I. Research Project Title, Purpose, Anticipated Project Duration and Inclusion of Proprietary Information

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Title:

Remote monitoring of symptoms and cognitive function using Telehealth: ***T- Liver*** project

Purpose:

End-Stage Liver Disease (**ESLD**) is one of the ten leading causes of death in US. It is marked by episodic acute exacerbations of the underlying liver disease which often leads to severe symptoms, poor quality of life, mental deterioration and repeated hospitalizations. The **overall purpose** of this project is to introduce a telehealth based intervention (involving remote monitoring of symptoms and cognitive function assessment) initiated during the time of hospital admission of ESLD patients. This will support enhanced clinical care and improve self-management in ESLD population. In addition, it will reduce healthcare utilization, improve medication adherence and overall health outcomes.

II. Research Project Overview

The **primary goal** is to develop and implement a systematic clinical approach for remote monitoring of symptoms and cognitive function in ESLD patients, through developing a telehealth based intervention. The intervention includes assembling specific apps on an ipad/smartphone/tablet through a web based secured system, having patients respond to periodic assessments and transmission of results instantly to providers, who will follow specified clinical pathways stratified by severity scores.

Methods: This is a single arm study to assess the effectiveness of an experimental telehealth intervention within the treatment of ESLD, and compare it with a historic cohort. All inpatients with advanced liver diseaseand at least 1 complication will be eligible to participate. the study group receives the Telehealth intervention and will be given an ipad/smartphone preloaded with the instruments used for symptom monitoring and cognitive function assessment during the hospital admission. A research coordinator will consent the patients and conduct a 30-minute introduction to use of device on the day of enrollment (within 24-48 hours of admission). The second assessment will be done on day 2, and third assessment on day of discharge. After that, the patient will be told to do the study assessments daily at home. The study assessment results will be reviewed by the providers on the same day, and based on the severity scores clinical actions will be taken and documented.

IV. Expected Research Outcomes and Benefits -

Primary Outcomes:

1) Healthcare utilization (30 and 90-day readmission)
2) Changes in severity scores of symptoms and quality of life over time.

3) Patient experience/satisfaction.

Benefits of the research: Applying telehealth intervention (inclusive of remote monitoring of symptoms and cognitive function) with a well-defined clinical algorithm at the time of discharge of patients with ESLD, who are prone to impaired quality of life, adds a **new dimension** to the care delivery model. This new post-hospital discharge algorithm is expected to have positive effects on many parameters, including readmission rates, patient satisfaction, and above all on the health outcomes. Arguably, these improvements will reduce health care costs among a group of patients with ESLD, who are high utilizers of healthcare services. Benefits to individual patients include monitoring of their own symptoms, and cognitive function, which will allow early detection of hepatic encephalopathy and/or other complications.

VII. Evaluation Component and Research Evaluative Procedures - Oversight and Statistical Tests

Oversight: The PI will be overseeing the implementation of the project along with the Co-Investigator. Since the study involves patients who are admitted to the hospital, and offers them a device to improve their own care, the likelihood of participation is high. We will assess the attrition rates and other technical issues during the project. Higher rates of no response to timed assessments from enrolled patients will trigger an alert to the research coordinator, who will then call the patients to make sure device is working appropriately and explore the reasons for missing responses. Furthermore, a detailed discussion at the time of enrollment about the project and expected responsibilities from patients will reduce the missing data points.

Statistical Tests: The data for study group will be described using both graphic and summary statistics. Process data on participation, usage and satisfaction with telehealth intervention will be collected and summarized to assess intervention fidelity. We will assess the change in percent readmissions at 30 days and 90 days in the study groupfrom baseline to 3 months. The average rate of change in the defined outcomes in longitudinal (overtime) analyses using paired t tests and 95%CIs of the differences in the two groups will be conducted. The trajectories of symptom and quality of life scores will be illustrated by graphing individual patient values over time course of the study for the intervention group. We will test whether the relationship between study outcome and study arm differ with the severity of disease as assessed by MELD (Model for End Stage Liver Disease) score using two-way analysis of variance for repeated measures.

(B) Performance Measures

B) Performance measures:

1) Number of patients enrolled in the study.
2) Completion of 7, 28 days and 3 months assessment of symptoms and cognitive function by the patients.

3) Attrition rates of enrolled patients.
4) Efficiency of the technical device provided to patients as assessed from ease of use by patients and providers.
5) Scholarly activities (publications and presentations) resulting from study data.

VIII. Health Disparities

This project will target the patient population at Einstein, which is largely underserved, and minority. No racial/ethnic or gender group will be excluded from the proposed study. Furthermore as the study involves providing an ipad/smartphone to patients, it eliminates any existing disparity of access for anyone who participates.

XI. Research Plan

(1) Specific Aims

The **specific aims** are:

1. To develop and implement a systematic clinical approach for remote monitoring of symptoms and cognitive function in ESLD patients, through assembling specific apps on an ipad/smartphone using web based cloud technology (referred to as telehealth intervention).
2. To evaluate the impact of our telehealth intervention on health care utilization (30/90 day readmissions)
3. To assess prospectively the comparative efficacy of telehealth intervention within the treatment of ESLD, in improving i) symptom scores, ii) patient reported quality of life, and iii) satisfaction with device and questionnaire. We hypothesize that Telehealth intervention will show improvement in these domainsover time [a 10% improvement in scores from baseline to 3 months will be considered clinically significant]

(2) Background and Significance

End-Stage Liver Disease (**ESLD**) is one of the ten leading causes of death in US. [i] Hospitalization rates due to ESLD and its complications have skyrocketed by 93% (due to *hepatorenal syndrome*), 62% (due to *portal hypertension*), and 190% due to Hepatitis C and its complications from 2004-05 to 2010-11.[ii] Developing interventions which can potentially reduce readmissions and healthcare utilization are a national priority according to the Affordable Care Act.[iii] **Telehealth** offers a unique platform to remotely monitor individual patients and offer enhanced care at the time of need, and has shown success in congestive heart failure, lung disease and diabetes.[iv] There is no research demonstrating its utilization or efficacy for liver disease patients. Hence, we propose to develop and test the effectiveness of a ***T-Liver intervention*** to remotely monitor the symptoms (pain, shortness of breath) weight, temperature, and cognitive function (using symptom questions and a stroop test) to reduce healthcare utilization, improve patient satisfaction and health outcomes.

"HGE healthcare solutions" is a group of experts who have pioneered some work in telehealth, and created a smartphone based COPD app (Chronic Obstructive Pulmonary Disease), which assesses daily symptoms and triggers alerts to providers for immediate treatments. This app has shown to improve health outcomes and reduce hospitalizations by changing the approach of health care to proactive than reactive. [v] [vi] We will be partnering with this company in creating and delivering our telehealth intervention. The company operates on a HIPAA secured platform, which maintains confidentiality and security of the data. They also offer technical assistance to end users during normal business hours.

(3) Research Design, Methods and Activities -

Methods: This is a single arm trial to assess the effectiveness of an experimental telehealth intervention within the treatment of ESLD, and compare it with a historic control. The study patients continue to receive the routine standard of care, which may involve addressing symptoms based on individual needs and circumstances. All participants will be given an ipad/smartphone preloaded with the instruments used for symptom monitoring and cognitive function assessment. A research coordinator will consent the patients and conduct a 30-minute introduction to use of device on the day of enrollment. Repeat assessments will be done as shown in **Table 1** above. All patients will receive the standard of care discharge planning, including discharge instructions and a confirmed follow-up ambulatory visit within 2-4 weeks.
Inclusion Criteria: All patients being discharged from the inpatient liver practice of the Einstein Healthcare Network (EHN) who meet the following criteria will be eligible.

- ✓ Patients must be age 18 years or older
- ✓ Ability to provide informed consent, and must be able to cognitively answer questionnaires
- ✓ Patients who received a diagnosis of Advanced Liver Disease with at least 1 of the complications (Hepatorenal Syndrome, Portal Hypertension, Ascites, Hepatic Encephalopathy)
- ✓ Patient must be able to read/ speak English
- ✓ Patient must have a support person

Exclusion Criteria:

- ✓ Cognitive impairment which precludes participation
- ✓ Projected survival, in the opinion of the provider, of less than six months
- ✓ Current psychosis or confusion, precluding a patient from being consented
- ✓ Patients being discharged to nursing homes
- ✓ Patients with red green color blindness (as they will not be able to respond to stroop test questions).

Telehealth Intervention:
Patients will receive a 30-minute introduction to the use of ipad/smartphone, and instructions to respond to the following assessments. Initial assessments will be performed on the day of enrollment, and all of them will be repeated periodically (**Table 1**), for a total of 3 months study

participation. The assessments include the following: Pain (severity, location), shortness of breath (at rest or with mild activity), cognitive function assessment (drowsy, hard time concentrating, irritable, trouble remembering things, slurred speech, unsteady gait), and stroop test (color matching test, one cycle lasts 45 seconds).

Weight monitoring: Monitoring weight will allow assessment of fluid retention in ESLD patients, and help detect any development/ worsening of ascites. Patients will be instructed to enter their daily weights for the first month, and then every week for next 2 months. Any weight gain of more than 2 lbs within 1-2 days for 3 consecutive days will trigger a phone call by the providers.

A simplified step by step guide summarizing the instructions will be included with the device. Patients will be given a toll-free number that will be available during work hours (9am to 5pm) for any technical issues, and will be urged to complete assessments by 11 am on a daily basis.

Site: Levy 7 is the home of the "Liver Care Center at Einstein", a 15 bed inpatient unit dedicated to the care of patients with liver disease. This inpatient unit is the site of identification and recruitment of patients in this project.

Recruitment methods: The research coordinator will contact eligible patients within 24-48 hours of admission and conduct informed consent. All patients who consent will be then randomized to either of the 2 groups. We assume 3-4 patients will be enrolled per week, for 7 months of enrollment period.

Sample size and power: Assuming a baseline risk of readmission in the historic control of 40% and 10% attrition rates, a sample size of 50 patients will be sufficient to detect a difference of 35% or greater in the intervention group. Accepting a type I error rate of no more than .05, and a Type II error rate of .20, we will have 80% statistical power to detect a difference of this magnitude or larger.

Retention strategies: Patients will be informed about the purpose of the study and their responsibilities at the time of consent by the research coordinator. All patients with a support person will be eligible. Strategies (i.e. education about value of study participation) will be added if recruitment rates fall within 20% of target.

Analysis plan: Medical records will be utilized to capture the disease severity, diagnosis, duration of liver disease and presence of comorbidities. Patients enrolled into the study will be followed up for 6 months. Descriptive and analytics statistics will be done using linear correlation and regression. We will compare the clinical markers at baseline with 3 month value using unpaired t test.. .

Limitations:

Patient Attrition: this is an anticipated problem, as physical and cognitive deterioration may make the completion of questionnaires difficult. This limitation will be minimized by the short interval assessments and completion of study at 3 months.

(4) Protection of Human Subjects -

(a) **Risks to subjects:** There is no medical risk to any participant and no sharing of protected health information in this project. It is completely up to the participants to agree for this study. Refusal for participation will not impact their health care in the office. There are minimal risks to participants related to their completion of survey questionnaires. There may be some emotional distress as they complete the symptom and quality of life questions, but this will influence and enhance their own care. Patients may have technical difficulties, which will be addressed through availability of a help desk and the research coordinator during work hours.

(b) **Adequacy of protection against risks**: There are no known risks in this study. All study personnel have completed the IRB required CITI training, and will be trained appropriately. Confidentiality is maintained through Einstein's secured system and the secure administration through HGE. The PI and Co-Investigator will be available to answer any of the patient's concerns. The research coordinator will conduct an in-depth informed consent explaining the purpose of the project, and the expectations from patients to respond to the assessments in a timely way. All the information collected is through a secured password protected system, which allows encrypted data transmission to the providers

(c) **Recruitment of subjects:** All patients discharged from the Inpatient liver unit who meet the eligibility criteria will be approached for consent. Once the patients agree to participate, the details of the study and device operations will be discussed. If the patient needs more time to decide, we will allow them to take the information home and get back to the research coordinator within 1-2 days.

(d) **Informed consent**: An in-depth informed consent will be conducted in person using paper version. The IRB approval will be attached.

(e) **Data confidentiality** and provision of medical or professional intervention, if needed: Einstein Healthcare Network's Human Research Protection Program (HRPP) is a comprehensive system to ensure the protection of the rights and welfare of subjects in Human Research. It is comprised of the EHN leadership, Office of Research and Technology Development (ORTD), Institutional Review Board (IRB), investigators and their study staff and relevant departments and units. The HRPP not only promotes compliance with relevant laws, regulations and professional and ethical standards at all levels, it addresses the needs and concerns of researchers and enhances support of their endeavors. The HGE has a secured system through which the patients will

complete the study assessments and communicate with providers. All data collected will be completely confidential, and will not be shared with anyone outside of this project.

(f) **Potential benefits** of the research to subjects: Since this study involves close monitoring of symptoms and development of any hepatic encephalopathy, it will enhance patient centered care through timely management of symptoms, and early detection of complications of ESLD.

(g) **Importance of knowledge to be gained**: The knowledge gained from this project will enable the use of technology in care of liver disease patients in a meaningful way, and allow early detection of symptoms/ problems which will trigger clinical actions as needed and thereby make the approach to care more proactive than reactive. This will potentially engage patients in their own care, and improve the healthcare service delivery model for ESLD.

(h) Inclusion of women, children and minorities in the research: All eligible candidates more than 18 years of age are included in this study, irrespective of any specific race / sex, etc.

Data Safety Monitoring Plan: During this study medical history and other lab values will be assessed at baseline, 4 weeks and 3 months from the medical records. Only the study personnel will have access to this information, and is not shared with any third party including the HGE company. All the data collected is for research purposes only. The data will be saved in a password protected format within Einstein's secured network drive. The PI and Co-Investigator will review the data on an ongoing basis for data completeness and accuracy including patient accrual, compliance with inclusion/ exclusion criteria, patient adherence to intervention. Study progress and safety will be reviewed monthly.

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