STUDY TEAM ROSTER

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Primary Registry and Trial Identifying Number	**ClinicalTrials: NCT02856594**
Date of Registration	July 29 2016
Secondary Identifying Numbers	IRB ID#: 2016 P000742
Source(s) of Monetary Support	National Institute on Aging Grant (Award Reference Number R01 AG053582-01)
Primary Sponsor	Department of Anesthesiology, Critical care and Pain Medicine Massachusetts General Hospital Boston, MA 02114
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Public Title	Protocol for the Minimizing ICU Neurological Dysfunction with Dexmedetomidine-induced Sleep (MINDDS) Trial
Scientific Title	Protocol for the Minimizing ICU Neurological Dysfunction with Dexmedetomidine-induced Sleep (MINDDS) Trial: a Randomized, Double blind, Parallel-arm, Placebo-controlled Clinical Trial

Countries of Recruitment	United States
Health Condition(s) or Problem(s) Studied	Postoperative delirium, predictors of delirium
Intervention(s)	Trial arm 1: Dexmedetomidine-induced Sleep Group (primary intervention) Post cardiac surgical patients admitted to the cardiac surgical intensive care unit (CSICU) and extubated at least 30 minutes prior to 8:30 PM would receive a sleep induction dose of dexmedetomidine (1mcg/kg over 40 minutes; maximum administered dose of 80mcg at any one instance) at 9 PM every night throughout their CSICU stay. Trial patients admitted to the CSICU and extubated after 8:30 PM, but before 2 AM, would receive a sleep induction dose of dexmedetomidine within 30 minutes of extubation. However, throughout the rest of the CSICU stay the dexmedetomidine administration time will be targeted for 9 PM. Trial patients admitted to the CSICU and remain intubated past 2 AM will begin trial procedures the following day, assuming they are extubated within 12 hours of admission to the CSICU. Trial arm 2: Placebo Control Group. Post cardiac surgical patients admitted to the CSICU and extubated at least 30 minutes prior to 8:30 PM would receive placebo (intravenous normal saline over 40 minutes) at 9 PM every night throughout their CSICU stay. Trial patients admitted to the CSICU and extubated after 8:30 PM, but before 2 AM, would receive the placebo infusion of normal saline within 30 minutes of extubation. However, throughout the rest of the CSICU stay the placebo administration time will be targeted for 9 PM. Trial patients who are admitted to the CSICU and remain intubated past 2 AM will begin trial procedures the following day, assuming they are extubated within 12 hours of admission to the CSICU.
Key Inclusion, Exclusion and Objective Drop Criteria	Inclusion Criteria 1. Age ≥ 60 2. Scheduled for a cardiac surgical procedure with planned postoperative admission to the CSICU for ≥ 24 hours 3. Scheduled same day surgical admission

Exclusion Criteria

1. Blindness, deafness or the inability to speak English
2. Greater than 2 days of ICU admission in the month preceding the current surgical procedure
3. Renal and liver failure requiring dialysis or Child-Pugh score > 5
4. Follow-up difficulties (i.e. active substance abuse, psychotic disorder, homelessness)
5. Previous cardiac surgery within 1 year of surgical procedure
6. Allergy to dexmedetomidine
7. Chronic therapy with benzodiazepines and/or antipsychotics
8. Severe neurological deficit due to structural or anoxic brain damage
9. Surgical procedures requiring total circulatory arrest

Objective Drop Criteria

1. Scheduled for a second surgical procedure during hospital stay
2. Post-operative intubation > 12 hours

Trial Type

Interventional
Allocation: Randomized
Intervention model: Parallel assignment
Blinding: Clinicians blinded to intervention, subject blinded to intervention, primary outcome assessor blinded to intervention
Assignment: Parallel
Primary purpose: Prevention

Date of First Enrollment

March, 2017

Target Sample Size

Recruiting until 370 patients receive the study intervention on Post Operative Day 0.

Recruitment Status

Enrolling

Primary Outcome(s)

Outcome name: Incidence of postoperative delirium

Method of measurement: The Long Confusion

	Assessment Method Time points of interest: Postoperative day 1
Key Secondary Outcomes	Outcome name: ICU and hospital delirium/coma-free days Method of measurement: Delirium assessment with: The Long Confusion Assessment Method Time points of interest: Up until postoperative day 3 if no delirium. Up until postoperative day 5 if delirium exhibited but resolved. Up until postoperative day 7 or discharge if delirium unresolved by postoperative day 5. Outcome name: Severity of Delirium Method of measurement: The Long Confusion Assessment Method Time points of interest: Up until postoperative day 3 if no delirium. Up until postoperative day 5 if delirium exhibited but resolved. Up until postoperative day 7 or discharge if delirium unresolved by postoperative day 5. Outcome name: Date of Hospital Discharge / Length of Hospital Stay Method of measurement: Medical record review Time points of interest: Up until hospital discharge Outcome name: 30-day, 90-day, and 180-day mortality Method of measurement: Medical record review Time points of interest: 30 days, 90 days and 180 days postoperatively Outcome name: Postoperative cognitive status Method of measurement: Abbreviated Montreal Cognitive Assessment, 3D-CAM and PROMIS-29 applied cognition abilities questionnaire Time points of interest: 30 days, 90 days and 180

days postoperatively

Outcome name: Postoperative health related quality of life

Method of measurement: PROMIS-29 physical function, global health, pain interference questionnaires, and sleep questionnaire

Time points of interest: 30 days, 90 days and 180 days postoperatively

ORGANIZATIONAL STRUCTURE AND RESPONSIBILITIES

Principal Investigator:
Oluwaseun Akeju, M.D., M.M.Sc.

Responsibilities include: design and conduct of the MINDDS trial, preparation of protocol and revisions, organization of steering committee meetings, and publication of trial reports.

Steering Committee:

Oluwaseun Akeju, M.D., MMSc
Federico Bilotta, MD
Alan DiBiasio, Pharm.D
Tim Houle, Ph.D
Gaston Cudemus, M.D.
Marco L Loggia, Ph.D.
Kara Pavone, B.SN., R.N
Jason Qu, M.D.
Shahzad Shaefi, M.D., MPH
Ken Shelton, M.D.
Brandon M Westover, M.D., Ph.D.

Responsibilities include: agreement of final protocol, reviewing progress of trial and if necessary, conducting changes to the protocol, coordinating with principal investigator, and communicating with trial management committee.

Trial Management Committee:
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Tim Houle, Ph.D.
Lauren E Hobbs, M.S.
Reine Ibala, B.S.
Eunice Hahm, B.S.
Jacob Gitlin, B.S.
Kara Pavone, B.S.N, R.N.
Jason Qu, M.D.
Ken Shelton, M.D.

Responsibilities include: trial planning, organization of steering committee meetings, reporting SAEs (Serious Adverse Events) to Partners Healthcare IRB (Institutional Review Board), maintaining REDCap electronic database, reporting to steering committee, conducting data verification, recruitment, randomization, and follow-up of trial participants

Data Management Committee:
Hao Deng, M.D., M.P.H.
Tim Houle, Ph.D.

Responsibilities include: statistical design of trial, data verification.

Data Adjudication Committee:
Oluwaseun Akeju, M.D., M.M.Sc.
Shahzad Shaefi, M.D., MPH

Brandon M Westover, M.D., Ph.D.

Responsibilities include: regularly reviewing delirium assessments, contacting trial management committee, retraining researchers if necessary.

Data and Safety Monitoring Committee:
Wie Chao, M.D., Ph.D. - University of Maryland School of Medicine
Jesse Ehrenfeld, M.D.,M.P.H. -Vanderbilt University Medical Center
Michael Gropper, M.D., Ph.D. - University of California San Francisco
Keith A. Jones, M.D. - The University of Alabama at Birmingham

Responsibilities include: reviewing and evaluating the trial data to ensure participant safety, trial conduct, progress, and efficacy, and making recommendations regarding the continuation, modification, and termination of the trial.