Elderly Trauma Medical Home

Principal Investigator's name and address
Ashley Meagher, MD, MPH
IU Department of Surgery

Sub-Investigators
Ben Zarzaur, MD, MPH

Malaz Boustani, MD, MPH, Richard M. Fairbanks Professor in Aging Research
Department of Internal Medicine
Indiana University School of Medicine

Sujuan Gao, PhD, Professor
Department of Biostatistics
Indiana University School of Medicine

Babar Khan, MD, MS, Assistant Professor
Department of Internal Medicine
Indiana University School of Medicine

Rita Sue Lasiter, PhD, RN, Associate Professor
UMKC School of Nursing and Health Studies

Dustin Douglas French, PhD, Assistant Professor
Department of Ophthalmology
Northwestern University

Table of Contents:

1.0 Background

Injury from motor vehicle crashes, falls, gunshot wounds, knife stab wounds, and natural or manmade disasters lead to over 2.5 million acute care hospitalizations every year. Older injured patients, those 50 and older, are particularly at risk for poor outcomes. Physical injury results in an early reduction in quality of life as measured by the Quality of Well Being Scale and the Short Form-36, when compared to population norms. Over the year following injury, quality of life improves for some, but, often does not return to the pre-injury baseline. There is a significant link between poor physical function and quality of life and the development of psychological symptoms. We are proposing a collaborative care intervention targeting non-neurologically injured survivors as a means of improving functional and psychological outcomes.

2.0 Rationale and Specific Aims

Every year, 1.4 million Americans over age 50 are hospitalized for severe injuries.[1] The majority of older injured patients have the potential for full recovery, yet studies have shown that the current fragmented American health care system is failing to optimally serve these injury survivors leading to residual functional disability and reduced quality of life for years after injury.[2,3] Disability after injury is expensive, with injuries accounting for over $83 billion in direct and indirect costs.[4] Timely and integrated rehabilitative services have the potential of reducing the personal and societal burden of disability after injury.

To address the current fragmented care, the Institute of Medicine and the Center for Medicare and Medicaid Services recommend implementing the **collaborative care model** within both primary care and specialty care settings.[5,6] The goal of such a model is to provide continuous, coordinated and personalized care to patients with a wide range of healthcare needs and to ensure that patients receive the right care in the right place at the right time. After injury, patients experience a diverse set of physical, psychological, and socioeconomic challenges that threaten their full functional recovery. Indiana University School of Medicine researchers have over 20 years of experience developing innovative and effective collaborative care models.[7-10] These models are integrated within primary care practices to address the complex biopsychosocial needs of frail elders with multiple chronic conditions and survivors of acute critical illnesses. Based on these successes, an Interdisciplinary team of clinical investigators at Indiana University revised the collaborative care model to meet the needs of **older injury survivors**. This Trauma specific collaborative care model is called the **Trauma Medical Home** (TMH). This proposal aims to conduct a randomized controlled trial to evaluate the efficacy of 6-month duration of TMH in improving the functional and psychological recovery of older injury survivors, enhancing their quality of life and reducing their acute health care utilization. The trial has the following *specific aims*:

Primary Objective: Evaluate the ability of the TMH intervention to improve the physical recovery of older injury survivors.

Primary hypothesis: In comparison to the older injury survivors randomized to usual care, those randomized to the TMH intervention will have the following at 6 and 12-month follow-ups:

- *Higher physical performance as measured by the short physical performance battery (SPPB);*
- *Higher scores on the Physical Component Summary (PCS) of the Medical Outcomes Study 36-time short form (SF-36).*

Secondary Objectives:

1: Evaluate the ability of the TMH intervention to improve the psychological recovery of older injury survivors.
Secondary hypothesis 1: In comparison to older injury survivors randomized to usual care, those who are randomized to the TMH intervention will have the following at 6 and 12-month follow-ups:

- *Lower mood and anxiety symptoms as measured by the Patient Health Questionnaire–9 (PHQ-9) and the Generalized Anxiety Disorder (GAD-7) scale;*
- *Higher scores on the Mental Component Summary (MCS) of the SF-36.*

2: Evaluate the ability of the TMH intervention to reduce health care cost of older injury survivors and evaluate the cost effectiveness of TMH.
Secondary hypothesis 2: In comparison to older injury survivors *randomized to usual care, those who are randomized to the TMH intervention will have the following at 6 and 12-month follow-ups:*

- *Lower emergency department and hospital related cost.*
- *Savings in healthcare utilization in the intervention arm that will offset the intervention costs.]*

Due to demographic shifts, changes in life expectancy and increased activity of older Americans – putting them at risk for injury – there is an urgent need to enhance the recovery care for older injury survivors. Trauma centers across the nation are in an extraordinary position to use the information generated from the proposed trial to intervene; so older injury survivors may enjoy the maximum level of functional ability and quality of life after injury.

3.0 Inclusion/Exclusion Criteria

Inclusion Criteria:

[1] English-speaking adult age 50 years and older;
[2] admitted to Methodist or Eskenazi hospitals;
[3] able to provide consent or has a legally authorized representative to provide consent;
[4] access to a telephone;
[5] and an injury severity score (ISS) of 9 or greater.

Exclusion Criteria:

[1] have a self-reported diagnosis of cancer with short life expectancy;
[2] have a history of dementing illnesses and other neurodegenerative disease such as Alzheimer disease, Parkinson disease, or vascular dementia;
[3] have a significant traumatic brain injury (defined as the presence of any intracranial blood on Computed Tomography scan of the head or best Glasgow Coma Scale Score of less than 13 at the time of study enrollment);
[4] have any spinal cord injury with persistent neurologic deficit at the time of study enrollment;
[5] are pregnant women (assessed by a urine pregnancy test);
[6] have a primary residence outside the state of Indiana;
[7] are incarcerated at the time of study enrollment;
[8] have an acute stroke upon admission or develop a stroke as a new event during the course of hospitalization;
[9] unable to complete study questionnaire due to severe hearing loss;
[10] recent history of alcohol or substance abuse;
[11] discharged to a permanent care facility;
[12] admitted with a burn affecting >10% total body surface area.

4.0 Enrollment/Randomization

Enrollment. A research coordinator (RC) will screen for eligible subjects each day using the trauma service census at each site. Eligible individuals (those who meet inclusion criteria and do not meet any exclusion criteria) will be approached prior hospital discharge for enrollment into the study. If an individual is interested in participating and discharged before enrollment could be completed, a RC may follow up with the individual and complete enrollment at their place of discharge.

The target population is 430 English-speaking adults age 50 years and older, admitted to Methodist or Eskenazi Hospitals.

5.0 Study Procedures

After obtaining approval from the local institutional Review Board (IRB) and the leadership of trauma services at each hospital, subjects or their legally authorized representative will be approached prior to hospital discharge for participation in the study. Patients may be consented after discharge if they expressed interest in the study at the hospital but were unable to complete the consent process at that time. After obtaining an informed consent, the Research Coordinator/Research Assistant (RC/RA) will complete the Initial Case Review (see below for description) and will obtain baseline measurements of physical function, depression and anxiety, and quality of life. The RC and RA will be

blinded to the treatment assignments, therefore, after consent and baseline measurements are made, subjects will be randomized by the Care Coordinator via a computer-generated stratified randomization scheme. This scheme will be used to assign consented patients to intervention or control groups within each of the three hospitals. *All subjects* will receive the interventions described in the usual care section below. Those randomized to the TMH intervention will *also* receive the collaborative care (TMH) intervention.

During the hospital stay, research coordinators/assistants will review the medical records and conduct screening to assess the eligibility criteria for potential subjects. Furthermore, blinded assessors will complete the baseline, and follow-up data collection at the subject's home. The data obtained from subjects will include self-report of demographics, health history, current medications, anxiety and mood symptoms, and quality of life questionnaire. The assessors will also be collecting information on cognitive and physical performance via objective tests. Finally, the assessors will conduct a medical record review to assess subject's chronic conditions (Charlson index), physiologic status (blood pressure, height, weight, heart rate), and severity of medical illness (APACHE index) as well as their injury severity (Injury Severity Score).

TMH Intervention:

The Initial Case Review: Patients randomized to the TMH intervention will receive the same intervention as described under Usual Care (See below) at the time of the Initial Care Review. A time will also be arranged for the First Home Visit – which is the beginning of the TMH intervention.

The First Home Visit: After completing a pre-home visit review, the CC will travel to the patient and conduct a face-to-face initial assessment. The Care Coordinator (CC) will conduct a physical, cognitive, and psychological assessment of the patient. The CC will also perform a social and community needs assessment for the patient and the informal caregiver and will reconcile all prescribed and over the counter medications. The CC will make note of all scheduled and recommended appointments with specialists, physical therapists and occupational therapists. The CC will use the Healthy Aging Brain Care Monitor (HABC-M) to monitor the cognitive, functional, and psychological symptoms of patient and caregiver stress and to trigger the utilization of specific treatment protocols. The CC will document the initial and the follow-up visits using a modified version of population health decision support software, called the eMR-TMH.

The Plan of Care Development: This phase is designed to facilitate the creation of an individualized care plan with an emphasis on coordinating services with the patient's primary care and specialty providers. This phase begins with the TMH CC's first home visit and concludes with the

second home visit. Using the information provided by the patient and the informal caregiver, the CC will collaborate with the remainder of the TMH team and the primary care provider to finalize the individualized care plan. Complex patients and patients with diseases that may benefit from specialty care may be recommended for specialty evaluation and co-management. If necessary, the patient will be referred for a more extensive cognitive and psychological evaluation at local mental health practices. The TMH CC, the TMH team members, and the patient's primary care provider would collaborate on this decision. Finally, the CC will schedule a second face-to-face home visit with the patient and the informal caregiver to occur within 1-2 weeks of the first home visit.

The Second Home Visit: During the second home visit, the CC will disclose and review the individualized recovery care plan with the patient and the informal caregiver. This process will include a) understanding the process of monitoring the patient's recovery progress; b) implementation of the appropriate care recovery protocols; c) distribution and explanation of the corresponding educational recovery handouts (patient and informal caregiver); and d) connection to in-home services and community resources as needed.

The 6-month Interaction Period: Follow-up includes a 6-month interaction period with the patients and/or their informal caregivers via face-to-face visit, phone contact, email, fax or mail. At the end of 6 months, the TMH team will transition the full care of every patient to his or her primary care physician. The minimum amount of contact during the intervention will be every two weeks. During these interactions, the TMH CC, will answer any questions generated from previous visits; collect patient and caregiver's feedback; review and reconcile medications and discuss adherence; review specialist and therapists appointment and adherence to care plans; have the patient and/or the informal caregiver complete the HABC Monitor to trigger the use of specific care recovery protocols (described below); and facilitate the informal caregiver's access to appropriate community resources. Throughout the duration of the follow-up phase, the TMH team will continue to work with the patients, their informal caregivers, and the patient's primary care providers and specialists to monitor, implement, and revise the individualized recovery care plan.

Usual Care:

The Initial Case Review: The Care Coordinator (CC) will conduct a medical record review of each eligible patient after consent is obtained. The CC will confirm eligibility criteria, obtain contact information for patient and his or her legally authorized representative, review hospital discharge and rehabilitation plan, identify the primary care physician responsible for the patient care, identify the residential location of the patient, compose and send a letter to the primary care provider that summarizes the

patient's injuries, new diagnosis, hospital course and discharge medications and dosages, and the plan for rehabilitation and post-injury care. Comorbid medical conditions and current treatments will also be determined. If the patient does not already have a primary care provider, the CC will work with the patient to identify a primary care provider. The patients will also receive education on communication skills; caregiver coping skills; and legal and financial advice. Patients randomized to usual care will receive no further interventions.

The Support Tools of the TMH

The TMH Care Protocols: Care protocols have already been developed by members of our interdisciplinary team of researchers and successfully utilized in previous studies. We have modified these evidence based care protocols to address the specific needs of the non-neurologically injured patient. Specifically, these protocols address: personal care, repetitive behavior, mobility, sleep disturbances, depression, agitation or aggression, delusions or hallucinations, the caregiver's physical health, driving safety, nutrition, and PTSD. The protocols also address medication adherence and compliance with physical therapy and occupational therapy recommendations. These protocols will be utilized as needed by the TMH team to address issues as they arise in the patient's recovery.

The TMH Population Health Decision Support Software*:* In order to efficiently deliver the various components of any collaborative care model, care-coordination decision support software must be developed. Using the software that was developed for the Healthy Aging Brain Center as a model, we have altered the software to meet the needs of the injured patients. This web-based care-coordination software includes the following functions: a) flexible and secure access to the platform from multiple locations and by various users; b) manual and web-based solutions to capture patient-centered symptoms such as cognitive, functional, and psychological symptoms; c) decision support to deliver personalized pharmacological and non-pharmacological care recovery protocols; d) tracking process of care coordination delivered by the care coordination team; e) monitoring patients' and informal caregivers' responses to care recovery protocols; f) monitoring population-based outcomes to guide the overall program performance; g) integration capacity with other informatics tools such as the local electronic medical record and regional health information exchange; and h) an easy interface to move data from the software to analyzable datasets. Each member of the TMH team will have access to this software via an electronic device with wireless capability to accommodate the TMH office mobility.

The Healthy Aging Brain Care (HABC) Monitor: The TMH team will use the HABC Monitor (HABC-M) to monitor the cognitive, functional, and psychological symptoms of patients and caregiver stress. The HABC-M is a reliable and practical tool to monitor biopsychosocial needs of the patient or the informal caregiver. The HABC-M is 32 items tapping the previously mentioned four constructs. While the total HABC-M score is

helpful to measure change over time, each question also indicates a specific care area where help or coping strategies might be indicated. The HABC-M also includes questions on dangerous behaviors such as falls, home safety and automobile driving.

The HABC-M is a process measurement tool that will guide the personalization of the TMH collaborative care protocols to the needs of the patient at any point in time during recovery. Our preliminary data indicate that recovery trajectories after non-neurologic injury are widely variable. When cognitive, functional, or psychological symptoms are identified, the TMH team can utilize the evidence based care protocols that our team has developed as a type of "drop down menu" of interventions that can be customized to the patient's particular needs at any point in time. Thus, the HABC-M is a part of a dynamic feedback loop that allows for adaptation and customization of the intervention in real time by the care coordinator. The TMH team will also work with the primary care clinician and other providers to communicate changes in the care plan and to begin initial pharmacological and non-pharmacological management if needed.

Data Collection.

All assessments will be completed in the participant's hospital room or home by trained RC. Frequency, timing of contacts and the intervention offered in the group receiving TMH will be tracked using the HABC Trauma Medical Home software which offers quantitative measures of intervention intensity in the TMH group. All of the cognitive, physical, psychological, and quality of life outcome measures, with the exception of the Katz and Lawton ADL scales, will be assessed at baseline (hospital discharge or shortly thereafter, if consented after discharge), and at 6 and 12-month follow-up. If study team is unable to contact the subject by telephone to set up home visit at any point in the study, study assessments may be sent by mail with return postage-paid envelope.

Outcome Measures.

Short Physical Performance Battery (SPPB)

Physical recovery effects will be assessed via the SPPB, a validated objective assessment. The SPPB yields a performance score of 0-12; 0-4 poor, 5-7 intermediate, 8-12 is good. Based on previous studies in similar patient populations the expected scores on the SPPB are 6.0 (SD 2.5) (at baseline), 7.5 (SD 2.5) at 6-months, and 8 (SD 2.5) at 12 months. A difference of more than 1.3 would be considered clinically significant.

Self-reported quality of life outcomes

Non-neurologically injured patient's health–related quality of life will be assessed using the Medical Outcome Study Short Form (SF-36). This scale has eight components (physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health) that are aggregated into a Physical Component Summary (PCS) and a Mental Component Summary (MCS). Expected scores on the PCS of the SF-36 are 40 (SD 5) at baseline, 49 (SD 5) at 6-months,

and 51 (SD 5) at 12-months. A difference of more than 2 would be considered clinically significant. Functional status prior to admission and 12 months after enrollment will be assessed using the Activities of Daily Living (Katz scale) and Instrumental Activities of Daily Living (Lawton Scale).

Self-reported Mood and Anxiety symptoms

We will use the Patient Health Questionnaire–9 (PHQ-9) and Generalized Anxiety Disorder Scale (GAD-7) to determine the impact of the intervention on non-neurologically injured patient's mood and anxiety. The PHQ-9 is a nine-item depression scale with a total score from 0 to 27 and the GAD-7 is a seven-item anxiety scale with a total score from 0 to 21. Both of these scales are derived from the Patient Health Questionnaire, have good internal consistency, and test–retest reliability as well as convergent, construct, criterion, procedural and factorial validity for the diagnosis of major depression and general anxiety disorder.[54,57]

Acute Health Care Utilization (Secondary Objective).

In addition to patient reported emergency department and hospital admission data, we will use the local data-warehouse of IUH and IUH Physician Group to capture all of the data needed to determine utilization. The IUH and IUH Physicians Group data warehouse includes detailed administrative, billing and hospital records of all patients seen within the IUH system. The IUH system has nearly 60% market share in the state of Indiana, so, using this database will likely capture the majority of healthcare encounters. Furthermore, we will also use the data from the Indiana Network for Patient Care (INPC) to compliment any data use outside of IUH system. INPC is the primary health information exchange in the state of Indiana and it provides data for acute care services from all of the health care systems within the state of Indiana. We will determine the number of emergency department visits and the number of rehospitalizations within 6 months of discharge as well as the diagnoses associated with each utilization episode. Based on previously published data we expect the cumulative readmission proportions at 30 days, 3 months, 6 months, and 12 months will be around 6%, 11%, 15%, and 20% respectively. We would expect the emergency department visits to be approximately 3-5% higher at each time point.

Other data collection.

At hospital discharge and baseline we will measure the subject's age, race, gender, years of education completed, visual acuity, height, weight, body mass index, heart rate, blood pressure, and Charlson Comorbidity Index. We will also establish a linkage to the trauma registries maintained at both Level I trauma centers. The trauma registries contain detailed, demographic, physiologic, injury type, injury location, injury severity, treatment and complication information. These measures will be used to describe the non-neurologically injured patient characteristics and as potential confounders. We will also utilize findings from previous studies in similar patient populations to act as historical, usual care controls. These data have been gathered as part of previous IRB approved studies or are published in the literature already.

Sources of Materials**:** During the hospital stay, RC will review the medical records and conduct screening to assess the eligibility criteria for potential subjects. Furthermore, assessors will complete the baseline, and follow-up data collection at the subject's home. The data obtained from subjects will include self-report of demographics, health history, current medications, anxiety and mood symptoms, and quality of life questionnaire. The assessors will also be collecting information on cognitive and physical performance via objective tests. Finally, the assessors will also conduct a medical record review to assess subject's chronic conditions (Charlson index), physiologic status (blood pressure, height, weight, heart rate), and severity of medical illness (APACHE index) as well as their injury severity (Injury Severity Score).

6.0 Reporting of Adverse Events or Unanticipated Problems involving Risk to Participants or Others

Potential Risks:

(1) *Fatigue, anxiety, stress, or embarrassment from the testing sessions.* Emotional distress may result from answering health and behavior questions. Testing may also create anxiety, stress, or embarrassment at perceived performance. Participants may also become fatigued during the testing sessions. Screening instruments for the presence of substance abuse, depression and significant anxiety will be used during this study. It is possible that subjects could feel embarrassed by these questions.

(2) *Falls and/or muscle stiffness and soreness from the physical assessment*. Based on piloting and published studies, the most likely adverse events risk is a fall, and mild muscle stiffness and soreness associated with increased exercise. Moderate-intensity physical activities are associated with a very low risk of musculoskeletal complications.

(3) *Exposure of confidential information.* There is the potential for loss of privacy or confidentiality due to the data collection efforts of this study.

Adequacy of Protection Against Risks.

Recruitment and Informed Consent**:** Eligible subjects will be identified through the intensive care units' census to which they are admitted. Study personnel will consent the patient or their legally authorized representative (if the patient is unable to consent for themselves).

Protections Against Risk**:**

(1) *Fatigue, anxiety, stress, or embarrassment from the testing sessions.* All questions planned for this study are part of validated standardized instruments, and we are not asking any questions that do not directly relate to the study purpose. Both Interventionists and Assessors will be trained in their proper use and in the importance of privacy and sensitivity to the participant's time. They will be trained to be alert and sensitive to signs of fatigue and other symptoms and to take appropriate actions when they are present. Breaks from testing will be offered as needed; assessment sessions can also be split into two sessions if a participant is tired or physically uncomfortable. Screening instruments for the presence of substance abuse, depression and significant anxiety will be used during this study. For persons who screen positive for any of these problems, we will make appropriate referrals for treatment based on our established referral patterns in our institution. We will follow-up with individuals who are referred for treatment to be sure that they have taken necessary steps to address their issue.

(2) *Falls and/or muscle stiffness and soreness from the physical assessment.* We have minimized the risk of a fall through and stiffness that may occur from the physical testing. We expect that any soreness that may occur during the testing will subside within a few days and be unlikely to occur again. Participants with persistent or very severe soreness will be encouraged to contact their primary care provider. In the ~2,000 in-home assessments that we have done in the similar studies which have extensive physical exam protocols, we have not had a single fall or other adverse event. We attribute this to our very careful training and supervision procedures, which we will also be using in the proposed trial. We will have an emergency plan in place to handle any emergencies that might occur.

(3) *Exposure of confidential information.* Indiana University requires certification of training in protection of human subjects in research. The investigators, interventionists, assessors, and all key personnel have or will have successfully completed training and certification in these courses. All research involving the use of these data must be reviewed and approved by the IRB. We will assure the privacy of subjects and confidentiality of study data by assigning unique identifiers to track participants' data (rather than using names or hospital or social security numbers) and keep all records under lock with access only by study personnel. These procedures have been dutifully adhered to in prior studies. The final data files for this study will be merged, maintained, and analyzed on servers managed by the Division of Biostatistics, Department of Medicine, Indiana University School of Medicine. This group has extensive experience in the handling and security of PHI. None of the individual participant data will be identifiable in published reports or

manuscripts and the analyzable datasets will not contain the participant's unique identifier.

Definitions:

An **adverse event** (AE) is defined as any unintended or abnormal reaction or clinical condition that is not of benefit to the participant. Either the response/condition was not present prior to exposure to the study or participation has worsened the intensity or frequency of the response/condition. A **reportable adverse event** is any unintended or abnormal reaction or clinical condition in a subject that (1) places the subject at increased risk of harm **and** (2) was unexpected **and** (3) was related to the research procedures. Any breach of patient confidentiality is considered a reportable adverse event.

Unanticipated problems involving risks to subjects or others will be reported **promptly** to the IRB if they:

1. were unexpected (in terms of nature, severity, or frequency);
2. were related or possibly related to participation in the research; and
3. suggest that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized. [Note that such events routinely warrant consideration of substantive changes in the research protocol or informed consent process/document or other corrective actions in order to protect the safety, welfare, or rights of subjects or others.]

The timeline for reporting **promptly** to the IRB is within **5** working days of notification.

Submit reports to:

Indiana University Institutional Review Board on Prompt Report form via the KC-IRB system.

Events not meeting requirements for prompt reporting will be recorded in the study record and summarized at time of continuing review.

Data and Safety Monitoring Plan.

This trial will be monitored by the PI and a three-member Data Safety and Monitoring Board (DSMB).

a. Qualifications and responsibilities of the Safety Officer: The safety officer for this trial will be a physician researcher experienced in running intervention studies, and will have an understanding of the types and severity of injuries or complications as a result of a collaborative care intervention. The safety officer

will review the reports sent by the study manager and will determine whether there is any corrective action, trigger of an ad hoc review, or stopping rule violation that should be communicated to the study investigator, the DSMB, the IU IRB, and the NIH. In addition, the safety officer may comment on whether the study investigator needs to report any specific out of range data to the participant and/or her physician.

b. Qualifications of the DSMB: The safety officer will be joined by an expert trauma surgeon and a biostatistician. These persons will not be otherwise affiliated with the project. The three member DSMB panel will meet at 6-month intervals.

c. Monitoring and Reporting: The frequency of data review for this study differs according to the type of data and can be summarized in the following table:

The study coordinator and biostatistician will generate reports for PI, safety officer, and DSMB that will contain:

a) summary of adverse events and an explanation of how each event was handled;

b) summary of complaints and how each complaint was handled;

c) subject retention, including the number and reasons of participant withdrawals;

d) intervention compliance (session attendance); and

e) summary of protocol violations and how each was handled.

All reports will be submitted to IU IRB at time of continuing review.

d. Measurement and reporting of adverse events: Adverse event rates associated with a collaborative care intervention are low. Therefore, adverse event rates are expected to vary little between the treatment and control groups. We will present blinded adverse event data to the statistician and PI throughout the trial. We plan to present unblinded adverse events data to the safety officer throughout this trial and to the DSMB panel when requested by the safety officer and at bi-annual meetings. If there is evidence of elevated adverse events, the safety officer will consult with the statistician and PIs. An adverse event form will be used by the study staff to report injuries or other adverse events caused by the intervention.

Data Type	Frequency of Review		
	Each Occurrence	Q 6-mo	Annual
Subject accrual (adherence to inclusion/exclusion); drop-out rates; randomization		X	
Adverse event rates (injuries)	X	X	
Subject complaints		X	
Compliance to interventions		X	
Protocol violations/noncompliance	X	X	
Out of range data		X	
Risk-benefit ratio assessment			X
Stopping rules report			X

e. Possible Adverse Events: Adverse events will be monitored on an ongoing basis by the study manager. The PIs will be notified within 24 hours of any adverse events. Serious adverse events will be reported within 5 business days to IU IRB, Safety Officer, DSMB, and NIH. Non-serious adverse events will be reported at time of continuing review to IU IRB. In cases where there is any question regarding the level of AE or attributable cause, we will consult with the DSMB and safety officer.

Serious adverse events are defined as:

1) death, life threatening event, prolonged inpatient hospitalization, permanent disability, clinically significant lab exam or any deemed by the reporter to be medically serious.

f. Stopping Rules: It is unlikely that the study would be stopped early due to important favorable differences in the intervention group compared to control group because of the short term nature of the intervention. However, the study could be stopped early due to adverse events. Some events of particular concern would be a high number of study withdrawals due to discontent with the study procedures. The NIH will make the final decision on whether or not to accept the DSMB's recommendation about discontinuation of any component of the study. Interim analysis of the study is planned according to the O'Brien-Fleming alpha spending rule. The p-values are constructed to maintain the overall study power of 0.05, two-sided. If the test statistic exceeds the boundary, then the study could be considered for early termination due to emerging differences. The interim look is planned after enrollment and follow-up of 200 patients. The study can also be stopped if continuing is considered futile after the interim analysis. Further, if dropout rates remain high after an extreme alert (see below for description) the study can be stopped early.

g. Limits of Assumptions: It is possible that baseline differences between the groups, excessive study dropouts and/or missing data by the interim measurement time point (midway point to targeted enrollment) will limit the value of data analysis of measurements at the one year time point. Baseline differences will be evaluated after the first measurement time point and effects on the power to detect differences in the primary outcome will be evaluated and

communicated to the PI, DSMB, and NIH. Given the monitoring plans outlined elsewhere in this document, it is exceedingly unlikely that there will be baseline differences between groups of any magnitude to threaten the validity of the study.

Dropout rates higher than 40% would be of concern, so we propose to monitor the dropout rate quarterly. Alert points are set at dropout rates of 20% (low alert), 35% (mid-alert), 45% (high alert) and 55% (extreme alert). With early alerts to problems, action would be taken to avoid higher level alerts; if a higher level alert should arise, more drastic remedial action would be invoked.
The actions taken at each level of alert are given below:

- Mid-level alert = Conference call between study investigators to discuss approaches to minimize further losses to follow-up/dropouts.
- High-level alert = Conference call between investigators and DSMB to determine further alterations of study protocol to complete the study with no further losses.
- Extreme-level alert = In the unlikely event of a 55% dropout rate occurs prior to the 1-year measurement time point, study investigators, the DSMB members, and the NIH program official would convene on a conference call to discuss the usefulness of continuing the study.

7.0 Study Withdrawal/Discontinuation

This study is voluntary and participants have the right to withdraw at anytime. Participants must notify the Principal Investigator that they choose to withdraw from the study:

Ashley Meagher, MD, MPH
Indiana University Department of Surgery
Trauma and Emergency General Surgery
1730 N. Capitol Avenue, Suite B249
Indianapolis, IN 46202
(317) 962-9231

Participants who choose to withdraw will be informed that no new procedures will be performed after receiving their notice that they choose to withdraw from the study. Information that has been obtained up to that point will remain as part of the study.

8.0 Statistical Considerations

We will compare randomization results to a pre-planned randomization schedule to ensure randomization integrity. To verify the comparability of the randomized groups, patients' baseline characteristics between the intervention and the usual care group will be compared using analysis of covariance (ANCOVA) for continuous variables and the Cochran-Mantel-Hansel statistic for categorical variables while adjusting for recruitment

sites. We will examine the distributions of continuous variables and use alternative approaches such as transformation or nonparametric methods in cases of violation to the normal distribution assumption. We will also examine the frequency distribution of all categorical variables and adopt exact inference procedures in cases of zero or small cell size. All analyses will be conducted using SAS 9.4 (SAS Institute, Cary, North Carolina).

Obective 1: Evaluate the ability of the TMH intervention to improve the physical recovery of the non-neurologically injured patient. Mixed effects models will be used with repeated physical function scores (SPPB and PCS on the SF-36) collected at baseline, 6 months and 12 months as the outcome measures, group, time, and a group and time interaction as independent variables while adjusting for stratification variables (recruitment site, injury severity and injury type) and other potential baseline covariates that are found to be different between the two groups. An unstructured variance-covariance matrix will be used in the mixed effects models to adjust for the potential correlations among SPPB and PCS obtained from the same individual over time. A significant interaction between group and time would indicate differences in changes of physical functions over time between the two groups. Post-hoc comparisons at each follow-up time will be conducted following a significant interaction between group and time to determine the time when a group difference can be detected. Parameter estimation and inference for the mixed-effects models are conducted using the maximum likelihood approach which are robust under many missing data mechanisms.[72] We will also include additional covariates to examine whether patients' characteristics or prior medical comorbidities are associated with the changes in physical function scores.

Objective 2: Evaluate the ability of the TMH intervention to improve the psychological recovery of the non-neurologically injured patient. Mixed effects models will be used with repeated PHQ-9, GAD-7 or MCS on SF-36 scores as the outcome variables, group, time and interactions between group and time as independent variables while adjusting for stratification variables and other baseline covariates that may be different between the two groups, similar to the approach described for Aim 1. Post-hoc analyses will also be conducted following significant interactions in the mixed effects models to examine differences in psychological outcome measures between intervention and usual care groups at 6 and 12 months.

Objective 3: Evaluate the ability of the TMH intervention to reduce health cost and the TMH cost effectiveness relative to usual care of the non-neurologically injured patient. Economic Value and Costs. Time from enrollment to *emergency department visits and hospital readmissions* will be used as the outcome variables in Cox's proportional hazard models and group as the independent variable while adjusting for sites and other baseline covariates. Patients who are followed to 12 months without experiencing any event will have their event time censored at 12 months and patients who died or were lost to follow-up will have their observation time censored at time of death or date of last contact. The proportional hazard assumption will be examined by including the interaction between the group indicator variable and time.

We will conduct a cost effectiveness analysis to determine if changes in health care utilization offset the intervention costs between treatment arm and usual care. To conduct this analysis, we will use established methods to estimate direct costs of the interventions and health care spending from a Medicare payment perspective. The conceptual proposition begins with our proposed TMH intervention, which requires healthcare and non-healthcare resources for delivery (e.g., therapists or transportation) and caregiver assistance. The foregone economic opportunities and ability for

successful return to activities of daily living and participation can be assessed in combination with recovery time in dollar value. Changes in patients' health status, long-term mobility, and community participation will be assessed using the SF-36 tools for measuring physical functioning and utility.[73-76] Changes in health status and community participation are captured. The cost effectiveness ratio is practically measured as the increment in cost summary to the increment in the effect measure.

Multivariate regression models will be constructed to examine total healthcare costs in the 12-month post index period. To address issues of skewness and violations of normality assumptions, and medical comorbidities, a generalized linear model with a gamma distribution and a log-link function will be used. Estimated parameters will be obtained using the maximum likelihood technique,[77-81] and adjusted results will be presented with 95% confidence interval (CI) estimates. Finally, the incremental cost to achieve a clinically meaningful change in SF-36 scores due to the interventions, i.e., the cost-effectiveness (CE) ratio, is the difference in intervention costs of the treatment arms, divided by the difference in effectiveness between groups; or

$$CE\ ratio = \frac{TMH\ Intervention\ costs + delta(\ Health\ care\ and\ opportunity\ costs)}{delta\ SF-36\ (TMH) - delta\ SF-36\ \ (Usual\ Care)}$$

Sensitivity analysis of all key assumptions and bootstrapping will be conducted. All analyses were conducted with Statistical Analysis Software (SAS, Version 9.3, Cary, NC).[46]

Missing Data: Two types of missing data are anticipated in this trial: those due to lost to follow-up and those due to death. There may be a potential for higher rate of lost to follow-up in the usual care group than in the intervention group because of the frequent contacts between the research team and study participants in the TMH group. The mixed effects model approach we propose to use for data analysis is robust under the missing at random assumption, i.e. the probability of missing is unrelated to the missing outcomes. We will compare baseline characteristics of patients with missing outcomes to completers in order to detect potential violation to the missing at random assumption. Sensitivity analyses will be performed if the missing at random assumption is violated using various methods of imputation or a full parametric likelihood approach assuming various patterns of missing data. Intention to treat analysis will be used in all models.

Sample Size and Power: Based on previous studies,[21,82-84] we assume a mean baseline SPPB score of 6.0 (SD=2.5) in this patient population. A sample size of 150 patients in each group will yield 80% power to detect a change score of 0.81 using a two-sample *t*-test at α=0.05. Since we expect balanced outcomes at baseline due to the RCT design, projected effect size is also the effect of the interaction in the mixed effects models. To be conservative and allowing 30% patients missing the 12-month assessments, we will need to enroll and randomize 430 patients (215 per group). Our enrollment sample size will allow us to detect significant effect of 0.325 SD or larger with 80% power on the PCS of SF-36, PHQ-9, GAD-7, MCS of the SF-36 and log-transformed total healthcare cost. We present effect sizes and estimated power in the study and within each stratum in the following table.

Detectable effect sizes and estimated power in the overall sample and each stratum. Projected sample size (n=300) is the number completing 12 month of follow-up.

Overall (n=300)	Randomization Stratum			
	Severity ISS 10-15 (n=136)		Severity ISS ≥ 16 (n=164)	
Combined	Fall (n=68)	Other Injuries (n=68)	Fall (n=82)	Other Injuries (n=82)
0.33 (81%)	0.33 (27%)	0.33 (27%)	0.33 (32%)	0.33 (32%)
0.34 (84%)	0.50 (53%)	0.40 (37%)	0.30 (27%)	0.20 (15%)
0.66 (99%)	0.69 (80%)	0.69 (80%)	0.63 (80%)	0.63 (80%)

This study is not powered to detect significant treatment effect within each randomization stratum unless there are large effect sizes in each stratum. Instead, stratified randomization was used to control for potential heterogeneity in patient outcomes in order to detect a significant treatment effect in the overall sample. Since we will have access to the electronic medical records on all enrolled patients, for the analysis on acute care utilization, data on all 430 randomized patients will be retrieved to determine status and time to ER visits and re-hospitalization. We will have 80% power to detect odds ratio of 1.8 or greater for ER visits assuming cumulative event rate of 25% in the usual care group and 82% power to detect odds ratio of 1.9 or greater for re-hospitalization assuming cumulative event rate of 20% in the usual care group using Chi-squared test at the 0.05 significance level.

Potential Problems and Alternative Strategies.

While recruitment into clinical trials is a challenge, retention of subjects over a period of time presents its own difficulty. For clinical trials of the type proposed, the control condition faces the greatest challenge to retention. We plan to mitigate withdrawals from both groups through several mechanisms. First, the control condition offers tangible, concrete, and immediate benefits. Second, our quality control procedures allow us to monitor subjects' perceptions about the risks and benefits of participation. Occasionally new and fixable issues arise that, if addressed, can prevent the withdrawal of subjects. We also recognize that approximately 10% of our participants will be African-American, 40% will be women, many will be socioeconomically disadvantaged, some will have cognitive impairment, and many will have other chronic conditions and unique vulnerabilities. We recruit research personnel representative of the target population by gender and race and we seek to identify personnel who have life experiences in this community. All research staff will complete specific training in working with research populations representing vulnerable subjects, including those with cognitive impairment. We will periodically measure retention. If retention drops below 80%, we will have the study staff follow-up with the participant to troubleshoot issues and provide coaching. We will also institute gift card incentives and we will use fair subject payments contingent on the completion of the baseline, 6 months and 12 months follow-up assessments. Loss of information could occur if subjects are unable to complete outcome assessments. We have a "step-down" battery if a participant is not able to tolerate the full outcome assessments, which will allow us to estimate the treatment effect in key domains (SPPB and PHQ). We also can provide assistive devices (glasses, headphones or pocket talker) if a participant's visual or auditory acuity declines and interferes with interventions or outcome assessments. Finally, the proposed intervention has multiple components and the study is not designed to test which of these components is most important or which represents the active ingredient. We do not believe that one component can be singled out as more important than another and we fully anticipate that ever more complex interventions will be required to

deliver excellent care. Our research team's capacity to design, to deliver, and to measure outcomes for a multi-component intervention is one of our key strengths.

9.0 Privacy/Confidentiality Issues

All data gathering is done initially with each subject or their legally authorized representative in the hospital and then with each subject in their home by a trained assessor. Data will be linked to participants through the use of a unique identifying number. Only persons on the research team will have access to the data. All data are collected for research purposes only. Case Report Forms (CRFs) will be stored in locked filing cabinets in the Department of Surgery and all data will be entered into electronic case report forms (eCRFs) in a secured password-protected database. All study data will be entered via a password-protected, study specific REDCap (Research Electronic Data Capture) database website. REDCap was developed specifically around HIPAA-Security guidelines and has been disseminated for use locally at other institutions and currently supports > 140 academic/non-profit consortium partners and 11,000 research end-users (www.project-redcap.org).

10.0 Follow-up and Record Retention

Subjects will be followed for 12 months after injury. Study records will be maintained for a minimum of seven years per state HIPAA guidelines.

Bibliography and References Cited

1. WISQARS [database online]. Atlanta, GA: Centers for Disease Control National Center For Injury Prevention and Control. Available at: http://wisqars.cdc.gov:8080/costT/cost_Part1_Intro.jsp/. Accessed January 23, 2014.

2. Holbrook TL, Anderson JP, Sieber WJ, Browner D, Hoyt DB. Outcome after major trauma: 12-month and 18-month follow-up results from the Trauma Recovery Project. J Trauma. 1999 May;46(5):765-71.

3. Michaels AJ, Michaels CE, Moon CH, Smith JS, Zimmerman MA, Taheri PA, Peterson C. Posttraumatic stress disorder after injury: impact on general health outcome and early risk assessment. J Trauma. 1999;47:460-467.

4. Corso P, Finkelstein E, Miller T, Fiebelkorn I, Zaloshnja E. Incidence and lifetime costs of injuries in the United States. Injury Prevention 2006;12:212–218. PMCID: PMC2586784.

5. Committee on Quality of Health Care in America. Crossing the quality chasm: a new health system for the 21st century. Washington, DC: National Academy Press; 2001.

6. Unützer, Jürgen, Henry Harbin, and M. D. Druss. "The collaborative care model: An approach for integrating physical and mental health care in Medicaid health homes." *Center for Health Care Strategies and Mathematica Policy Research, May* (2013).

7. Callahan CM, Boustani M, Unverzagt FW, et al. Effectiveness of collaborative care for older adults with Alzheimer disease in primary care: a randomized controlled trial. *JAMA.* 2006 May 10;295(18):2148-57.

8. Boustani MA, Sachs GA, Alder CA, et al. Implementing innovative models of dementia care: The Healthy Aging Brain Center. *Aging Ment Health*. 2011 Jan;15(1):13-22, PMCID: PMC3077086.

9. Khan B, Boustani M. The Critical Care Recovery Center. Annual Meeting of the American Delirium Society. June 2-4 2013.

10. Khan BA, Zawahiri M, Campbell NL, et al. Delirium in hospitalized patients: implications of current evidence on clinical practice and future avenues for research -- a systematic evidence review. *J Hosp Med*. 2012 Sep 7;7(7):580-9, PMCID: PMC3640527.

11. Holbrook TL, Hoyt DB, Stein MB, et al. Perceived threat to life predicts posttraumatic stress disorder after major trauma: risk factors and functional outcome. J Trauma 2001;51:287.

12. Zatzick D. Posttraumatic stress, functional impairment, and service utilization after injury: a public health approach. Semin Clin Neuropsychiatry 2003;8:149.

13. Zatzick D, Jurkovich G, Russo J, et al. Posttraumatic distress, alcohol disorders, and recurrent trauma across level 1 trauma centers. J Trauma 2004;57:360.

14. Zatzick D, Jurkovich GJ, Gentilello LM, et al. Posttraumatic stress, problem drinking, and functional outcomes after injury. Arch Surg 2002;137:200.

15. Zatzick D, Kang SM, Muller HG, et al. Predicting posttraumatic distress in hospitalized trauma survivors with acute injuries. Am J Psychiatry 2002;159:941.

16. Soderstrom CA, Smith GS, Dischinger PC, et al. Psychoactive substance use disorders among seriously injured trauma center patients. J Am Med Assoc 1997;277:1769.

17. Gentilello LM, Rivara FP, Donovan DM, et al. Alcohol interventions in a trauma center as a means of reducing the risk of injury recurrence. Ann Surg. 1999 Oct;230(4):473-80.

18. Schermer CR, Moyers TB, Miller WR, Bloomfield LA. Trauma center brief interventions for alcohol disorders decrease subsequent driving under the influence arrests. J Trauma. 2006 Jan;60(1):29-34.

19. Michaels AJ, Michaels CE, Moon CH, et al. Posttraumatic stress disorder after injury: impact on general health outcome and early risk assessment. J Trauma 1999;47:460.

20. Zarzaur BL, Bell TM. Trajectory subtypes after injury and patient-centered outcomes. J Surg Res. 2016 May 1;202(1):103-10.

21. Zatzick D, Jurkovich GJ, Rivara FP, et al. A national US study of posttraumatic stress disorder, depression, and work and functional outcomes after hospitalization for traumatic injury. Ann Surg. 2008 Sep;248(3):429-37.

22. Sabin JA, Zatzick D, Jurkovich G, et al. Primary care utilization and detection of emotional distress after adolescent traumatic injury: identifying an unmet need. Pediatrics 2006;117:130.

23. Zatzick DF, Roy-Byrne P, Russo J, Rivara FP, Koike A, Jurkovich GJ, Katon W. Collaborative interventions for physically injured trauma survivors: a pilot randomized effectiveness trial. Gen Hosp Psychiatry. 2001;23:114-123.

24. Zatzick D1, Roy-Byrne P, Russo J, et al. A randomized effectiveness trial of stepped collaborative care for acutely injured trauma survivors. Arch Gen Psychiatry. 2004 May;61(5):498-506.

25. Ghaffar O, McCullagh S, Ouchterlony D, Feinstein A. Randomized treatment trial in mild traumatic brain injury. J Psychosom Res. 2006;61(2):153–160.

26. Wade DT, Crawford S, Wenden FJ, King N, Moss NE. Does routine follow up after head injury help? A randomised controlled trial. J Neurol Neurosurg Psychiatry. 1997;62(5):478–484, PMCID: PMC486856.

27. Wade DT, King NS, Wenden FJ, Crawford S, Caldwell FE. Routine follow up after head injury: a second randomised controlled trial. J Neurol Neurosurg Psychiatry. 1998;65(2):177–183, PMCID: PMC2170203.

28. Whiteneck GG1, Gassaway J, Dijkers MP, et al. Inpatient and postdischarge rehabilitation services provided in the first year after spinal cord injury: findings from the SCIRehab Study. Arch Phys Med Rehabil. 2011 Mar;92(3):361-8.

29. Dijkers MP. Quality of life after traumatic brain injury: a review of research approaches and findings. Arch Phys Med Rehabil. 2004;85:S21-S35.

30. McCarthy ML, MacKenzie EJ, Durbin DR, Aitken ME, Jaffe KM, Paidas CN, Slomine BS, Dorsch AM, Christensen JR, Ding R; Children's Health After Trauma Study Group. Health-related quality of life during the first year after traumatic brain injury. Arch Pediatr Adolesc Med 2006;160:252-260.

31. Wilson IB, Cleary PD. Linking clinical variables with health-related quality of life: A conceptual model of patient outcomes. JAMA. 1995 Jan 4;273(1):59-65.

32. Van Beeck EF, Larsen CF, Lyons RA, Meerding WJ, Mulder S, Essink-Bot ML. 2007. Guidelines for the conduction of follow-up studies measuring injury-related disability. J Trauma. 62:534-50.

33. Unutzer J, Katon W, Callahan CM, et al. Collaborative care management of late-life depression in the primary care setting: a randomized controlled trial. JAMA. Dec 11 2002;288(22):2836-2845.

34. Callahan CM, Boustani MA, Weiner M et al. Implementing dementia care models in primary care settings:The Aging Brain Care Medical Home. *Aging and Mental Health*. 2011; 15(1): 5-12, PMCID: PMC3030631.

35. Frame A, LaMantia M, Reddy Bynagari BA, et al. Development and Implementation of an Electronic Decision Support to Manage the Health of a High-Risk Population: The enhanced Electronic Medical Record Aging Brain Care Software (eMR-ABC). eGEM *2013;*1: Article 8.

36. Defining the Patient Centered Medical Home: Patient Centered Medical Home Resource Center Rockville, MD: Agency for Healthcare Research and Quality. Available at: http://www.pcmh.ahrq.gov/page/defining-pcmh. Accessed January 23, 2014

37. Elliott D, McKinley S, Alison J, et al. Health-related quality of life and physical recovery after a critical illness: a multi-centre randomised controlled trial of a home-based physical rehabilitation program. *Critical care (London, England).* 2011;15(3):R142.

38. Khan BA, Fadel WF, Tricker JL, et al. Effectiveness of implementing a wake-up and breathe program on sedation and delirium in the intensive care unit. Critical Care Medicine 2014. *Crit Care Med. 2014 Dec;42(12):e791-5*, PMCID: PMC4311879.

39. Khan BA, Guzman O, Campbell NL, et al. Comparison and agreement between the Richmond Agitation-Sedation Scale and the Riker Sedation-Agitation Scale in evaluating patients' eligibility for delirium assessment in the ICU. *Chest.* Jul 2012;142(1):48-54, PMCID: PMC3610594.

40. Khan BA, Calvo-Ayala E, Campbell N, et al. Clinical decision support system and incidence of delirium in cognitively impaired older adults transferred to intensive care. *American journal of critical care : an official publication, American Association of Critical-Care Nurses.* May 2013;22(3):257-262, PMCID: PMC3752665.

41. Khan BA, Farber MO, Campbell N, et al. S100 calcium binding protein B as a biomarker of delirium duration in the intensive care unit - an exploratory analysis. *International journal of general medicine.* 2013;6:855-861, PMCID: PMC3855164.

42. Counsell SR, Callahan CM, Tu W, et al. Cost analysis of the Geriatrics Resources for Assessment and Care of Elders care management intervention. J Am Geriatr Soc. 2009 Aug;57(8):1420-6, PMCID: PMC3874584.

43. Katon WJ, Schoenbaum M, Fan MY, et al. Cost-effectiveness of improving primary care treatment of late-life depression. *Arch Gen Psychiatry*. 2005 Dec;62(12):1313-20.

44. Callahan CM, Kroenke K, Counsell SR, et al (IMPACT Investigators). Treatment of depression improves physical functioning in older adults. J Am Geriatr Soc. 2005 Mar;53(3):367-73.

45. LaMantia MA, Alder CA, Callahan CM, Gao S, French DD, Austrom MG, Boustany K, Livin L, Bynagari B, Boustani MA. The Aging Brain Care Medical Home: Preliminary Data. J Am Geriatr Soc. 2015 Jun;63(6):1209-13.

46. French DD, LaMantia MA, Livin LR, Herceg D, Alder CA, Boustani MA. Healthy Aging Brain Center improved care coordination and produced net savings. Health Aff (Millwood). 2014 Apr;33(4):613-8.

47. Monahan PO, Boustani M, Alder C, et al. Practical clinical tool to monitor dementia symptoms: The HABC Monitor. *Clin Interv Aging.* 2012; 7: 143–157, PMCID: PMC3393358.

48. Khan BA, Lasiter S, Boustani MA. Critical Care Recovery Center. Making the case for an innovative collaborative care model for ICU survivors. Am J Nurs. 2015 Mar;115(3):24-31. PMCID: PMC4608259

49. Stevenson M, Segui-Gomez M, Lescohier I, Di Scala C, McDonald-Smith G. An overview of the injury severity score and the new injury severity score. Inj Prev 2001;7:10-3, PMCID: PMC1730702.

50. Baker SP, O'Neill B, Haddon W Jr, Long WB. 1974. The injury severity score: a method for describing patients with multiple injuries and evaluating emergency care. J Trauma 14:187-96.

51. Glancy KE, Glancy CJ, Lucke JF, Mahurin K, Rhodes M, Tinkoff GH. 1992. A study of recovery in trauma patients. J Trauma 33:602-609.

52. Halcomb E, Daly J, Davidson P, Elliott D, Griffiths R. Life beyond severe traumatic injury: an integrative review of the literature. Aust Crit Care. 2005 Feb;18(1):17-8, 20-4.

53. Sluys K, Häggmark T, Iselius L. Outcome and quality of life 5 years after major trauma. J Trauma. 2005 Jul;59(1):223-32.

54. Hoffman K, Cole E, Playford ED, Grill E, Soberg HL, Brohi K. Health outcome after major trauma: what are we measuring? PLoS One. 2014 Jul 22;9(7):e103082.

55. Watne LO1, Torbergsen AC, Conroy S, Engedal K, Frihagen F, Hjorthaug GA, Juliebo V, Raeder J, Saltvedt I, Skovlund E, Wyller TB. The effect of a pre- and postoperative orthogeriatric service on cognitive function in patients with hip

fracture: randomized controlled trial (Oslo Orthogeriatric Trial). BMC Med. 2014 Apr 15;12:63.

56. Volpato S, Cavalieri M, Guerra G, Sioulis F, Ranzini M, Maraldi C, Fellin R, Guralnik JM. Performance-based functional assessment in older hospitalized patients: feasibility and clinical correlates. J Gerontol A Biol Sci Med Sci. 2008 Dec;63(12):1393-8.

57. Latham NK, Harris BA, Bean JF, Heeren T, Goodyear C, Zawacki S, Heislein DM, Mustafa J, Pardasaney P, Giorgetti M, Holt N, Goehring L, Jette AM. Effect of a home-based exercise program on functional recovery following rehabilitation after hip fracture: a randomized clinical trial. JAMA. 2014 Feb 19;311(7):700-8. PMCID: PMC4454368

58. Prestmo A, Hagen G, Sletvold O, Helbostad JL, Thingstad P, Taraldsen K, Lydersen S, Halsteinli V, Saltnes T, Lamb SE, Johnsen LG, Saltvedt I. Comprehensive geriatric care for patients with hip fractures: a prospective, randomised, controlled trial. Lancet. 2015 Apr 25;385(9978):1623-33.

59. Perera S, Mody SH, Woodman RC, Studenski SA. Meaningful change and responsiveness in common physical performance measures in older adults. J Am Geriatr Soc. 2006 May;54(5):743-9.

60. Ware JE Jr, Sherbourne CD. 1992. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care 30:473-83.

61. Kopjar B. 1996. The SF-36 health survey: a valid measure of changes in health status after injury. Inj Prev 2:135–139, PMCID: PMC1067678.

62. Michaels AJ, Michaels CE, Smith JS, Moon CH, Peterson C, Long WB. 2000. Outcome from injury: general health, work status, and satisfaction 12 months after trauma. J Trauma 48:841-8.

63. Van Beeck EF, Larsen CF, Lyons RA, Meerding WJ, Mulder S, Essink-Bot ML. 2007. Guidelines for the conduction of follow-up studies measuring injury-related disability. J Trauma. 62:534-50.

64. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *Journal of general internal medicine.* Sep 2001;16(9):606-613, PMCID: PMC1495268.

65. Lowe B, Unutzer J, Callahan CM, Perkins AJ, Kroenke K. Monitoring depression treatment outcomes with the patient health questionnaire-9. *Medical care.* Dec 2004;42(12):1194-1201.

66. Kroenke K, Spitzer RL, Williams JB, Monahan PO, Lowe B. Anxiety disorders in primary care: prevalence, impairment, comorbidity, and detection. *Annals of internal medicine.* Mar 6 2007;146(5):317-325.

67. Spitzer RL, Kroenke K, Williams JB, Lowe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Archives of internal medicine.* May 22 2006;166(10):1092-1097.

68. Löwe 1, Unützer J, Callahan CM, Perkins AJ, Kroenke K. Monitoring depression treatment outcomes with the patient health questionnaire-9. Med Care. 2004 Dec;42(12):1194-201.

69. McDonald CJ, Overhage JM, Barnes M, Schadow G, Blevins L, Dexter PR, et al. The Indiana network for patient care: a working local health information infrastructure. An example of a working infrastructure collaboration that links data from five health systems and hundreds of millions of entries. Health Aff (Millwood) 2005;24(5):1214–1220.

70. Indiana Network For Patient Care [Internet]. [cited 2013 Oct 1]. Available from: http://www.ihie.org/indiana-network-for-patient-care.

71. Moore L, Clark DE. The value of trauma registries. Injury. 2008 Jun;39(6):686-95.

72. Little, R.J.A. and Rubin, D.B. (2002). *Statistical Analysis with Missing Data*, 2nd edition, New York: John Wiley

73. The University of Sheffield SF-36 Software to Utility Conversion FAQ. Available at: https://www.shef.ac.uk/scharr/sections/heds/mvh/sf-6d/faqs (Accessed June 17, 2016).

74. Brazier, JE, Roberts, JR,. The estimation of a preference-based index from the SF-12. Medical Care, 2004;42(9):851-859.

75. Kharroubi, S, Brazier, JE, Roberts, JR, et al. Modelling SF-6D health state preference data using a nonparametric Bayesian method. Journal of Health Economics, 2007;26(3):597-612.

76. McCabe, C, Brazier, JE, Gilks, P, et al. Using rank data to estimate health state utility models. Journal of Health Economics, 2006;25(3):418-431.

77. Elixhauser A, Steiner C, Harris R, Coffey RM. Comorbidity measures for use with administrative data. Med Care. 1998;36(1):8-27.

78. Agency for Healthcare Research and Quality (AHRQ), Healthcare Cost and Utilization Project, Comorbidity Software [Internet]. [cited 2013 Oct 4]. Available from: http://www.hcup-us.ahrq.gov/toolssoftware/comorbidity/comorbidity.jsp

79. Blough DK, Ramsey SD. Using generalized linear models to assess medical care costs. Health Serv Outcome Res Methodology. 2000;1(2):185–202.

80. Buntin MB, Zaslavsky AM. Too much ado about two-part models and transformation? Comparing methods of modeling Medicare expenditures. J Health Econ. 2004;23(3):525–542.

81. Manning WG, Mullahy J. Estimating log models: to transform or not to transform? J Health Econ. 2001;20(4):461–494.

82. Guralnik JM, Ferrucci L, Pieper CF, et al. Lower extremity function and subsequent disability: consistency across studies, predictive models, and value of gait speed alone compared with the short physical performance battery. The journals of gerontology. Series A, Biological sciences and medical sciences. Apr 2000;55(4):M221-231.

83. Latham NK, Harris BA, Bean JF, et al. Effect of a home-based exercise program on functional recovery following rehabilitation after hip fracture: a randomized clinical trial. JAMA. 2014 Feb 19;311(7):700-8.

84. Pan SL, Liang HW, Hou WH, Yeh TS. Responsiveness of SF-36 and Lower Extremity Functional Scale for assessing outcomes in traumatic injuries of lower extremities. Injury. 2014 Nov;45(11):1759-63.