Coversheet

Study title: Pediatric Guideline Adherence and Outcomes- Argentina (PEGASUS)

NCT number: NCT03896789

PI name: Monica Vavilala

Document name: Analysis plan Aim 1A_CTgov resubmit_2

Initial RB approval date: 9/28/2018

Continuing IRB approval date: 8/15/2019

Protocol modification and continuing IRB approval date: 8/7/2020

Continuing IRB approval date: 7/10/2021

Final statistical analysis plan documents date: 3/10/2022

Analysis plan Aim 1A_ PEGASUS Argentina_031022

Paper title: TBD

Specific Aim 1: *Determine the relationship between PEGASUS program implementation and TBI guideline adherence (Aim 1a)*

Hypothesis: Centers that receive the PEGASUS program have higher TBI guideline adherence (main outcome), as well as better discharge survival and 3-month Glasgow Outcome Scale-Extended (GOSE) score (secondary outcomes) than centers who receive usual care.

Authors: TBD

Questions of interest:

1) Does PEGASUS implementation improve guideline adherence?
2) Are there any imbalances between the study arms that need to be addressed?

Study Design: 2-arm parallel cluster RCT

Study population: Pediatric (<18) ICU patients with severe TBI at 16 sites

Exposure variable(s): Study Arm (binary)

Outcome variable(s): (1) TBI guideline adherence

"The main outcome is TBI guideline adherence during first 3 days ICU stay, calculated via our previously developed TBI guideline adherence scorecard.[12] Using patient charts, we measure presence or absence of adherence to the indicators and capture time since injury for any observed indicators, including the main protective KPIs (ventilation, nutrition, CPP). Patient guideline adherence is defined as the sum of indicators to which care was adhered divided by the number of relevant adherence indicators for a given patient. Mean adherence scores are calculated for each site individually and across all sites."

Describe:
(2) Extracranial injuries
(3) Discharge GOS
(4) Discharge survival
(5) 3-month GOSE-Peds
(6) 3-month mortality
(7) KPIs?

Covariates/confounders:

- patient (demographics, ISS, LOS, presence of extracranial injuries, and surgery (yes/no) for up to 7 days after severe TBI in case report forms. If a child is discharged or dies prior to day 7, data collection will stop. Recorded radiographic evidence of cerebral edema, subdural hematoma, and intracranial hemorrhage on first head CT)
- implementation (reach, dose, fidelity from medical records),
- organizational (annual trauma volumes, and physician & nurse staffing)

Methods:

1. Descriptive statistics for all measures at the facility level, within treatment and control arms. Potential differences in patient (age, sex, race/ethnicity) and injury characteristics will be examined using bivariate analyses by center using **X2** tests (categorical) and t-tests (continuous).
2. ITT analysis: multi-level mixed effects Poisson regression with robust variance estimation and clustering by site to estimate the relative risk of PEGASUS implementation on TBI guideline adherence and stratified by extracranial injury, as described in Zou, et al.
   Per protocol: As with ITT, but potentially including implementation dose/fidelity as covariate and interaction with intervention.
3. Secondary analyses (Following ITT for primary analysis): Poisson regression with robust variance estimation and clustering by site to estimate separately the relative likelihood of program implementation on these outcomes:1) in-hospital mortality; and 2) GOSE-Peds at 3 months post TBI, analyzing GOS score as a dichotomous measure (minor-moderate impairment vs major impairment-vegetative state and death). Multivariable Cox regression model to examine the marginal effect of PEGASUS on mortality during the 3 months post discharge, averaged over all centers.
4. Sensitivity analyses: repeated analysis on ICP monitoring patients
5. Subgroups: COVID effect and geographic effect

Potential products:

a) Descriptive table
b) Outcome table
c) Figure showing 3-month mortality in Cox model
d) Figure showing variation in intervention dose/fidelity within and between sites