1. Introduction and Methodology

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1. Introduction and Methodology

1.1 Introduction
The Evidence-Based Review of Rehabilitation of Moderate to Severe Acquired Brain Injuries (ERABI) was designed to comprehensively review current practices in acquired brain injury (ABI) rehabilitation with the eventual aim of 1) identifying effective treatment interventions; 2) identifying gaps in the literature deserving further research and; 3) to serve as an accessible tool for clinicians in an effort to encourage improved evidence-based practice.

1.1.1 Defining Acquired Brain Injury
ABI is an umbrella term, encompassing a wide spectrum of brain injuries that generally includes traumatic and non-traumatic etiologies such as cerebral concussion, brain contusions, subarachnoid hemorrhages or other ‘acquired’ problems. ABI typically produces a potentially wide range of impairment affecting physical, neurocognitive and/or psychological functioning. A person with ‘ABI’ might therefore refer to an individual with a mild, moderate or severe traumatic brain injury (TBI), a person with Herpes encephalitis, viral meningitis or acute hypertensive encephalopathy. As opposed to an insidious developmental process, an ‘ABI’ infers that a person previously intact from a neurological perspective who subsequently ‘acquires’ some form of brain pathology at some point during his or her lifespan. ABI can therefore result from traumatic and non-traumatic causes. Common traumatic causes include motor vehicle accidents, falls, assaults, gunshot wounds, and sport injuries (Greenwald et al., 2003). Non-traumatic causes of ABI include focal brain lesions, anoxia, tumors, aneurysm, vascular malformations, and infections of the brain (Toronto Acquired Brain Injury Network 2005).

Given that ‘ABI’ is a loosely defined, vague rubric, studies referencing ‘ABI’ are often similarly vague as regards to their subject populations, and might include any combination of persons with traumatic brain injuries, diffuse cerebrovascular events (such as a subarachnoid hemorrhage) or diffuse infectious disorders (such as encephalitis or meningitis). For example, some studies might include as ‘ABI’ subjects, persons with all types of brain lesions apart from stroke (e.g., brain tumours). Most ABI patients have a traumatic etiology; in fact, many of the studies are of TBI patients alone.

For the purposes of this evidence-based review, we used the definition of ABI employed by the Toronto Acquired Brain Injury Network (2005). ABI is defined as damage to the brain that occurs after birth and which is not related to congenital disorders, developmental disabilities, or processes that progressively damage the brain.
Table 1.1 Defining Acquired Brain Injury

<table>
<thead>
<tr>
<th>Included in ABI definition</th>
<th>Excluded from ABI definition</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Traumatic Causes</strong></td>
<td></td>
</tr>
<tr>
<td>- Motor vehicle accidents</td>
<td>- Stroke</td>
</tr>
<tr>
<td>- Falls</td>
<td>- Intracerebral hemorrhage (focal)</td>
</tr>
<tr>
<td>- Assaults</td>
<td>- “CVA” Cerebrovascular accident (i.e. stroke)</td>
</tr>
<tr>
<td>- Gunshot wounds</td>
<td>- Vascular accidents</td>
</tr>
<tr>
<td>- Sport Injuries</td>
<td>- Malignant/metastatic tumours should be excluded</td>
</tr>
<tr>
<td><strong>Non-traumatic Causes</strong></td>
<td></td>
</tr>
<tr>
<td>- Tumors (benign/meningioma only)</td>
<td></td>
</tr>
<tr>
<td>- Anoxia</td>
<td></td>
</tr>
<tr>
<td>- Subarachnoid hemorrhage (non-focal)</td>
<td></td>
</tr>
<tr>
<td>- Meningitis</td>
<td></td>
</tr>
<tr>
<td>- Encephalitis/encephalopathy (viral, bacterial, drug, hepatic)</td>
<td></td>
</tr>
<tr>
<td><strong>Congenital and Developmental Problems</strong></td>
<td></td>
</tr>
<tr>
<td>- Cerebral Palsy</td>
<td></td>
</tr>
<tr>
<td>- Autism</td>
<td></td>
</tr>
<tr>
<td>- Developmental delay</td>
<td></td>
</tr>
<tr>
<td>- Down’s syndrome</td>
<td></td>
</tr>
<tr>
<td>- Spina bifida with hydrocephalus</td>
<td></td>
</tr>
<tr>
<td>- Muscular dystrophy</td>
<td></td>
</tr>
<tr>
<td><strong>Progressive Processes</strong></td>
<td></td>
</tr>
<tr>
<td>- Alzheimer’s disease</td>
<td></td>
</tr>
<tr>
<td>- Pick’s disease</td>
<td></td>
</tr>
<tr>
<td>- Dementia</td>
<td></td>
</tr>
<tr>
<td>- Amyotrophic Lateral Sclerosis</td>
<td></td>
</tr>
<tr>
<td>- Multiple Sclerosis</td>
<td></td>
</tr>
<tr>
<td>- Parkinson’s disease</td>
<td></td>
</tr>
<tr>
<td>Huntington’s disease</td>
<td></td>
</tr>
</tbody>
</table>

For the purpose of this review, we first selected those studies where more than 50% of the subject populations met our criteria for ABI or where a subset of ABI participants was independently reported on. The purpose of this evidence-based review was to investigate the efficacy of interventions or treatments for “moderate” to “severe” acquired brain injury. Thus, for the purposes of this review, any studies dealing with “mild” forms of ABI were to be excluded and defining severity of the brain injury took on special significance.

1.2 Defining Severity of Injury

ABI severity is usually classified according to the level of altered consciousness experienced by the patient following injury. Consciousness levels following ABI can range from transient disorientation to deep coma. Patients are classified as having a “mild”, “moderate” or “severe” ABI according to their level of consciousness at the time of initial assessment.

Various measures of altered consciousness are used in practice to determine injury severity following ABI. The most common measures of ABI severity include the Glasgow Coma Scale (GCS), the duration of loss of consciousness (LOC), and the duration of post-traumatic amnesia (PTA).
1.2.1 The Glasgow Coma Scale
Developed by Teasdale and Jennett (1974; 1976) the GCS is one of the most widely used standard measures of altered consciousness.

The GCS comprises 3 subsections (see table 1.1): eye opening (ranging from 4 points for spontaneous eye opening to 1 point for no response), best motor response (from 6 points for obeying commands to 1 point for no response) and verbal response (from 5 points for oriented to 1 point for no response). Higher scores on the GCS are indicative of an increased level of consciousness.

The total score on the GCS (i.e. sum of the scores on the 3 subsections) ranges from 3 –15, with a score of 13-15 indicating a mild injury, a score of 9-12 indicating a moderate injury, and a score of 8-3 indicating a severe injury (Murdoch and Theodoros 2001; Campbell 2000).

1.2.2 Duration of Loss of Consciousness
For moderate to severe TBI, duration of Loss of Consciousness (LOC) appears to be a valid measure of injury severity. LOC of less than 15 minutes is considered to represent a “mild” injury; up to 6 hours LOC is considered as a moderate injury; and between 6-48 hours is considered severe. When LOC exceeds 48 hours, the injury is considered as being very severe (Campbell, 2000).

1.2.3 Post-Traumatic Amnesia
Post-traumatic amnesia is the time period post-trauma for which the conscious patient has no recall for events. PTA is formally defined by some authors as the period following emergence from coma in which the patient may appear confused, disoriented, or agitated (Campbell 2000). Research indicates a dose-response relationship; the length of PTA frequently is proportional to the severity of injury. Injury severity is defined as “mild” if the duration of PTA is less than 1 hour; moderate if between 1 – 24 hours and severe if PTA is between 1 – 7 days. PTA exceeding 7 days is considered to represent a very severe injury (Campbell 2000; Russell 1932).

Table 1.3 Definitions of Injury Severity

<table>
<thead>
<tr>
<th>Mild:</th>
<th>Moderate:</th>
<th>Severe:</th>
<th>Very Severe:</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTA &lt; 1 hour</td>
<td>PTA 1-24 hours</td>
<td>PTA 1 – 7 days</td>
<td>PTA &gt; 7 days</td>
</tr>
<tr>
<td>GCS 13-15</td>
<td>GCS 9 – 12</td>
<td>GCS between 3 and 8</td>
<td>LOC &gt; 48 hours</td>
</tr>
<tr>
<td>LOC &lt; 15 minutes</td>
<td>LOC &lt; 6 hours</td>
<td>LOC 6-48 hours</td>
<td>LOC &gt; 48 hours</td>
</tr>
</tbody>
</table>

Table 1.2 The Glasgow Coma Scale

<table>
<thead>
<tr>
<th>Response/Item</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eye Opening</td>
<td></td>
</tr>
<tr>
<td>Spontaneous</td>
<td>4</td>
</tr>
<tr>
<td>To speech</td>
<td>3</td>
</tr>
<tr>
<td>To pain</td>
<td>2</td>
</tr>
<tr>
<td>None</td>
<td>1</td>
</tr>
<tr>
<td>Motor Response</td>
<td></td>
</tr>
<tr>
<td>Obey commands</td>
<td>6</td>
</tr>
<tr>
<td>Localizes pain</td>
<td>5</td>
</tr>
<tr>
<td>Withdrawal (from painful stimulus)</td>
<td>4</td>
</tr>
<tr>
<td>Abnormal flexion</td>
<td>3</td>
</tr>
<tr>
<td>Extension</td>
<td>2</td>
</tr>
<tr>
<td>None</td>
<td>1</td>
</tr>
<tr>
<td>Verbal Response</td>
<td></td>
</tr>
<tr>
<td>Oriented</td>
<td>5</td>
</tr>
<tr>
<td>Confused</td>
<td>4</td>
</tr>
<tr>
<td>Inappropriate</td>
<td>3</td>
</tr>
<tr>
<td>Incomprehensible</td>
<td>2</td>
</tr>
<tr>
<td>None</td>
<td>1</td>
</tr>
</tbody>
</table>
1.3 Challenges in ABI Rehabilitation Research

Comparative research in the field of complex disability following ABI poses several major challenges (Turner-Stokes 2004):

- There is marked heterogeneity with respect to the patient group, the intervention and setting, and to the outcomes that are relevant at each stage of recovery.
- The application of randomized controlled trial designs is limited by small numbers of patients at each site, and by ethical considerations, because many patients with ABI lack the mental capacity to give fully informed consent.
- Lack of Equipoise: The expanding body of evidence for effectiveness of multidisciplinary rehabilitation in other conditions (particularly stroke) makes it increasingly unethical to randomize patients to 'no treatment' or even 'standard' care.
- The length of time over which rehabilitation may have its effects (often months or years) is often longer than funding for research projects and hinders the use of 'wait-list' control groups.

As a result of these challenges, there are few large experimental design studies in this field.

Evaluating the impact of ABI rehabilitation programs is difficult because interventions are often multiple and their pathways to impacting outcomes are complex and subject to effect modification. An intervention that works well in one given setting may be ineffective in another setting, presenting a challenge for the development of clinical practice guidelines. Evidence-based rehabilitation must rely on a variety of types of evidence, often in combination (Victora et al., 2004). Current trends towards the acceptance of RCTs as the gold standard source of evidence may limit the knowledge base needed to make sound decisions about ABI rehabilitation priorities and policies. As RCTs have not been widely applied to traumatic brain injury rehabilitation, rigorous observational alternatives to the RCT are still of significant value (Whyte 2002).

There are also a wide variety of nonrandomized designs that can contribute important data on the efficacy or effectiveness of interventions, such as quasi-experimental designs, nonrandomized trials, and natural experiments. Including these types of designs in developing evidence-based recommendations can provide a more complete picture of the existing evidence, particularly where RCTs are lacking, and could thereby advise ABI practice, albeit not as strongly. Excluding data collected under such designs would undoubtedly bias the evidence base toward interventions that are “easier” to evaluate but not necessarily more effective or cost-effective (Des Jarlais et al., 2004).

The aim of this project was to conduct a comprehensive review of the literature regarding rehabilitation treatment of moderate to severe acquired brain injury. Each study was carefully reviewed for data extraction and quality assessment of study methodology. Levels of evidence were then determined for all elements of rehabilitation management of patients with moderate to severe acquired brain injuries.
1.4 Objective of the ABI Evidence Based Review (ERABI)
This project was designed to develop an evidence-based review of the literature for rehabilitation interventions for ABI. We reviewed research evidence of direct relevance and material benefit to clinicians and researchers in the rehabilitation of moderate to severe ABI patients. From this review, we developed a mechanism for continued collection and dissemination of research and information about ABI rehabilitation.

1.5 Methodology

1.5.1 Literature Search Strategy
An extensive literature search using multiple databases (CINAHL, EMBASE, MEDLINE, and PsycINFO) covering the years 1980 – 2009 was initially used to identify all published literature which evaluated the effectiveness of any treatment or intervention related to acquired brain injury. For the most current edition a search of other databases, such as Social Work Abstracts, Family and Society, and Child Development & Adolescent Studies was conducted. Studies related to a specific topic but not identified by the original four databases were sought. Both prospective and retrospective studies were considered, as were studies that used either experimental (randomized trials) or non-experimental designs (prospective and retrospective controlled trials, single group interventions, retrospective studies and cases studies).

Single case studies, single subject designs or a collection of case studies were included only for areas lacking studies of other designs. Studies cited in review articles, meta-analyses, systematic reviews, or in selected study articles but not identified through the original literature search were also included. Unpublished data or studies were not included. We limited our search to articles written in English. However, under special circumstances when no other studies were available, we included studies written in other languages (French and Spanish) as long as the abstract was available in English. Such studies were not scored unless we were able find a reviewer who was proficient in the given language. Reference Manager 17.0 ® was used for database management.

Specific subject headings related to acquired brain injury (ABI) were used as the search terms for each database. These search terms were selected with the assistance of a medical staff librarian. Using a specific database’s subject heading allowed for all other terms in the database’s subject heading hierarchy related to acquired brain injury to also be included in order to broaden the search. The database subject headings used for CINAHL were “brain injuries” and “head injuries”, for EMBASE “brain injury” and “head injury” were used, for MEDLINE “brain injuries” and “craniocerebral trauma” were used, for PsycINFO “brain injuries” and “traumatic brain injury” were used as search terms, for Social Work Abstracts and finally for Family and Society Studies Worldwide community integration and community rehabilitation were paired with head injury, brain injury, brain impaired, brain injured and brain lesion.
Module 3: Efficacy & Models of Care: Background information was identified using general internet searches, popular media links, and searches within key ABI websites. MEDLINE, CINAHL, EMBASE and PsycINFO were searched for combinations of “head injury” or “brain injury” and “rehabilitation”, “outpatient”, “inpatient”, “models”, “systems”, “pre-hospital”, “acute”, and “therapy”. Reviews and summary papers were targeted for references. Key authors were then identified and searched using MEDLINE. Search strategies for the Fatigue and Sleep Disorders post TBI module included: searching the following databases PubMed, CINAHL, EMBASE, PsycINFO using the following subject headings: fatigue and sleep disorders post TBI.

Module 4: Sensory and Motor Impairments post ABI. The modules authors paired the following each words or word phrases with brain injury, traumatic brain injury, closed head injury, with each: oculomotor rehabilitation, visual dysfunction, optometric rehabilitation, vision rehabilitation, vestibular dysfunction, vestibular rehabilitation, vertigo, balance problems, constraint induced movement therapy, splinting, fine motor, serial casting, orthosis, botulinum toxin, baclofen, tizanidine, electrical stimulation, exercise and aerobic training. For this current edition a section looking at pain post ABI/TBI has been added. The section focuses on central nervous system pain, neuropathic pain and post traumatic headaches. Both the pharmacological and non-pharmacological treatments were reviewed.

Module 5: Dysphagia & Nutritional Interventions for Patients with Acquired Brain Injuries revisiting the four main databases and the grey literature (dysphagia websites, various texts written by Jerri Logemann and others) to broaden our scope of the information available. This also allowed us to examine and include, not only the tests used to diagnosis dysphagia but the various treatments available even though many of these have not yet been tested specifically within the ABI population. In this current edition the modules authors investigated the connection between oral hygiene or the lack of oral hygiene and dysphagia post ABI.

Module 6: Cognition Interventions Post ABI. In an effort to clarify the information presented a reorganization of the material was needed. The chapter is now organized into 4 main sections: Remediation of Attention, Concentration & Information Processing Speed, Remediation of Learning and Memory Deficits, Remediation of Executive and General Cognitive Functioning, and Pharmacological Interventions to Assist with Cognitive Recovery Post ABI. The following search terms brain injury, brain injured, and closed head injury were matched with the following: donepezil, amantadine, pramiracetam, physostigmine, methylphenidate, bromocriptine, cerebrolysin, dual-task training, reaction time, attention retraining, attention deficits, attentional deficits, attention process training, external aids, memory, memory aid, memory training, memory retraining, memory therapy, memory rehabilitation, cognitive therapy, memory remediation, electronic aids, training intervention, learning, memory impaired, memory strategies, electrical stimulation, group therapy, group rehabilitation, goal management, cognitive rehabilitation, computer training, computer rehabilitation, and virtual reality.
Module 7: Cognitive-Communication Treatments Post Acquired Brain Injury. For this module we focus on the years 1992 to present. Following an Acquired Brain Injury, we engaged in an expanded search of the literature using the subject headings in the module and the following: social communication (discourse, pragmatics, social communication/social cognition, social perception, self regulation and ABI, TBI or BI; verbal expression (word finding, word retrieval, naming, language formulation, verbal expression, sentence formulation) and ABI, TBI or BI; auditory or listening comprehension (auditory and listening comprehension, receptive language, inference and figurative language); reading comprehension (visual processing, and oral reading) and ABI, TBI and BI; written expression (discourse and formulation) and community and family communication, academic and academic supports and vocational communication and ABI, TBI and BI. This allowed us to capture all available published available.

Module 8: Mental Health Issues Post ABI: This module discusses the treatments used to deal with challenging behaviors, affective disorders and substance addiction post ABI. Terms such as “behavior modification”, “modification, behavior”, “conditioning therapy”, “therapy, behavior” paired with “traumatic brain injury”, “acquired brain injury” closed head injury, “diffuse axonal injury” and “brain injury” was conducted. To assist us in broadening our search of substance addiction post ABI were included the terms alcohol, substance abuse, drug abuse with brain injury, head injured, head injury and brain injured. We looked at the pharmacological treatments and non-pharmacological treatments for behavioural and mental health issues that may arise as a result of the injury. Along with the five databases used in all the searches, a search through very specific journals such as: Journal of Rational Emotive Cognitive Behavior Therapy, Journal of Behavior Therapy Experiment Psychiatry, Journal of Applied Behavior Analysis, Behavior Modification, and Journal of Positive Behavior Intervention was also conducted. We limited our search to studies dealing with rehabilitation and therapy. In V9 of ERABI we decided to include a section looking at the issue and use of restraints in both acute care and rehabilitation settings. We looked at how they are used, when, why and who decides. This controversial issue we felt needed to be explored.

Module 9: Neuroendocrine Disorders Following Acquired Brain Injury: We used the following terms to guide in our search: incidence and prevalence of endocrine issues post ABI/TBI; laboratory testing used to diagnosis the disorders; physiological deficits such as posterior and anterior pituitary dysfunction; and treatments available. We conducted this search by using the 4 main databases and various other medical texts available to us.

Module 10: Post-Traumatic Seizure Disorder: Post traumatic seizure disorder, although identified as a serious consequence of TBI, remains an understudied problem. It is believed TBIs result in 20% of symptomatic epilepsy in the general population. Of all TBI patients who are hospitalized 5% to 7% will experience post-traumatic seizures (PTS). However, the incidence of PTS is much higher on rehabilitation units (as high as 17%) which is felt to reflect the increased severity of the injury and a higher number of risk factors in this population. For this module the following terms: traumatic brain injury, acquired brain injury, brain injury, closed head injury, diffuse axonal injury, were paired with each of the various anticonvulsants used to treat seizure disorders.
Module 11: Heterotopic Ossification and Deep Venous Thrombosis: Heterotopic ossification (HO) is a process where new bone forms within tissues where bone formation does not usually occur. In traumatic brain injury (TBI) patients, the areas which are most commonly involved are the soft tissues around the hip, elbow, shoulder and knee with the incidence of HO in TBI patients has been reported as ranging from 11% to 77%. Venous thromboembolism, including deep venous thrombosis and pulmonary embolism, remains a common complication in patients who have sustained an acquired brain injury; however, the scientific literature, specific to ABI, is quite limited on this topic even though it is quite extensive on venous thromboembolism in general. As with the other modules the following databases were searched: PubMed/Medline, CINAHL and EMBASE. For these two topics the stroke literature and spinal cord literature were also reviewed.

Module 12: Neuropharmacological Interventions Post ABI: For a number of years, it has been recognized that brain injury causes alterations in neurotransmitter levels through a number of pathways including direct neuronal cell trauma, changes in neuronal membranes, and through secondary injury such as alterations in cerebral perfusion. A number of both clinical and basic science researchers have attempted to find pharmacological treatments in an attempt to normalize neurotransmitter levels and enhance brain recovery. This module is a composite of the various pharmacological interventions used to assist in the recovery of an ABI or TBI in both the acute and rehabilitation phases post injury.

Module 13: Community Reintegration Post ABI: Community reintegration is the ultimate goal of brain injury rehabilitation. However, the evidence supporting many widely held beliefs about outcomes in this domain is limited. The evaluation of clinical work in this domain may not lend itself well to the rigor of a randomized controlled trial, as the situations, circumstances, deficits, and supports are as complex and varied as the individuals themselves. This chapter will review the evidence pertaining to community integration and is divided into five primary themes: Independence and Social Integration; Caregiver Burden; Satisfaction with Quality of Life; Productivity; and Return to Driving. For this particular area both the grey literature and the scientific literature were examined.

Module 14: Pediatric Interventions in Acquired Brain Injury Rehabilitation: To broaden our search for pediatric materials (especially materials looking at communication deficits in the pediatric population) we included the database Child Development and Adolescent Studies. Here “brain injury was paired with “communication”, “speech”, “language”, and finally “cognitive-communication”. In addition to updating the section on rehabilitation, Shaking Baby Syndrome and mild TBI, in this current Module an effort was made to include more literature that addresses treatments tried in the acute stage of recovery.

Module 15: Fatigue and Sleep Disorders Post TBI: Fatigue and sleep disorders post injury are two of the more common symptoms associated with and reported on by survivors of a brain injury. Over the years, researchers, physicians and psychologists have all tried to define fatigue: What is it? How do we measure it? How do we treat it? It is believed that fatigue is a subjective
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Experience and thus not easily assessed by objective measures. It is also believed that because fatigue is common with all who sustain a brain injury, it is therefore not related to damage within a specific area of the brain. Sleep disturbances or disorders tend to be classified as insomnia, excessive sleep, or excessive daytime sleepiness (EDS). This module looks at both disorders and their treatments.

Module 16: Acute Interventions for Acquired Brain Injury: Traumatic brain injury is currently one of the leading causes of death and disability worldwide. The true incidences and prevalence remains unknown. Up to 40% with severe TBI die as a result of their injury. Currently there is an increase in the knowledge that these individuals must be monitored closely. Module 16 investigates the steps taken to reduce the risk of death and improve outcomes in the first few weeks post injury.

Module 17: Assessment of Outcomes Following Acquired/Traumatic Brain Injury: This module examines the various outcome measures/tools used to assess severity of injury, and long term outcomes. The list of tools choses was originally derived by a consensus of experts working on the Evidence-Based Review of Acquired Brain Injury (ABI) literature. Tools such as the Glasgow Come Scale, Glasgow outcome Scale, Community Integration Questionnaire, Functional Independence Measure Scale, the Medical Outcomes Study SF-36, Rancho Los Amigos Scale, the Satisfaction with Life Scale, Galveston Orientation and Amnesia Test. To see the full list of tools examined, please see module 17. Evaluation criteria for each measure included: appropriateness, reliability, validity, responsiveness, precision, interpretability, acceptability, and feasibility. For this module tools were selected based upon a 3-step process. The first was the development of an inventory of current outcome measures based upon both the literature and discussions held with the rehabilitation team members who actually used the tools. The second was a consensus agreement among a panel of experts as to which was most important. Finally, there had to be sufficient research on the outcome measure in ABI populations to allow a meaningful analysis of the psychometric qualities of the tools.

Module 18: Aging and Traumatic Brain Injury: This particular module looks at the impact a TBI or ABI has on the elderly population. To assist us in finding the most recent literature looking at the impact a brain injury has on those over the age of 60, the following search terms were used: brain injury, traumatic brain injury, brain injured, head injured, and head injury. To allow for a thorough search the following on-line databases were used: Medline, EMBASE, CINAHL, Web of Science and PsycINFO.

Module 19: Traumatic Brain Injury and Animal Research: For this module authors conducted a similar search using the same databases. The same search terms used for module 18 were coupled with animal (rats, mice, dogs, cats, etc), animal model and neuroprotection.

1.5.2 Study Inclusion Criteria
Every effort was made to identify all relevant articles that evaluated any rehabilitation intervention which assessed any outcome measure during any timeframe within the recovery period following brain injury. Two independent reviewers (including one of the primary
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authors) evaluated all reference titles obtained from the various databases or from other sources. Any reference title that appeared to involve ABI and a treatment was selected. The abstracts from these selected reference titles were then reviewed by another 2 independent reviewers (including one of the primary authors) to determine if the studies met the criteria for full review.

Studies where at least 50% of the population included patients with ABI and which involved the evaluation of a treatment with measurable outcomes were selected. Studies underwent full review only when 2 independent reviewers agreed that a study met the 2 inclusion criteria stated above based on the information available in the article’s abstract. A third independent reviewer settled discrepancies.

Background information, for the Models of Care subsection of the Efficacy Module, was drawn from the grey literature and peer reviewed articles. Papers were considered for analysis if they focused on a generalized system of care and were published in a recognized peer reviewed journal. Since our aim was to compare systems of rehabilitation and not rehabilitation itself, only papers which compare at least two distinct rehabilitation groups were included. These could include separate hospitals, separate treatment groups within one center or comparisons between patients in the same center before and after systemic changes. Papers were then subdivided into two groups: those which included an empirical, objective analysis of an outcome related to a system of care and those which provided a descriptive comparison of a component of their system. Empirical studies were scored using the PEDro evaluation tool. Descriptive papers were given no score and only information pertaining to models of care was extracted and summarized.

1.5.3 Data Extraction
Once an article was selected for full review, the following data was extracted: authors, place and date of publication, inclusion and exclusion criteria, sample sizes, details regarding the population studied (i.e. type of injury, severity, source, sex, age, time since injury), treatment, outcome measures, and results. Articles which did not meet our definition of ABI or which did not fall under the moderate to severe range of injury severity were excluded. This data was summarized using large tables. Articles evaluating similar treatments were grouped together.

1.5.4 Methodological Quality Assessments of RCTs
Two independent reviewers, each blinded to the other’s results rated the methodological quality of all selected articles. For randomized controlled trials the Physiotherapy Evidence Database (PEDro) rating scale developed by the Centre for Evidence-Based Physiotherapy (CEBP) in Australia was used (Moseley et al., 2002).

http://www.pedro.fhs.usyd.edu.au/FAQs/Scale/scaleitems.htm
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Studies that used a non-experimental or uncontrolled design (non-randomized comparative trials, cohort studies, or retrospective trials) cannot be evaluated using the PEDro scale; therefore these studies are no longer evaluated.

Table 1.4 PEDro Scale (Moseley et al., 2002)

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>“Subjects were randomly allocated to groups.” (in a crossover study, subjects were randomly allocated an order in which treatments were received). A point for random allocation was awarded if random allocation of patients was stated in its methods. The precise method of randomization need not be specified. Procedures such as coin-tossing and dice-rolling were considered random. Quasi-randomization allocation procedures such as allocation by bed availability did not satisfy this criterion.</td>
</tr>
<tr>
<td>2.</td>
<td>“Allocation was concealed.” A point was awarded for concealed allocation if this was explicitly stated in the methods section or if there was reference that allocation was by sealed opaque envelopes or that allocation involved contacting the holder of the allocation schedule who was &quot;off-site.&quot;</td>
</tr>
<tr>
<td>3.</td>
<td>“The groups were similar at baseline regarding the most important prognostic indicators.” A trial was awarded a point for baseline comparability if at least one key outcome measure at baseline was reported for the study and control groups. This criterion was satisfied even if only baseline data of study completed-only subjects were presented.</td>
</tr>
<tr>
<td>4.</td>
<td>“There was blinding of all subjects.” The person in question (subject, therapist or assessor) was considered blinded if he/she did not know which group the subject had been allocated to. In addition, subjects and therapists were only considered to be &quot;blind&quot; if it could be expected that they would have been unable to distinguish between the treatments applied to different groups. In drug therapy trials, the administrator of the drug was considered the therapist and was considered blinded if he/she did not prepare the drug and was unaware of the drug being administered.</td>
</tr>
<tr>
<td>5.</td>
<td>“There was blinding of all therapists who administered the therapy.” (criteria 4.)</td>
</tr>
<tr>
<td>6.</td>
<td>“There was blinding of all assessors who measured at least one key outcome” (criteria 4).</td>
</tr>
<tr>
<td>7.</td>
<td>“Adequacy of follow-up.” For the purposes of this review, follow-up was considered adequate if all of the subjects that had been originally randomized could be accounted for at the end of the study. The interpretation of this criterion differs from that described by PEDro, where adequacy is defined as the measurement of the main outcome in more than 85% of subjects.</td>
</tr>
<tr>
<td>8.</td>
<td>“Intention to treat.” All subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome was analyzed by &quot;intention to treat&quot;. For purpose of the present evidence-based review, a trial was awarded a point for intention-to-treat if the trial explicitly stated that an intention-to-treat analysis was performed.</td>
</tr>
<tr>
<td>9.</td>
<td>The results of between-group statistical comparisons are reported for at least one key outcome.” Scoring of this criterion was design dependent. As such, between groups comparison may have involved comparison of two or more treatments, or comparison of treatment with a control condition. The analysis was considered a between-group analysis if either a simple comparison of outcomes measured after the treatment was administered was made, or a comparison of the change in one group with the change in another was made. The comparison</td>
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</table>
Evidence-Based Review of Moderate to Severe Brain Injury

Module 1 - Introduction and Methodology

1.6 Determining Levels of Evidence

1.6.1 Interpreting the Results of Individual Studies

For RCTs, studies scoring 9-10 on the PEDro scale were considered methodologically to be of “excellent” quality. Studies with PEDro scores ranging from 6-8 were considered to be of “good” quality, while studies scoring 4 or 5 were of “fair” quality. Studies that scored below 4 were felt to be of “poor” quality. The authors arrived at these descriptive terms of quality assessment arbitrarily in an effort to simplify the interpretation of results. Studies employing a non-experimental or uncontrolled design were considered an inferior form of evidence. They were used only to formulate conclusions only in the absence of RCTs.

1.6.2 Formulating Conclusions Based on Levels of Evidence

The levels of evidence used to summarize the findings are based, in part on the Eastern Ontario/Queen’s Evidence Based Report, which in turn was based on the levels of evidence used by the United States Agency for Health Care Policy and Research (AHCPR) Guidelines for Stroke Rehabilitation. We chose these over a multitude of similar levels of evidence because it fit well with the rehabilitation model where RCTs with small “n’s” were the rule.

The following definitions of evidence were used:

- **Evidence**
  - May be in the form of hypothesis testing (e.g. p-value) or in the form of an estimate (e.g. the mean, median difference, difference in proportion, number needed to treat, and relative risk or hazard ratio) and its confidence interval. A trial was awarded a point for this criterion if between group comparison on at least one outcome measure was made and its analysis of comparison was provided.
  - **The study provides both point measures and measures of variability for at least one key outcome.** A point measure was referred as to the measure of the size of the treatment effect. The treatment effect was described as being either a difference in group outcomes, or as the outcome in (each of) all groups. Measures of variability included standard deviations, standard errors, confidence intervals, interquartile ranges (or other quartile ranges), and ranges. Point measures and/or measures of variability that were provided graphically (for example, standard deviations (SDs) may be given as error bars in a Figure) were awarded a point as long as it was clear what was being graphed (e.g. whether error bars represent SDs or standard error (SEs)). For those outcomes that were categorical, this criterion was considered to have been met if the number of subjects in each category was given for each group.

Although the identification of eligibility criteria is also considered under the PEDro scoring system, it was not used to calculate PEDro scores for this review. Subject selection influences the external validity, not the internal or statistical validity of a study.

The maximum score a study could receive was 10. Whenever rating discrepancies occurred, the 2 reviewers reached consensus or a third independent reviewer evaluated the study to settle any disagreements.
• **Level 1a:** More than one RCT: Randomized Controlled Trial, PEDro score ≥6. Included within subjects comparison with randomized conditions and crossover designs.

• **Level 1B:** 1 Higher Randomized Controlled Trial, (≥6 on PEDro).

• **Level 2:** The findings are supported by a single RCT of a least “fair” quality (RCT<6 PEDro), non-RCTs and Cohort

• **Level 3:** A retrospective study comparing conditions including historical controls.

• **Level 4:** The findings are supported by at least one:
  - **Pre-Post test**—a prospective trial with a baseline measure, intervention, and a post test using a single group of subjects;
  - **Post-test**—a prospective intervention study using a post intervention measure only (no pre-test or baseline measurement) with 1 or more groups
  - **Case Series**—a retrospective study usually collecting variables from a chart review.

• **Level 5:** The findings are supported by at least one:
  - **Observational study**—using cross sectional analysis to interpret relations;
  - **Clinical Consensus**—expert opinion without explicit critical appraisal or based on physiology, biomechanics or “first principles”;
  - **Case Reports**—pre-post case series involving one subject.

The levels of evidence used to summarize the findings are based on the levels of evidence developed by Straus et al. (2005) The levels proposed by Straus et al. (2005) were modified to collapse the subcategories within a level (e.g., level 1a, 1b, 1c, 2a, 2b) in all but the first level. Here we modified Sacketts original scale from 1a-1c to 1a or 1 b. we have therefore reduced the categories from 10 to 6. Straus et al. (2005) distinguishes high and low quality randomized controlled trials (RCTs) into level 1b and level 2b, respectively. To provide a more reliable decision-making process, we required that a level 1 RCT had a PEDro score of 6 or higher (good to excellent quality), while a level 2 RCT had a PEDro score of 5 or less.

Using this system, conclusions were easily formed when the results of multiple studies were in agreement. However, interpretation became difficult when the study results conflicted. In cases where RCTs also differed in terms of methodological quality, the results of the study (or studies) with the higher PEDro score(s) were more heavily weighted to arrive at the final conclusions. However, there were still some instances where interpretation remained problematic. For instance, the authors needed to make a judgment when the results of a single study of higher quality conflicted with those of several studies of inferior quality. In these cases we attempted to provide a rationale for our decision and to make the process as transparent as possible. In the end the reader is encouraged to be a “critical consumer” of all of the material presented.

**1.7 The Importance of Evidence-Based Practice**

Evidence-based practice, because of its potential to improve patient care, is clearly the way of the future. Medicine has a long history of relying on anecdotal experiences, which runs the danger of promoting practices that are ineffective and in some cases, produce less than optimal outcomes.
Evidence-based practice is therefore an increasingly important element of clinical care. It is a tool to improve on rehabilitation, which remains delivery of care by a rehabilitation clinician or a team on a one-on-one basis. The fact that therapy is delivered on a one-on-one basis means that there are other factors, other than the actual treatment, which will influence the outcomes (Banja 1997). The chronic and ever-evolving nature of many patients’ conditions makes it difficult to decide the optimum amount of therapy at the outset of treatment (Purtill 1992). The experience, enthusiasm and empathy of the rehabilitation clinician still plays an extremely important role in the rehabilitation of ABI/TBI patients but these qualities are difficult to fully capture within the structure of evidence-based practice. Also ABI/TBI rehabilitation outcomes reflect a process in which various decisions are made by different stakeholders. These stakeholders consider what is desirable, acceptable, reasonable, and appropriate, and how these decisions produce an outcome to which subjective assessments of worth or value will be attached (Banja, 1997). Nevertheless, evidence-based practice is the most important improvement on the care delivered by even the most experienced clinician.

1.8 The Limitations of Evidence-Based Practice
Evidence-based practice does have limitations. One of the limitations alluded to above is its focus on the treatment of groups rather than individuals. Therefore, the evidence provides guidelines as to how patients as a group should be treated and in that way also provides some guidance as to how the individual patient should be treated; however, in the end how a patient is treated is an individual clinician’s decision. There are times when the evidence will need to be put aside for a specific case. The important element is that these cases should not be common but rather uncommon and the majority of patients should be managed according to the evidence.

Evidence-based practice can also be problematic when the evidence is misinterpreted. The most common scenario occurs when results of a trial are generalized to a wider group than they should be. Evidence is a tool, and as such it can be used for both good and bad.

Regardless of which outcome measures and data analysis methods are used, there continues to be a need for examining how values determine rehabilitation outcomes if for no other reason than that most outcomes cannot be guaranteed (Englehardt 1996). As Banja (1997) has illustrated, “Even if an outcome study found a particular treatment to be successful 33% of the time, it would still be an entirely speculative matter as to whether or not a 33% rate of success was acceptable. A treatment success rate of 33% might be marvellous if it could save a life, but considerably less marvellous if the person’s quality of life would only be barely improved.” (p.54).
1.9 Reference List


Purtill RB. Whom to treat first, and how much is enough? Ethical dilemmas that physical therapists confront as they compare individual patients’ needs for treatment. International Journal of Technology Assessment in Health Care 1992; 8: 26-34.


