from RCTs (such as the establishment of new services) without valuable knowledge gained from such studies could result in care that is not effective, compassionate and accepted. However, there remains a lack of syntheses of qualitative studies, despite the development of the metasynthesis methodology over the past decade. For example, a search of the literature, combining keywords of interest\(^1\) with metasynthesis, identified a disappointing number of such studies (five studies in stroke, spinal cord injury, community rehabilitation, fibromyalgia and driving).

The use of mixed methods to evaluate complex interventions is also gaining increasing recognition, with many funders (e.g. UK Medical Research Council) specifying that RCTs should be accompanied by qualitative and economic evaluations (35). Indeed, Daley et al. suggest a qualitative hierarchy that might provide the strongest basis for action for practitioners or policy (37). They contend that qualitative studies may illuminate treatment issues, for example, indicating why some patients respond in a particular way to treatment; its use in generating critique of current practice, indicating where standard practice may not be beneficial to one or more groups of people; provide evidence for or against public health or prevention programs and evidence relevant to the formulation of better health policy.

\(^1\) Keywords of interest: rehabilitation, rehabilitation medicine, physiotherapy, occupational therapy, speech and language therapy, clinical psychology, rehabilitation nursing
Knowledge/evidence use

When creating research knowledge we should be aware of the needs/preferences of those who are using it. Having explored various methodologies in rehabilitation research it would be interesting to explore what sources of research evidence rehabilitation professions, commissioners and patients draw on in order to inform their decisions. In order to explore the sources of knowledge available for professional groups in rehabilitation we decided to focus on three key rehabilitation professions: occupational therapy, physiotherapy and nursing. These professions were only chosen as an example, since they reflect the professional backgrounds of the authors, but not to draw specific attention to them over other professions. For physiotherapy and occupational therapy we scanned all abstracts of research published in profession-specific journals (for the UK, Australia, the USA and New Zealand) over a one-year period (summer 2008 to summer 2009). Figure 1 demonstrates that physiotherapy research was dominated by quantitative studies (79%) with very few qualitative studies (7%). By contrast occupational therapy research consisted of fewer quantitative research (51%, which was mostly observational in design) and more qualitative research (23%). The occupational therapy journals included far more non-systematic reviews and discussion papers than the physiotherapy journals (22% versus 12%), suggesting that occupational therapists possibly rely more on expert knowledge than physiotherapists. Further, 20% of published research in the physiotherapy journals was based on trial data (systematic reviews and trials) compared to 3% in occupational therapy journals. The dominance of quantitative research amongst physiotherapists was also noted by Rauscher and Greenfield who contended that physiotherapists should consider using both quantitative and qualitative research, either sequentially or as a mixed methods
approach (43). Further, a recent paper in physiotherapy argued that interventions should only be adopted in physiotherapy practice if it has been established to be effective with an RCT (44). However, in reality this doesn’t happen and many continue with practices which have become established over time without evidence or in the face of damning evidence. The distribution of research methods in occupational therapy was observed by Case-Smith and Powell (45) who pointed out that occupational therapy research remains focused on understanding the complexities of the human experience as an appropriate approach to underpin their professional practice. However, the lack of involvement of occupational therapists in systematic reviews has also been noted as a negative issue (46). A recent study of nursing research was very similar in its findings to our findings in occupational therapy with 51% quantitative studies (though only 7% were experimental studies) and 37% qualitative studies (47). Of course, a tally of research types in professional journals cannot be considered comprehensive since many therapists are engaged in multidisciplinary research of complex interventions and publish in a wide range of multidisciplinary journals. Also, publication bias can result in greater likelihood for certain studies to be accepted in multi-professional journals with higher impact. Nevertheless, these profession specific journals are most easily accessed by practitioners since they come through the letter box once they are a member and the influence on non-research active practitioners should therefore not be underestimated.

Commissioners (who may or may not be clinicians) are of course also key users of evidence and are keen to know that services are effective. Indeed, the utilisation of evidence based practice remains at the heart of delivering high quality care for all (48). However, the influence of research evidence on decision making can be tempered by ‘financial constraints, shifting timescales and decision makers’ own
experiential knowledge’ (49). In addition, for many rehabilitation services often no specific research has been carried out, and so research evidence may not feature as highly in commissioning priorities. This means that they need to use other forms of information to shape their decision making. National strategies increasingly provide a focus for commissioners for service and pathway redesign. These strategies provide key quality markers to help improve outcomes. For example, the UK national stroke strategy has 20 quality markers, and many of these were not informed by RCT’s but by user engagement and consultation (50). NHS evidence has been launched (51) enabling clinicians and commissioners to make informed decisions around service redesign. With the economic downturn it will become even more important for commissioners not only to focus on the quality of a service or clinical pathway but also on how productive it is, and the need for detailed economic analysis will become greater. Studies utilising qualitative and observational methodology are also increasingly used to develop a greater understanding in service design. For example, in a recent stroke service development an action research approach was used to ensure services would meet the needs of people who had experienced a stroke and their carers (52).

**Conclusion**

Quantitative studies and the associated hierarchy currently remain the most accepted form of evidence. RCTs clearly have their merits, particularly in establishing causal relationships. They provide a strong methodology to evaluate the effectiveness of a new intervention using an experimental approach, e.g. the causal effect of an intervention upon individuals. However, in neurological conditions, the RCT is not always the most appropriate method for answering certain questions, in particular those about ‘how’ and ‘why’. The hierarchy of evidence assumes greater value attached to the RCT. This preference given to the RCT over and above other study designs has arguably failed us both in relation to the research carried out, and to the important questions we have yet to ask. It has led to a lack of growth in other areas such as good observational studies and qualitative research, in particular metasyntheses. The prioritisation of trials has not stopped clinicians operating in a belief driven or faith model (53) as we have seen in the large number of non-systematic and expert papers published in some fields. It is time therefore to ask ourselves whether we need more trials in neurological conditions? In some cases the
answer is an unequivocal yes but in other cases, such as stroke where we do have good trial data already, we suggest there is a strong argument for focusing more on research that identifies the best way to operationalise and implement findings in delivery of rehabilitation, i.e. translation of research into practice. Do we always need randomised controlled trials before we can treat our patients? The answer here has to be ‘no’ for the reasons outlined above. Do we need to question the evidence for what we do? The answer here is undeniably ‘yes’. However, the best answers about how to enhance rehabilitation outcomes are likely to come from a combination and integration of the most appropriate methods (54). If we, as care recipients, researchers, professionals, providers or commissioners don’t all value, understand and importantly integrate different sorts of knowledge then we will not be able to reach towards a more complete picture of what is needed in rehabilitation; the more we understand the more effective the intervention can be. We urge therefore for more joined up thinking, for learning from different fields so that we can begin to develop more effective and appropriate health care and rehabilitation. And in some cases this might mean we won’t, or can’t, conduct an RCT.
Reference List


(15) Horn SD, DeJong G, Ryser DK, Veazie PJ, Teraoka J. Another look at observational studies in rehabilitation research: Going beyond the holy grail of


(43) Rauscher L, Greenfield BH. Advancements in contemporary physical therapy research: use of mixed methods designs. Physical Therapy 2009 January;89(1):91-100.


(46) Martin E, Baggaley K, Buchbinder R, Johnston R, Santesso N. Occupational therapists should be more involved in the Cochrane Collaboration: The
example of the Australian Cochrane Musculoskeletal Review Group.


Figure 1 Different types of research (in percentages) published in physiotherapy and occupational therapy profession-specific journals* over a 12-month period in 2008-9

* The journals included were: Australian Journal of Physiotherapy, Physical Therapy (USA), Physiotherapy (UK), New Zealand Journal of Physiotherapy, Australian Occupational Therapy Journal, American Journal of Occupational Therapy, British Journal of Occupational Therapy