A. Specific Aims

**This research summarized in one case:** Bernice is an 82 year old woman who lived independently despite multiple medical problems until she suffered a hip fracture. After surgery, she was admitted to a Skilled Nursing Facility (SNF) for post-acute rehabilitation with the goal of returning home. Depressed and mildly cognitively impaired, she was difficult to engage and showed little progress in therapy. She failed to regain the ability to walk and is now in long-term SNF care.

1. What if there is a better way to rehabilitate Bernice?
2. What if this enhanced rehabilitation overcame the barriers posed by Bernice’s depression and cognitive problems, so that she successfully rehabilitated?

**The problem:** For millions of disabled older adults each year, post-acute care in skilled nursing facilities (SNFs) is a brief window of opportunity to regain enough function to return home and live independently -- but too often they fail due to problems such as depression that undermine rehabilitation’s benefits.

**Our treatment development:** We created Enhanced Medical Rehabilitation (EMR) for older adults in post-acute care rehabilitation. Based on models of behavior change, EMR is a set of patient engagement skills for physical and occupational therapists (PT/OT) that transform standard care through: (1) a patient-directed, interactive approach (2) increased rehabilitation intensity (3) frequent feedback to patients on their effort and progress. We developed successful training and supervision techniques such that PT/OTs carried out these skills with high treatment fidelity.

**In NIMH R34 pilot work:** We found (1) EMR is high-intensity and high-engagement. Therapy by PT/OTs trained and supervised in EMR is greatly amplified in intensity and patient engagement compared to standard-of-care rehabilitation. (2) EMR improves functional and affective recovery. Patients randomized to EMR had better improvement of function, physical performance, and affect. (3) EMR overcomes barriers to successful rehabilitation. Those most vulnerable to poor rehabilitation outcome – patients with depression, cognitive impairment, or multiple medical problems – benefitted most from EMR relative to standard rehabilitation.

**Now:** We propose a randomized trial in 252 older adults, 50% of whom have clinical depression, to test EMR’s benefits over standard-of-care rehabilitation.

**Aim 1:** Examine the effectiveness of EMR for improving functional and affective outcomes in older adults admitted to SNFs for post-acute rehabilitation.  
**H1:** EMR will improve functional and affective recovery to a greater extent than standard-of-care rehabilitation.  
**Rationale:** This test could demonstrate EMR’s effectiveness, a key step toward establishing EMR as the gold-standard practice for post-acute rehabilitation, to the benefit of millions of older adults.

**Aim 2:** Examine EMR’s ability to overcome patient-level barriers to successful rehabilitation.  
**H2:** The effectiveness of EMR for functional recovery will be greatest in: (a) patients with clinical depression; (b) patients with high levels of medical comorbidity; (c) patients with cognitive impairment.  
**Rationale:** Demonstrating that EMR is particularly effective in the most vulnerable patients could overturn conventional wisdom that such persons should be excluded from intensive rehabilitation.

The **innovation** of this project is high: it is a novel application of theories of behavior change, to improve both depression and function. It responds to NIMH strategic plan objective 3, “Develop new and better interventions for mental disorders that incorporate the diverse needs and circumstances of people with mental illness.”

The **public health significance** is also high: recovery from disablement is a health issue of enormous human and economic significance. Success in this line of research could establish EMR as the gold standard, making rehabilitation more effective. Doing so would benefit all older adults in this sector of care but particularly those with depression, cognitive impairment, and other complications, who are at most risk for poor outcomes with the existing standard-of-care rehabilitation. **This project addresses NIMH’s goal of interventions to improve mental health and related health outcomes in real-world settings.**
Research Strategy: Significance

The growing role of post-acute rehabilitation

Americans are aging and having more medical events such as heart attack, stroke, and hip fracture. More than ever, older adults are surviving these events and leaving the hospital, alive but severely disabled. The solution for these highly disabled older adults is rehabilitation in the post-acute care setting, a large and rapidly-growing sector of care. Post-acute rehabilitation consists of daily physical therapy (PT) and occupational therapy (OT) to achieve restoration (e.g., regain walking ability and counteract bone and muscle loss by gait and muscle strengthening exercises), and adaptation (e.g., learn to perform activities of daily living and safely live at home).

The most common setting for post-acute rehabilitation is a skilled nursing facility (SNF). Length of stay is about 3 weeks, a narrow window in which to recover and return home or be institutionalized.

Depression is the most common and deleterious mental disorder in post-acute rehabilitation.

Disabled older adults have high rates of depressive symptoms and disorders which lead to and amplify disability. This bidirectional relationship between late-life depression and disability is intensified in post-acute rehabilitation, where affective impairments are barriers to successful rehabilitation. In other words, in this population, depressive symptoms are both an outcome of rehabilitation (as disability is depressogenic) and moderate (reduce) rehabilitation success. Additionally, cognitive impairment and high levels of medical complexity impede rehabilitation success.

Existing mental health interventions are a poor fit for these disabled and depressed older adults. Post-acute rehabilitation is a difficult setting in which to integrate evidence-based mental health treatments, due to short stays, difficulty of case detection, and competing demands (most notably from the rehabilitation itself). Additionally, frail and medically ill older adults have less benefit and greater risks from antidepressants. Finally, the affective state of these older adults appears tightly linked to the disablement itself. Therefore, an optimal intervention would use a common conceptual model to address affective impairments together with the disablement.

Do we need to enhance rehabilitation?

Post-acute PT/OT itself could be this optimal intervention, ameliorating affective impairments and disablement via intensive goal-oriented interactions with highly-trained providers. Yet two factors have been observed to undermine rehabilitation, particularly for depressed older adults: (1) The PT and OT is of low intensity, often too low to provide adequate restoration of function and improve affect; (2) The interaction with patients is unengaging because (a) therapists are directive, telling patients what to do, and (b) therapists do not provide adequate feedback on patients' effort and progress in therapy, such that patients will know where they stand in their recovery and why their therapy activities are important.

From a behavior change standpoint, standard rehabilitation fails because it is a traditional Action-oriented program, assuming that patients are motivated to carry out therapeutic activities and not demoralized or uninsightful. Yet our research in post-acute rehabilitation shows that a substantial proportion are not adequately motivated and do not participate well in their therapy, particularly when they have depressive symptoms and/or cognitive impairment. When participation in therapy is poorer, recovery is poorer.

The conventional wisdom in rehabilitation practice guidelines is a distortion of this observation; it states that inadequately motivated patients are "poor candidates" for high-intensity rehabilitation. This conventional wisdom not only ignores behavior change research, it has no evidence basis; indeed, it runs counter to our observation that depressed and apathetic older adults do better in high-intensity than lower-intensity rehabilitation. Yet, no research has clearly refuted this wisdom. The resultant disparity is that older adults most at risk for poor outcomes after disablement – such as those with depression or cognitive impairment – may be relegated to the least intense rehabilitation.

To summarize the significance, post-acute rehabilitation is low-intensity, low-engagement and too often fails to achieve functional recovery, especially in the most vulnerable individuals. This problem should be remediable by applying the science of behavior change to this setting. We therefore developed Enhanced Medical Rehabilitation.
Approach: Preliminary Studies
Enhancing post-acute rehabilitation is feasible: results of a pilot study
From 2010-2011 we carried out an **NIMH R34 treatment development grant** to develop and preliminarily test Enhanced Medical Rehabilitation (EMR), a novel PT and OT intervention. Our goal was to apply the science of behavior change to overcome shortcomings of standard of care rehabilitation, namely that it does not provide high-intensity and highly engaging therapy.18,19

EMR is a set of skills for PT and OT to increase both intensity and the engagement of all therapeutic sessions. It has three foci for therapy sessions: high intensity, feedback to patients on their effort and progress, and a patient-directed approach. EMR is a “how” intervention, not a “what” intervention: its skill set integrates into existing OT/PT, rather than adding new activities or exercises or adding another specialist to the setting. In other words, OT or PT in the EMR model is still OT or PT (which in this setting is individualized by the therapist to the patient's impairments, abilities, home environment, and other contextual factors). The difference is in the effort to engage the patient and provide high-intensity therapy. **For this reason, EMR can integrate well into post-acute OT/PT no matter what the patient’s primary impairment, comorbidities (cognitive, medical), or other contextual factors.**

EMR’s foci have deep roots in the science of behavior change, including social cognitive theory,33 self-regulatory theory,34 the Theory of Planned Behavior,35 and the Transtheoretical Model which encompasses these and other theories.21 **EMR’s three foci are described with an explanation of their innovation for rehabilitation and their link to theories of behavior change here:**

1. Interactive, patient-directed approach
   a. In the first session, OT and PT elicit the patient’s own goals for rehabilitation using the Rehabilitation Goals Interview, a brief (15 minute) semi-structured interview to generate patient-nominated therapy goals.36 Up to 5 goals are nominated by the patient as most important to them. We found this technique to provide more rich and precise information than the standard rehabilitation technique of simply asking patients what their goals are. This interview is linked to the Transtheoretical (Stages of Change) Model in that it raises the patient's awareness of themselves presently in contrast to where they want to be. The interview frequently produces an emotional experience by the patient, and so therapists are also trained to expect this and work with it. Regarding innovation: no rehabilitation therapists, to our knowledge, use a structured interview to discern patients’ goals (they typically ask “what are your goals?” which is generic and insufficient).
   b. These patient-reported goals become the basis for all interactions:
      i. “You decided that helping care for your grandchildren, getting to church, and walking your dog are your goals. Which one of those would you like to focus on today?”
      ii. “Okay, so we’ll focus today’s therapy on activities that will get you closer to your goal of being able to help take care of your grandchildren again. What will you need to be able to do so that you can get back to doing that?”
      iii. “Just to make sure we’re on the same page, can you talk me through how this activity will get you closer to your goal of helping care for your grandchildren?”
      iv. Additionally, study staff (not blinded raters) make a videotape of the patient’s home, which the therapists watch alone and again with the patient. This helps to further link (for both patient and therapist) rehabilitation activities with goals related to functioning at home safely. Linking actions to patient goals helps move patients into an action phase, in accordance with the Transtheoretical (Stages of Change) Model; similarly it increases intention according to the Theory of Planned Behavior. This explicit linking of therapy activities with the patient’s goals is novel; it is not done repeatedly and purposefully by any rehabilitation therapist, in our experience.
   c. To choose therapy activities, therapists “ask, don’t tell”: “What activity would you like to do next?” Non-directive interaction is consistent with Social Cognitive Therapy (increasing self-control), Self-Determination Theory, and the Transtheoretical Model (self-liberation). In post-pilot study interviews, the real-world therapists told us that this skill was one of the more novel (i.e., not part of their previous training or practice) and important features of EMR.
   d. Along the same lines, therapists check in with the patient after each activity or exercise: “How do you feel you did with those stairs?”…“It seems you weren’t happy with how you did; how can you make getting from the bed to the wheelchair easier or safer?”
   e. These interaction strategies are also used at a therapist meeting with the patient and caregiver(s).
f. Therapists are trained and supervised to use open-ended questions when appropriate, to avoid directive language in general, and to avoid the use of jargon. Points d-f help EMR therapists to increase their patient’s sense of self-control and perceived behavioral control, as well as maintain patient investment, and increase rapport.

2. Increased intensity
   a. Therapist guides patient towards higher-intensity activities:
      i. “Let’s start off with a challenging activity. Which one of those activities we just discussed would you like to try first?”
      ii. “How hard are you working?” (patient responds “4” on 1-10 scale, indicating that therapeutic exercise requires little effort) “We’d like to get you even stronger. What would it take to get you up to a 7 or 8 while doing this activity?”
   b. Exercises and activities are individualized to maximize effort (“Do you want to see how much farther down the hall you can walk?”), not of arbitrary length (“now walk 10 feet”).
   c. Therapists are trained and supervised to minimize down-time during therapy sessions. The focus on maximizing intensity is both novel and an advance over standard therapy in which the level of intensity is either arbitrary or at most is encouraged non-specifically. Increased intensity is also closely linked to the other EMR foci and their behavioral theory underpinnings. The 1-10 perceived effort scale, and feedback ensuing from it, is an innovation of EMR for rehabilitation settings. It is based on a scale developed for community-dwelling elders relative to exercise prescription.

3. Frequent feedback on effort and progress
   a. Therapist tells patient the benefits when therapeutic activity/exercise was hard: “How hard is this exercise?” (patient responds “9”, indicating that therapeutic exercise was very difficult) “I can see you are working hard, and your heart is beating fast. That means right now you are increasing your stamina…your endurance and your heart and lung capacity are getting better.”
   b. Therapist comments on progress when an activity becomes easier: “You rated your effort a 3 on this stair-climbing, and last week you rated it an 8. Can you see that you are getting stronger and closer to your goals?”
   c. Therapist links patient’s progress in activities to goal achievement: “Remember when you told me that you wanted to be able to walk your dog again? Well, today, you were able to walk 15 feet without much assistance. You’re closer to your goal.”
   d. Therapists use a progress binder to systematically review progress with patients in all activities, each Monday, Wednesday, and Friday after therapy, and link it to goal attainment.
   a-d above are consistent with the feedback focus of self-regulatory theory and also with social cognitive theory and the Transtheoretical Model in that they are intended to increase self-efficacy (or perceived behavioral control) and improve outcome expectations.
   e. Therapists are trained to understand and manage displays of affect by the patient. If a patient shows emotional distress, the therapist shows empathy, acknowledging the affect prior to continuing therapy. If a patient appears to the therapist as amotivated or disinterested, the therapist conceptualizes this as a temporary state (rather than an immutable trait) and tries to find a solution with the patient.
   f. Therapists are supervised regarding communication skills such as eye contact, speaking at the level of the patient, and avoiding jargon.
   e-f are critical interaction skills to improve rapport-building, and they underlie all other aspects of EMR. They require de novo training (in the case of managing affect) or retraining (in the case of basic communication skills because they are not reinforced to therapists in real world settings).

What EMR is not: (1) …psychotherapy, nor is it an attempt to convert PT/OTs into mental health specialists. In fact, therapists do not spend more time talking with patients in EMR than they do in standard-of-care therapy (but their speech is more precise and more engaging). (2) …marketed as a “mental health intervention.” EMR is a depression intervention but not “depression-only intervention,” as we observed benefits of EMR to a wide range of patients, suggesting that it could be universally applied.

EMR is designed to work in the real world. EMR was developed for real-world rehabilitation and thus overcame two challenges: First, skills must be used while the therapists are conducting their PT or OT, with frail patients in a hectic SNF environment. Therefore, (1) EMR focuses on easily teachable points that are in sync with PT/OT principles and can be carried out throughout therapy sessions automatically after sufficient practice. As a result, our manual (appended) has the simplicity of a prompt sheet, and uses structure and
langauge (e.g., “goal, plan, do, check”) familiar to PTs and OTs.\textsuperscript{38,39} (2) EMR’s feedback focus uses a measuring of effort (via a 0-10 scale), which fits well with OT and PT. (3) Our training and supervision (described in\textsuperscript{40}) focused heavily on repetition, using role-playing and feedback, which was a good fit for the SNF therapists. We also provided the same reinforcing feedback to the therapists (“Did you see how you gave your patient feedback on her progress, and she brightened up and became more motivated?”) as they were providing to patients. Anecdotally, it helped that therapists could easily tell that patients were more motivated.

Second, training, supervision, and treatment fidelity monitoring do not exist in rehabilitation research (as they do in psychotherapy research): in a systematic review of 100 recent trials of OT and/or PT, we found that few contained any mention of training or supervision, and none measured treatment fidelity using either external monitors or a validated scale.\textsuperscript{40} Therefore, we developed training and supervision methods to get therapists up to a high level of adherence and competence with EMR (included in the appended manual).\textsuperscript{40} There have been calls for OT and PT to use treatment fidelity methodology,\textsuperscript{41-43} suggesting that the rehabilitation sector is ripe for this methodological innovation that has been so important in advancing psychotherapy research.\textsuperscript{44,45}

We trained and supervised four therapists (2 OT, 2 PT) and we monitored their fidelity to the EMR model. In a case series, we found excellent functional recovery and reduction of depressive symptoms with EMR.\textsuperscript{46} Then, we carried out a pilot RCT,\textsuperscript{47} randomizing 26 participants to EMR by the trained therapists or standard of care rehabilitation by non-trained therapists. Only 6 eligible persons refused to participate. The sample was 74\% female and ethnically diverse: 48\% Caucasian, 48\% African-American, 4\% Asian. This was an older group (mean 77yr) with considerable medical comorbidity and disability; often participants had 8 or more medical comorbidities, were cognitively impaired, and/or had significantly elevated depressive symptoms.

**Pilot RCT Results part 1: Good treatment fidelity and differentiation from standard of care.** These data collected by external raters in a random sample of EMR and standard-of-care sessions, demonstrate that our training and supervision achieved the two features of good treatment fidelity in treatment research:\textsuperscript{45} high treatment integrity (high adherence and competence scores in the EMR-trained therapists) and high treatment differentiation (adherence and competence scores in EMR are easily contrasted from non-trained therapists, p<0.001 for all comparisons).\textsuperscript{40} Our assessment of treatment fidelity takes a “more is better” approach with respect to many EMR principles: therapists are graded during each monitored therapy session not just whether they carried out a certain EMR principle (e.g., “commented on effort”) but how often they did so, and how many chances they missed to do so. These large differences in adherence and competence scores between EMR and standard of care therapy demonstrate that the EMR training and supervision produces a substantially different and novel skillset, not simply a quality improvement.

**OT/PT therapists’ adherence and competence to the most commonly-used EMR foci:**

**Adherence:**

<table>
<thead>
<tr>
<th>Metric</th>
<th>Standard of Care</th>
<th>EMR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Related progress in activities to goal achievement</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Asked for patient feedback</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>Asked about effort level</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Tailored activities to patients home environment</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Clarified the relationship of activity to patient goals</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Guided patient towards higher-intensity activities</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Patient helped decide what activities to perform</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Patient decided which goal to work on</td>
<td>1</td>
<td>4</td>
</tr>
</tbody>
</table>

**Competence:**

<table>
<thead>
<tr>
<th>Metric</th>
<th>Standard of Care</th>
<th>EMR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feedback on Effort and Progress</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Interactive patient-directed approach</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>High Intensity</td>
<td>3</td>
<td>9</td>
</tr>
</tbody>
</table>

Also informative were the OT/PT therapists’ reactions.\textsuperscript{48} They reported high satisfaction with it. They commented “The supervision greatly helped me”; “I gained skills that I can use with all of my patients”, and simply “This has made me a better therapist.” This feedback speaks well to the sustainability of EMR. Our demonstration that PT/OT therapists could carry out protocolized treatment with high treatment fidelity, is the first in the rehabilitation field. More work in this direction – adapting both theories and methods of mental health research – could significantly advance all of rehabilitation treatment research.
Pilot RCT Results part 2: The mechanism of EMR is “high intensity, high engagement”

The mechanism of EMR is increased engagement and increased intensity in therapy sessions; both constructs are considered critical in the rehabilitation sector, yet surprisingly little research has advanced their measurement. Therefore we developed and tested measures for intensity and engagement.

**Intensity:** We developed two complementary methods to measure rehabilitation intensity: first, a rating of Patient Active Time; i.e., the amount of time during a PT/OT session in which patients were observed actively doing a therapeutic activity (e.g., walking or practicing an ADL) as opposed to sitting and doing nothing (resting or listening). Interrater reliability of this rating was excellent (ICC >0.9 for both PT and OT). Second, we used actigraphs on the patient’s 4 extremities to measure all movements during the therapy session (expressed as total activity counts, or activity counts per minute). As the figures below show, EMR sessions markedly outpaced standard-of-care sessions (by 2-3 fold) in both of these novel measures of therapy intensity.

EMR PT/OT therapy sessions are high-intensity as measured by per-session:

**Engagement:** We used the Rehabilitation Participation Scale, which measures patient participation in each therapy session using a 1-6 scale; a score of 5-6 demonstrates active engagement in the therapy session, i.e., showing interest in and intentional effort to work towards rehabilitation goals. EMR participation scores were higher, indicating more active engagement by patients. In contrast, scores from the Working Alliance Inventory (WAI) are similar (and high) in both EMR and SOC. The WAI examines non-specific therapist variables and may therefore be a technique-independent predictor of positive rehabilitation outcomes (as it predicts psychotherapy outcomes). Thus, these data indicate that the differences seen are specifically related to higher therapy engagement in EMR, not non-specific factors (such as liking the therapist).

Non-specific vs. Engagement-specific processes in EMR vs. Standard of Care (SOC) therapy
Pilot RCT Results part 3: EMR results in superior functional and affective outcomes

These figures show change in functional and performance outcome measures from baseline to discharge. EMR outpaced standard of care therapy in each.

Barthel Index (ADLs/mobility)  
Six-minute walk  
Gait speed

Additionally, among those with high baseline depressive symptoms, EMR resulted in greater improvement in negative affect: a mean reduction of 5.6 points, vs 2.2 points in SOC rehabilitation (scale’s range was 8-40).

Pilot RCT Results part 4: The relative benefits of EMR may be greatest in patients with depression, cognitive impairment, and multiple medical comorbidities.

We developed EMR because these common comorbidities often undermine successful rehabilitation, so we examined them as moderator variables. When we dichotomized the sample based on present/absent cognitive impairment, high/low medical complexity (number of medical conditions), or high/low depressive symptoms at baseline, in each case we found trends for greater relative recovery in EMR compared to SOC among those with higher impairments (see figure below). This appeared to be because SOC did not work as well (lower functional recovery in those with these comorbidities) while EMR did work as well (similar functional recovery with or without these comorbidities). These results, while very preliminary, suggest that EMR overcomes barriers to successful rehabilitation in the most vulnerable patient groups.

In summary:

- This pilot RCT showed promising results.
- We randomized 26 individuals over one year and attrition was <5%.
- Real-world therapists showed good treatment fidelity with our novel methods for training, supervision, and fidelity monitoring.
- EMR-randomized participants had much higher therapy intensity and engagement, as measured by our novel methods.
- EMR-randomized participants had better functional recovery.
- Among those with depression, EMR-randomized participants had more reduction in negative affect.
- Participants with depression, cognitive impairment, or high medical complexity had the best results with EMR relative to SOC.
Approach: Research Design and Methods

Summary of Study:

N = 252 participants
- Age 65+
- Admitted to skilled nursing facility (SNF) for post-acute care rehabilitation ≥2 weeks
- 50% with SCID-diagnosed depression

Enhanced Medical Rehabilitation during SNF stay (n = 126)

Standard of Care Rehabilitation during SNF stay (n = 126)

180-day follow-up

Baseline (day 0 of rehabilitation)
Function: Barthel Index (H1a)
Depression: Cornell Scale for Depression in Dementia (H1b)
Secondary measures: Gait speed, 6-minute walk, positive and negative affect
Short blessed test

Repeat (day 21: primary endpoint)
Function: Barthel Index (H1a)
Depression: Cornell Scale (H1b)
Secondary: Gait speed, 6-minute walk, positive and negative affect

Same assessments as above plus Rehospitalizations and disposition (e.g., home, institutionalization)

Summary of study design decisions:
Our trial has features of an explanatory (efficacy) trial, because it must test the benefits of EMR, and a pragmatic (effectiveness) trial, because of the real-world setting. The table below summarizes our design decisions using the Pragmatic-explanatory continuum indicator summary, a format showing what extent a study is pragmatic vs. explanatory (as most trials have features of both).

<table>
<thead>
<tr>
<th>Enhanced Medical Rehabilitation R01</th>
<th>Pragmatic-explanatory continuum rating</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Summary of design decisions:</strong></td>
<td>Explanatory--------------------------Pragmatic</td>
</tr>
<tr>
<td><strong>Participant eligibility:</strong> Recruit from real-world sites, include all impairment groups likely to benefit, few exclusions.</td>
<td>---------------------------------------X--</td>
</tr>
<tr>
<td><strong>EMR intervention flexibility:</strong> Instructions for each component of EMR, with supervision/training to achieve high fidelity.</td>
<td>----X-----------------------------------</td>
</tr>
<tr>
<td><strong>EMR therapist expertise:</strong> OT/PTs and OT/PT assistants from real-world post-acute care site.</td>
<td>-----------------------------X-----</td>
</tr>
<tr>
<td><strong>Control group:</strong> standard-of-care rehabilitation, with no explicit instructions (but all control participants definitely get therapy).</td>
<td>-----------------------------X-----</td>
</tr>
<tr>
<td><strong>Control therapist expertise:</strong> Same as EMR therapist expertise, matched to EMR group in expertise level.</td>
<td>-----------------------------X-----</td>
</tr>
<tr>
<td><strong>Follow-up intensity:</strong> involves participant, but with minimal number/burden of assessments.</td>
<td>---------------------------------------X--</td>
</tr>
<tr>
<td><strong>Primary trial outcome:</strong> clinically meaningful measures of function and affect, brief and very low-burden to patients.</td>
<td>---------------------------------------X--</td>
</tr>
<tr>
<td><strong>Participant compliance:</strong> All levels of adherence are allowed.</td>
<td>-----------------------------X-----</td>
</tr>
<tr>
<td><strong>Practitioner adherence:</strong> EMR therapists must maintain adequate treatment fidelity. Fidelity monitored in all.</td>
<td>--X-----------------------------------</td>
</tr>
<tr>
<td><strong>Analysis of primary outcome:</strong> all randomized (“Intent-to-treat”).</td>
<td>-----------------------------X-----</td>
</tr>
</tbody>
</table>

Site: We will collaborate with Delmar Gardens Nursing and Rehabilitation Inc., a leading provider of post-acute rehabilitation in the St. Louis area (a letter of support from the Vice President of Delmar Gardens is appended). We will recruit patients upon their admission to two facilities within the Delmar Gardens system, chosen based on proximity and positive feedback regarding the project from the rehabilitation team leaders at those facilities. At each facility, we will train and supervise at least six therapists in EMR; the remainder will be SOC therapists. The two facilities are the same in their models of care and length of stay (average 17-21 days) and are staffed
by salaried (rather than contracted) physical and occupational therapists. The two facilities have an average of 780 Medicare admissions per year in 107 available Medicare Certified Beds, with an average census of 45 Medicare patients, the vast majority of whom are aged 65+. Few to none are expected to have such severe cognitive impairment or medical exclusions (e.g., hospice) that would exclude them from the study – these patients are common in SNFs in general but rare in SNF post-acute rehabilitation. Based on these data, 250-450 study-eligible patients (based on age and expected length of stay) are anticipated to be admitted per year. This is more than sufficient for our recruitment needs. The two facilities differ in racial/SES make-up, with an expected 55-60% African-American, predominantly low SES population at the larger facility (2/3rds of eligible patients) and 5-10% African-American, predominantly higher SES population at the smaller facility. This variability will improve the study’s generalizability. Additional facilities are available in the system if needed.

Key inclusion/exclusion criteria: Inclusion: Aged 65+ admitted to the SNF for post-acute care PT and OT (≥2 week stay); 50% will have a current depressive disorder diagnosis (major or minor depressive episode) as diagnosed by the Structured Clinical Interview for DSM-IV (SCID). Exclusions: medical illness preventing study participation or accurate data collection (e.g., highly unstable cardiac illness such that early re-hospitalization is expected; metastatic or other cancer such that hospice is recommended or survival is limited; progressive neurological condition such that recovery of function is not feasible.

Justifications for inclusion/exclusion criteria: (1) We include a wide spectrum of disablement (not restricting to stroke or hip fracture, for example) based on epidemiologic findings and our pilot study observations that a typical older adult is admitted with multiple sources of disability, and it allows findings to be generalizable to a sector of care, not a specific medical illness. (2) A focus on depression has the highest public health impact – major/minor depression was by far the most common diagnosable mental health issue in our pilot (25% of participants). We will enrich for depression (50%) so that we will have a sufficient sample to examine EMR’s antidepressant effectiveness; but we will include 50% without a depression diagnosis. Our rationale is that EMR is a depression intervention, but not a “depression-only” intervention, as our pilot study suggested it may be effective for a range of patients (e.g., those with cognitive impairments, multiple medical comorbidities). If EMR is seen by the rehabilitation community as a rehabilitation practice for the post-acute sector (rather than a “mental health treatment for depression”), it is likely to have more reach and more likely to be implemented. (3) the exclusion of progressive neurological illness excludes those unlikely to benefit from post-acute rehabilitation but won’t exclude individuals with cognitive impairment, including mild dementia.

Randomization: We will randomize 1:1 to EMR (i.e., all OT/PT sessions done by EMR-trained and supervised therapists) or SOC (i.e., all sessions done by non-EMR-trained therapists), as in our pilot RCT. We will stratify by SNF site and by baseline depression status. To prevent subversion of randomization, the statistician will hold the randomization list, releasing an assignment once a participant is consented and eligible.

EMR group: The EMR group will be the same as in our pilot study; participants who are randomized to the EMR group will receive therapy only from therapists who are trained and supervised in EMR. Their therapy sessions will follow the EMR protocol. Otherwise their SNF care will not differ from usual care.

SOC group: The standard-of-care (SOC) group will receive therapy only from PT/OTs (or assistants) who are not trained nor supervised in EMR. These therapists are monitored (videotaped or observed) but not asked to do anything differently with their patients. This SOC control is different than a typical usual-care control. We determined that this control group was more feasible than an experimental control (e.g., in which participants would be randomized to specific treatment), because post-acute care PT and OT is personalized to the patient.

Two methodological concerns: first, do study observations change SOC therapy? Second, is there risk of contamination to the SOC? We observed closely for these effects in our pilot RCT and found little evidence of either. SOC was good therapy – higher in intensity and functional outcome than reports in the literature, similar levels of engagement as in good-quality inpatient rehabilitation facilities, and high therapeutic alliance. But there was no trend towards increasing intensity, engagement, or adherence/competence with any EMR foci in the SOC group; they remained far lower than EMR throughout the RCT. We conclude that SOC is a valid control group for EMR. Though in the pilot study the observation process or nearby EMR had no effect on SOC, our plans for potential contamination in this project are “prevent, monitor, mitigate”: prevent by ensuring with training and supervision that EMR therapists know not to talk about their training or technique, and that SNF leadership keeps therapists separated (not putting EMR and SOC therapists on the same team); monitor using fidelity measurement to make sure the SOC therapists don’t start using EMR techniques (it would be obvious on such observation if they did); mitigate if contamination occurs: remove “contaminated” SOC therapists from the SOC pool, and if large-scale contamination occurs, stop recruiting at that facility.
### Schedule of assessments

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>SNF admit (baseline)</th>
<th>Day 21 (primary endpoint)</th>
<th>SNF discharge</th>
<th>Day 60</th>
<th>Day 90 and 180</th>
</tr>
</thead>
<tbody>
<tr>
<td>Function</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Barthel Index (primary outcome)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gait speed</td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>6-minute walk</td>
<td></td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression (measured as outcome if current depression diagnosis)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Cornell Scale for Depression in Dementia (primary outcome)</td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>positive and negative affect scale</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Processes</td>
<td>Patient active time &amp; actigraphy (at each session)</td>
<td>collected each session throughout stay</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment engagement</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rehabilitation Participation Scale (at each session)</td>
<td></td>
<td>collected each session throughout stay</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Fidelity data (at each session)</td>
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<td>collected each session throughout stay</td>
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<td></td>
<td></td>
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<tr>
<td>Other rehabilitation variables</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rehospitalization</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Disposition (home, long-term care)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Outcome:** Consistent with the common conceptual model of EMR improving affective and functional recovery, this project has two co-primary outcomes, one of functional recovery, and one of affective recovery. Our primary measure of functional outcome is the Barthel Index, a 0-100 scale that measures ability (time and physical assistance required) to perform 10 basic Activities of Daily Living or mobility items making it optimal for this highly debilitated population. The Barthel Index has excellent external validity: a higher score predicts greater likelihood of being able to live at home and degree of independence following discharge from the hospital. Secondary measures are gait speed (time to walk 6 meters, in meters/second) and 6 minute walk (number of feet walked in 6 minutes). These performance-based measures of physical function have found increasing favor as outcome measures in rehabilitation intervention studies, because of their strong external validity in predicting clinical outcomes such as hospitalization and mortality.

The primary measure of change in depression is the Cornell Scale for Depression in Dementia. The Cornell scale was created for older adults with cognitive and medical comorbidity and insight problems and has adequate psychometric properties (including sensitivity to change) in this population; we have used it in prior hip fracture studies. Our secondary measure is an 18-item positive and negative affect scale that measures positive and negative (depressed and anxious) affect. It measures the dominant dimensions of human emotional experience, which have important roles in both quality of life and as a predictor of success in geriatric rehabilitation. It is a combination of the full 10-item positive affect scale of the Positive and Negative Affect Schedule (PANAS), plus five items from the brief PANAS measuring negative affect and the three non-reverse coded items from a brief State Anxiety Scale derived from the State Trait Anxiety Inventory to measure negative (anxious) affect. This scale uses participants’ responses to questions (e.g., “how anxious do you feel at present”) to assess their current feeling or affective states. The PANAS has excellent reliability in post-acute rehabilitation, where it is considered valuable in capturing the range of mood and motivational issues in this setting. Our addition of specific anxiety items reflects the high rate of anxiety problems in post-acute rehabilitation. Additionally, this dimensional assessment of affect responds to calls by NIMH to use as outcomes dimensions that reflect more basic, validated emotional or behavioral states, as reflected in the Research Domain Criteria. These depression/affect measures will only be carried out in participants with a baseline clinical diagnosis of current major or minor depressive episode, based on the Structured Clinical Interview for DSM-IV (SCID) which we will carry out at baseline prior to randomization. We have considerable experience with the SCID in this population from prior NIMH-funded studies. Based on our pilot RCT experience, about 25% of eligible participants will have a current diagnosis; we will enrich the sample by continuing to recruit to ensure that 50% of randomized participants have a depression diagnosis, so that this study is adequately informative regarding benefits for late-life depression in this setting. Our test-retest Kappa (using different, blinded raters) for major/minor depression in this setting is 0.8 (good).
The measures we have chosen have adequate psychometric characteristics in this setting and are minimally burdensome. We will monitor all of the assessment procedures closely during the RCT (inter-rater and test-retest), and if reliability of any measure falls below ICC=.8 (or Kappa 0.7) we will re-train research staff.

Our primary endpoint measurement will be 21 days post-randomization (or upon dropout in the unlikely event that a participant elects to drop out of the study prior to day 21). We will gather all outcomes at additional timepoints up to 180 days, to examine durability of gains similar to psychotherapy clinical trials, as additional problems (e.g., medical/cognitive issues, low SES or loneliness) may impact outcomes.

Rehospitalization occurs in a substantial percentage (~20%) of post-acute rehabilitation patients. We will adhere to the intent to treat principle as in our pilot study, following all randomized participants. Two complications: (1) participants might be medically unstable (e.g., at day 21), in which case we would delay assessments until the participant is medically stable; (2) participants might not return to the same facility for rehabilitation, in which case we will continue to measure outcomes but will consider non-study rehabilitation as a covariate (this is unlikely to be the case by day 21, which is our primary endpoint). Outcomes will be gathered by raters blinded to intervention group, as we did during our pilot RCT.

Processes and fidelity: EMR therapists once trained will have all sessions taped (or directly observed by research staff) and assessed using our validated treatment fidelity scale (appended). Once EMR-trained therapists demonstrate adequate treatment integrity (expected to take approximately 1 month of project time, based on our pilot RCT experience), the RCT will begin. Then, 20% of EMR and SOC sessions chosen at random will be observed by an external (blinded) monitor, consultant Mary Hildebrand, OTD. One change from the pilot RCT is that we will also monitor treatment fidelity in all therapists PRIOR to training in EMR. This will allow us to ensure that EMR-trained therapists are equated to SOC therapists in treatment quality and experience and thus provide further evidence that any results showing superior in outcomes in the EMR group will be attributable to the EMR (rather than a therapist effect).

Rehabilitation intensity: We will use the same methods as in our pilot study to measure each EMR and SOC therapy session: (1) Patient active time: total time in minutes that the patient is observed doing a therapy activity or exercise (as opposed to sitting), measured by research staff. In our pilot study, we developed a protocol for this measurement and were able to measure it with excellent interrater reliability (ICC >.9). (2) Mini-accelerometers on all four (patient) limbs will measure total activity counts (via actigraphy).

Treatment engagement: We will use the Rehabilitation Participation Scale during each EMR and SOC therapy session, as in our pilot study. Research staff will rate the patient’s participation on the 1-6 scale, in which higher scores (5-6) demonstrate active patient engagement for a given therapy session.

Burden? The above process measures (fidelity, intensity, engagement) are intensive and time-consuming – for the research staff, but not for the patients. In our pilot study, no patients had concerns about videotaping or wearing accelerometers, and no one refused or dropped out of the study related to this measurement.

Other rehabilitation variables: We will collect data on rehospitalizations (dates, causes) and disposition (home, institutionalization), as these are key outcomes of interest to the post-acute care field (i.e., how quality of post-acute care is measured). We acknowledge limited power for these given their categorical nature; yet, if EMR benefits functional outcomes, these downstream outcomes ought to be influenced as well.

Clinical measures and confounds: (1) We will collect detailed information on medical illnesses (summarized using the Cumulative Illness Rating Scale for Geriatrics) and medication use including psychotropic use and any changes made during the study. (2) We will measure cognitive status at baseline with the Short Blessed Test. (3) We will measure SNF length of stay. (4) We will measure non-technique specific therapeutic interaction via the Working Alliance Inventory at day 8 and 15, as we did in the pilot study.

Data analysis: In this section, we describe first, the management and statistical testing of our hypotheses and second, a conceptual summary of our potential findings and their implications.

David Dixon, Ph.D., Statistical Data Analyst, has over 35 years of experience designing and conducting statistical analyses for research projects. Dr. Dixon has authored over 30 professional papers, with biostatistics research contributions in psychiatry, social work, orthopedics, pediatrics, cardiology, and surgery. His expertise includes sample design, randomization, statistical consultation, statistical input on grant and paper submissions, and conducting statistical analyses (see biosketch).
Data management and analysis, general: Data will be managed at Washington University by Peter Doré, M.A., who will customize databases for the study. Data will be stored in Microsoft Access databases. Two databases will be used: one for subject tracking and one for research data. Data analysis will be led by Dr. Dixon using SAS and Mplus. The continuous demographic and clinical variables at baseline will be compared between the EMR group and the SOC group using the Two Independent Sample t Test or the Wilcoxon Two Sample Test, whichever is appropriate. Baseline categorical variables (e.g., race) will be compared between the groups using either the Chi Square Test or Fisher’s Exact Test, whichever is appropriate. We will examine data descriptively using crosstabulations, histograms, and tests for normality (with corrective actions, data transformation or nonparametric alternatives, as needed). An analysis-appropriate technique will handle missing data.

Aim 1: Examine the effectiveness of EMR for improving functional and affective outcomes.

H1: EMR will improve functional and affective recovery to a greater extent than standard-of-care rehabilitation.

Our pre-specified primary outcome measures are:

a. Barthel Index to assess functional recovery.

b. Cornell Scale for Depression in Dementia (in those with depression) to assess affective recovery.

Explanation of H1: The purpose of H1 is to examine the effectiveness of EMR. If H1 is supported, this could establish EMR as the gold-standard practice for post-acute rehabilitation. Our primary analysis is the change from baseline to Day 21. This single primary endpoint allows for an effectiveness test that is not confounded by length of stay differences or post-discharge issues beyond the reach of EMR. Missing data are expected to be minimal and possibly non-existent for this analysis: the only missing observation in our pilot study was due to a subject whose rehabilitation was interrupted by a lengthy hospitalization due to a progressive neurological condition (Guillain-Barré syndrome) which would be an exclusion criterion for the proposed project. Time course analyses will be conducted to investigate the differences between pre and post outcome measures. These analyses will be used to ascertain whether there is a statistically significant difference in change over time between the EMR group and the SOC group, controlling for baseline values. Analyses of the outcome measures for normality will be carried out. Time course analysis techniques such as mixed effects models, t test of the differences, Wilcoxon test of the differences, or ANCOVA on the differences (using baseline value as the covariate) will then be conducted, depending on the normality tests. Our favored method for the primary analysis of baseline to day 21 (i.e., pre-post treatment) effects is the ANCOVA approach, comparing the EMR and standard-of-care groups in change scores, covarying for baseline scores. This approach is recommended as the superior and most well-powered approach for examining pre-post RCT data.91 Our tests of the pilot data agreed with this: the ANCOVA approach had as much or more statistical power than other approaches (t-test, Wilcoxon, mixed-effect model) for all outcomes.

Participants will be randomized within each facility (i.e., stratified by facility) and then receive a PT/OT therapist pair who either is or is not trained/supervised in EMR based on randomization assignment. Thus participants are nested within therapists and therapists are nested within facilities. This multi-stage nested (hierarchical) design structure introduces possible correlation of participant outcomes with therapist. Such classification effects (facility/therapist) will be analyzed using Proc Nested in SAS or with the multi-level modeling available in Mplus that deals with stratification, clustering, and weighting.

We will also examine all time points to Day 180, to provide a real-world estimate of EMR and improve power to detect important secondary outcomes such as rehospitalization and institutionalization. We acknowledge these data may become somewhat naturalistic in a rehabilitation population, given differences in length of stay, transfers to different facilities, and re-hospitalizations. Mixed effects models are the preferred method for these multiple-time-point analyses, especially as some missing data are to be expected post-discharge.92

Our sample size is based on 80% power to detect a Cohen’s d=0.4 effect size on the ANCOVA difference in treatments at day 21, based on a two-tailed p<0.025 (because two outcome measures are used). G*Power 3.1.2 was used for power calculations. A Cohen’s d=0.4 is between “small” (0.2) and “medium” (0.5) effect sizes. Effect sizes for function were in the “large” range, d=0.7-0.9, but we acknowledge that these observed effect sizes are qualified by the small sample size, and it makes most sense to be more cautious regarding likely effect sizes in a full-scale study, hence our choice to power at d=0.4. Such an effect size is clinically relevant for the functional outcomes.3 We will only examine affective recovery as an outcome for those who are “affectively impaired” to begin with; i.e., those with clinical depression at baseline; with this reduced N, we are powered at 80% for a d=0.54. This same power analysis would apply for any subgroup analysis of
depressed; i.e., if we wish to demonstrate that EMR is effective both in the case of clinical depression and in “non-depressed” older adults.

Secondary measures to assess function are gait speed and 6 minute walk; secondary measure to assess affect is the positive and negative affect scale (positive and negative affect are examined separately). We will also examine for any site differences.

Aim 2: Examine EMR’s ability to overcome patient-level barriers to successful rehabilitation.

H2: The effectiveness of EMR for functional recovery will be greatest in: (a) patients with clinical depression; (b) patients with high levels of medical comorbidity; (c) patients with cognitive impairment.

Explanation of H2: EMR was designed to overcome barriers to rehabilitation (for example, due to depression); therefore, the difference in functional recovery between EMR and SOC should be greater in the most vulnerable older adults. If H2 is supported, we will demonstrate that older adults with these common comorbidities benefit the most from high intensity, high engagement rehabilitation. If so, this would refute conventional wisdom in post-acute rehabilitation, codified in admission criteria for rehabilitation facilities, regarding the appropriate candidates for rehabilitation (as described in Significance).32

If H1 testing shows effectiveness of EMR for functional recovery, we will then test depression (SCID diagnosis, dichotomized as yes/no current depression), medical comorbidity (CIRS-G score, dichotomized by median split), and cognitive impairment (Short Blessed score, dichotomized by ≥10 vs. <10) as moderators.33-35 Starting with the ANCOVA from H1, we would test each clinical variable separately as a moderator by adding the moderator variable and treatment group x moderator interaction to the ANCOVA. The interaction will determine the “difference of differences”; e.g., whether the relative change in functional outcome of EMR compared to SOC is greater in the presence of clinical depression. Our sample size of 252 provides 80% power to detect a medium interaction effect size of f=0.26.

Additional analyses: 1. A goal of this study is to test additional endpoints recommended by stakeholders as key quality indicators: time to return home, and rehospitalization and institutionalization rates. Therefore, we will compare the two treatment groups on these variables using survival analyses out to day 180 (i.e., time to discharge home, time to rehospitalization, and time to institutionalization analyses).

2. Another goal of this study is to move post-acute rehabilitation from idiosyncratic96 therapy to a precision therapy in which therapists have an evidence base for determining level of intensity. To do so, we will use growth mixture modeling (GMM)97 to categorize participants based on their temporal patterns of rehabilitation intensity through day 21. GMM is a technique to classify individuals into patterns of change, or trajectories. To do so, we will fit GMMS with linear, quadratic, and cubic growth factors and piecewise models with 1-2 transition points using Mplus, version 5.1,98 Dr. Dixon has experience with this technique and program.99 We will then choose a parsimonious set of naturally-occurring latent trajectories that provides better fit than a single-class model and is clinically meaningful in predicting functional change.

“So what?” Four high-impact products of this grant if hypotheses are supported:

1. This will be the first step of demonstrating that EMR is an evidence-based intervention. Additional studies would replicate findings100 and examine cost-effectiveness. Then, implementation into post-acute and other sectors of rehabilitation would likely follow efforts underway in mental health101-105 as it would need training and supervision that is central to EMR. Washington University’s resources (see Resources section) will help in implementation efforts, should EMR be demonstrated effective. While, many barriers to implementation are anticipated,105 the move in post-acute rehabilitation towards performance-based payment (better functional recovery = more reimbursement) would be a major incentive for uptake of EMR. EMR’s impact would be great given the reach of medical rehabilitation – almost all of us need it at some point.

2. A demonstration that EMR works in patients with depression or cognitive impairment would challenge the conventional wisdom codified in rehabilitation guidelines that such individuals are poor candidates for more intensive post-acute rehabilitation.30,31 This could help eliminate a disparity in which the most vulnerable older adults actually receive less rehabilitation.32

3. Our methods to achieve and measure treatment fidelity, and measure intensity and engagement, will get uptake in PT/OT research if they are demonstrated to be robust in this study. This could accelerate evidence-based medicine in PT/OT (just as similar methodological advances did in psychotherapy research106).

4. Our examination of trajectories of rehabilitation intensity would be a first step towards an evidence-based personalization of post-acute rehabilitation. This is not only a goal of the NIMH,107 it is also described as “absolutely essential” for the post-acute rehabilitation sector.96