Comparative Effectiveness and Implementation Research for Neurocognitive Disorders: Concepts Relevant to Cognitive Rehabilitation Therapy for TBI

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GOAL: Identify specific CRT interventions with sufficient evidence base to support widespread use in military health system and TRICARE coverage

TASKS:
• Assess not only efficacy but also safety, effectiveness
• Evaluate current state of practice of CRT interventions identified as effective, by mild/mod/severe - and “training, education, and experience” of providers within MHS and likely association with current quality
• Current care within military health service (access, patterns, quality?)
**Neuroscience Research Continuum**

Basic Research → Translation from Basic Neuroscience to Human Studies → Clinical Science and Knowledge of Potential Value under *ideal* Conditions → Translation into "real-world" settings

- Higher use of RCT-proven treatments* → Improved population health
- Lower, delayed, or inappropriate use of RCT-proven treatments → Clinical Quality Improvement or Policy Interventions

*If diffusion occurs in population for whom there is greater harm than benefit, high diffusion may decrease population health.*
CONCEPTS

1) The translation of evidence into practice & improved population health outcomes typically is phased and entails a series of studies beginning with small pilot projects, to larger trials in more diverse settings with less investigator control over implementation.

2) Ultimate goal of treatment for TBI is rarely the dissemination of one evidence-based therapy to target a single dimension of cognition, but to improve patient health outcomes broadly. To do this requires conceptualizing healthcare interventions as multi-modal, addressing comorbidities of PTSD, depression, and physical impairments that may have occurred with polytrauma.

3) Registries and prospectively planned analyses are increasingly used to monitor and evaluate the implementation and impact of clinical and policy interventions in healthcare, in order to reassess effectiveness, including both benefits and harms.

4) As with CER on different modes of healthcare delivery, CRT for TBI ideally would take into account subgroup level results, given the heterogeneity of populations and forthcoming advances in disease mechanisms/markers.
1) The translation of evidence into practice & improved population health outcomes typically is phased and entails a series of studies beginning with small pilot projects, to larger trials in more diverse settings with less investigator control over implementation.
Well-Established Evidence on What Works for Hypertension

Large number of medications of proven efficacy; numerous guidelines on recommended pharmacologic algorithms

“Lifestyle” goals requiring behavioral change

a) Exercise (Whelton et al, 2002)
b) Healthy body weight
c) Moderate alcohol
d) Low salt, “DASH” diet:

Appel LJ. *J Am Soc Nephrol* 2003;14:S100
Counseling, patient self-monitoring of BP, and structured training – all are effective.

(But counseling effective only when given by nurse or pharmacist…)

Efficacy of a behavioral intervention targeting multiple lifestyle changes in 810 adults with “above-optimal” BP on:
- weight loss
- sodium reduction
- physical activity
- alcohol intake
- DASH dietary intake

Control: one 30-min session with dietitian; print matter

Behavioral Intervention (over 6 months):
- 14 group meetings and 4 individual counseling sessions
- self-monitoring logs (exercise, food diaries, sodium intake)

Systolic BP decreased ~4 mmHg; HTN at 6 months 26% vs. 12%

Appel et al  

Effects of Comprehensive Lifestyle Modification on Blood Pressure Control: Main Results of the PREMIER Clinical Trial  

*JAMA 2003;289:2083-2093*
So…behavioral interventions to modify lifestyle habits (as well as medications) are effective at reducing blood pressure and reducing the prevalence of hypertension.

Then what are the barriers to converting clinical trial knowledge (that is, scientific evidence) into better population health [reduced blood pressure]?
Barriers & Limitations to Use of Evidence-Based Interventions for Treatment of HTN

Hypertension is long-term duration but behavioral interventions are typically not.

Generalizability is uncertain (for example, literacy; having safe place to exercise; pt attitudes to change) because context matters.

Intervention costs may be prohibitive for broad dissemination.

Materials or training used in interventions may not be available.

Do not address lack of detection of hypertension.

Do not take into account access to guideline-recommended medication management and challenges in adherence to medication.

Implementation science addresses***
Refined research-implementation pipeline

Implementation Research

Effectiveness; G/Ls and SRs (Step C, 2)

Interventional implementation studies (4/5/6)

Obs’l: Quality gaps, implement processes (3, O)

Phase 1: Pilot Projects

Phase 2: Small-Scale Efficacy Trials

Phase 3: Large-Scale Effectiveness Trials

Phase 4: “Post-Marketing” Monitoring, Refinement

Improved Health Processes, Outcomes

Figure from Brian Mittman, PhD
2) Ultimate goal of treatment for TBI is rarely the dissemination of one evidence-based therapy to target a single dimension of cognition, but to improve patient health outcomes broadly. To do this requires conceptualizing healthcare interventions as *multi-modal*, addressing comorbidities of PTSD, depression, and physical impairments that may have occurred with polytrauma.
ANALOGY: RCT to Increase Translation of Evidence to Outcomes for Dementia

Not focus on one treatment or one outcome, but quality of care broadly:

- **Non-pharmacologic approaches reduce behavior problems (agitation and anxiety; Sloane, *JAGS*, 2004)**

- **Cholinesterase inhibitors can delay aspects of cognitive decline (Doody, *Neurology*, 2001)**

- **Caregiver receipt of support and respite services can delay nursing home placement (Mohide, *JAGS*, 1990)**
Current, Usual Care for Dementia

Patient Caregiver(s)

Health Care Systems
- Primary Care Physicians
- Neurologists, Other Care Providers

Community Agencies
- Usual Care Providers
“Re-engineered” Dementia Care Intervention Model

Activated Patient/Caregiver(s)

Health Care Orgs
- Dementia Care Managers;
  Evidence-Based Protocols
- Primary Care Physicians
- Other Care Providers

Community Agencies
- Dementia Care Managers;
  Evidence-Based Protocols
- Usual Care Providers and Services

Proactive case ascertainment and follow-up

Information Technology Prompts

Your ACCESS Care Manager at UCSD Health Care:

Contact Information:
Title: Registered Nurse
Organization: UCSD Health Care

[Image]
Trial Design: Testing Re-Engineered System of Dementia Care

- Pre-post, experimental design (intervention vs. usual care) with ~18-month follow-up
- Cluster RCT with clinic as randomization unit: stratified randomization of 18 clinics across 3 healthcare organizations in San Diego
- Medicare enrollees ≥65 yrs with dementia (>95% non-institutionalized)
- 408 patient/caregiver dyads enrolled

Effectiveness of Re-engineered Dementia Care Model in Improving Use of Evidence-Based Dementia Treatments


*p < 0.001 for all*
### Re-engineered Care Yielded Better Patient and Caregiver Health Outcomes than Usual Care

<table>
<thead>
<tr>
<th></th>
<th>Usual Care Mean</th>
<th>Intervention Mean</th>
<th>Adjusted Between-Group Difference</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient’s health related</td>
<td>0.03</td>
<td>0.10</td>
<td>0.06</td>
<td>0.03</td>
</tr>
<tr>
<td>quality of life (0-1 range)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall quality of healthcare</td>
<td>7.9</td>
<td>8.2</td>
<td>0.5</td>
<td>0.003</td>
</tr>
<tr>
<td>(0-10)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caregiver Confidence in</td>
<td>60</td>
<td>67</td>
<td>6.4</td>
<td>0.001</td>
</tr>
<tr>
<td>Caregiving (0-100)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caregiving Health Strain</td>
<td>60</td>
<td>64</td>
<td>4.3</td>
<td>0.06</td>
</tr>
<tr>
<td>(0-100)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Higher scores mean better outcomes*
EXAMPLE STRATEGY: Create public-accessible database of effective caregiving interventions, including tools; analyze (qualitatively) what components appear common to effective interventions.

Source: http://www.rosalynncarter.org/

**What Makes A Caregiver Program Effective?**

Programs that have been demonstrated to help caregivers under "real world conditions" are said to be effective. Generally, this means taking a program that has been rigorously tested under controlled conditions and implementing it successfully in a community agency. If the program as adopted demonstrates the ability to improve caregiver knowledge, skills, morale and health, and/or reduce depression, injury, ill-health and social isolation when provided in the community to caregivers, it is said to be "effective". Effectiveness, then, is the ultimate measure of whether a program "works" to help caregivers. Even the best evidence-based program may not be effective if it is poorly implemented, if staff are not properly trained, if the program varies too much from the original design and so on.

Evidence-based interventions are those that have a documented record of positive outcomes for caregivers. Not all evidence based interventions are effective in practice because of poor implementation, poor staff training, and other factors. Read more about evidence-based interventions.
Effective programs appear to share several characteristics. Specifically, the following factors have been associated with the most positive outcomes for family caregivers. These factors should be carefully studied and built into efforts to support family caregivers:

1. **Contact with a helper over time**, (NINR, 2001; Teri, 1999; Thompson & Gallagher-Thompson, 1996.)

2. **Contact with a helper who has specific intervention protocols to follow** (Schulz, 2000; Schulz, Gallagher-Thompson, Haley, & Czaja, 2000)

3. **Interventions and care plans tailored to the caregiver’s specific needs** (Chwalisz, 1995, Mittelman, Roth, Coon, and Haley, 2004; Schulz, Gallagher-Thompson, Haley, & Czaja, 2000).

4. **Multi-component interventions that include a combination of knowledge, skill building, problem solving and counseling** (Carnevale, Anselmi, Busichio, & Millis, 2002; Grant, Elliott, Giger, & Bartolucci, 2001; Paun, Farran, Peraud, & Loukissa, 2004; Query & Wright, 2003; Schulz, Martire & Klinger, 2005).

5. **Interventions with higher intensity** (e.g. greater frequency and duration) (Schulz et. al. 2005)

6. **Using a combination of home-visiting, telephone follow-up, internet and telehealth technology to deliver**, (Davis, Burgio, Buckwalter, & Weaver, 2004; Eisdorfer et al., 2003; Mahoney, Tarlow, & Jones, 2003; NINR, 2001) and,

7. **Programs developed and implemented locally and involving agency collaboration** (Felicreek, 2003; Tremethick et. al. 2004; Wilken, Tremethick, Walker, & Meier, 1999).

Other examples:

1. Administration On Aging: “Translation to Care” grants

2. Gitlin: OT interventions for dementia translated to reimbursable service

3. IMPACT depression care management dissemination: workshops and manuals

Source: [www.rosalynncarter.org/](http://www.rosalynncarter.org/)
CONCEPT

3) Registries and prospectively planned analyses are increasingly used to monitor and evaluate the implementation and impact of clinical and policy interventions in healthcare, in order to re-assess effectiveness, including both benefits and harms.
# Summary of Health Database Sources and Variables Typically Contained

<table>
<thead>
<tr>
<th>DATABASE</th>
<th>ENROLLMENT</th>
<th>DRUGS/PROCEDURES</th>
<th>DIAGNOSES</th>
<th>LABS</th>
<th>PHYSIOLOGIC VARS</th>
<th>PATIENT REPORT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Claims/Admin data</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>no</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td>Electronic Medical Record (EMR)</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>Registry</td>
<td>Can be</td>
<td>Can be</td>
<td>Can be</td>
<td>Can be</td>
<td>Can be</td>
<td>Can be</td>
</tr>
<tr>
<td>Registry linked to EMR</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
</tbody>
</table>

Adapted from Joe Selby, fall 2009
Registries for Evaluation of Health Care

Agency for HealthCare Research and Quality (AHRQ)

Purpose: “serve as a guide to the design and implementation of patient registries, the analysis and interpretation of data from patient registries, and the evaluation of the quality of a registry or one of its components.”
CONCEPT

4) As with CER on different modes of healthcare delivery, CRT for TBI ideally would take into account subgroup level results, given the heterogeneity of populations and forthcoming advances in disease mechanisms/markers.
"...describes results at the population and subgroup levels....By its focus on subgroup results and clinical prediction rules to identify patients likely to benefit from an intervention, CER assists providers and patients in individualizing decisions – going beyond the average effects to the effect in subjects with common clinical characteristics. This focus of CER reflects the growing potential for individualized and predictive medicine – based on advances in genomics, systems biology, and other biomedical sciences – through the analysis of subgroups with demographic, ethnic, physiologic, and genetic characteristics that could be useful factors in clinical decisions."

Effectiveness of Re-engineered Dementia Care Model in Improving Use of Evidence-Based Dementia Treatments

Mean % of Care Goals Met

Assessment Treatment Knowledge/Support Safety

Usual Care Intervention

p < 0.001 for all
Associations of Degree of Benefit from Dementia Care Management Intervention and Level of Caregiver Education

P=0.001 for interaction of intervention effect by caregiver education
### Assessing and reporting heterogeneity in treatment effects in clinical trials: a proposal

David M Kent, Peter M Rothwell, John PA Ioannidis, Doug G Altman, Rodney A Hayward

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**Table 1: How summary results of clinical trials can be misleading even when everyone gets the same relative risk reduction**

Assumption: Treatment reduces baseline risk by 25% without any treatment related harm

<table>
<thead>
<tr>
<th></th>
<th>Control Event Rate* (%)</th>
<th>Experimental Event Rate (%)</th>
<th>Relative Risk Reduction (RRR)</th>
<th>Absolute Risk Reduction (ARR)</th>
<th>Number Needed to Treat (NNT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall result (100%)</td>
<td>8</td>
<td>6</td>
<td>0.25</td>
<td>0.02</td>
<td>50</td>
</tr>
<tr>
<td>Average risk subjects (75%)</td>
<td>4</td>
<td>3</td>
<td>0.25</td>
<td>0.01</td>
<td>100</td>
</tr>
<tr>
<td>High risk subjects (25%)</td>
<td>20</td>
<td>15</td>
<td>0.25</td>
<td>0.05</td>
<td>20</td>
</tr>
</tbody>
</table>
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