*The CONCERN Early Warning System:*

*Study Protocol and Analysis Plan*

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Communicating Narrative Concerns Entered by RNs (CONCERN): Clinical Decision Support Communication for Risky Patient States
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## 1. Original Study Protocol and Analysis Plan

*Aim 3 below is focused on the CONCERN Early Warning Score Trial Design and Analysis Plan and is excerpted from R01 grant funded in 2017 (NINR 1R01NR016941, COmmunicating Narrative Concerns Entered by RNs (CONCERN): Clinical Decision Support Communication for Risky Patient States). Protocol below was IRB approved November 2016.*

**Aim 3**. Evaluate the impact of the CONCERN SMARTapp notification system on patient outcomes, for the primary outcomes of in-hospital mortality and length of stay (LOS) and secondary outcomes of cardiac arrest, unanticipated transfers to the intensive care unit, and 30-day hospital readmission rates.

Table 1. Sample and Setting Calendar Year 2014 (all adult patients)

| Site | Beds | Occupancy Rate | In-patient Mortality | 30-day Readmit |
|---|---|---|---|---|
| PHS-BWH | 777 | 95% | 1001 | 18% |
| PHS-NWH | 300 | 94% | 312 | 10% |
| NYP-CUMC | 745 | 95% | 1261 | 18% |
| NYP-Allen | 300 | 75% | 98 | 10% |

*CONCERN implementation processes* will use open source tools, APIs (application program interfaces), web services, and SMART tools developed at Harvard Medical School. The need for site specific, local EHR configurations will be minimized using this approach. Our technology solution will allow for continuous refinement of algorithm, pushing out a new version every 3 months to provide consistent amount of time to evaluate and track outcomes for each version.

*CONCERN Intervention Trial Design* will be a multiple time-series intervention (see Table 2). Please also refer to Table 1 for study sites and samples. Baseline data will be collected at all study sites. Silent release mode (no SMARTapp notification) will be used in non-equivalent control units and as a post-intervention unit control to evaluate if notifying clinicians can decrease rates of length of stay on non-ICU units and rates of 30-day hospital readmissions. In Table 2 the different versions indicate dynamic, adaptive functionality. The adaptive function utilizes Dr. Alber's inpatient acuity calculation[118] to determine if the pattern of nursing documentation has changed. We have built in time for a "burn-in" phase to evaluate adoption and adaptation to our algorithm.

Table 2. Trial Design with Multiple Time-series Intervention

| Study Arm | Site | Pre-intervention (6 months) | XXX | Phase 1 (3 months) [burn-in phase] | XXX | Phase 2a (3 months) | Phase 2b (3 months) | XXX | Phase 3 (3 months) |
|---|---|---|---|---|---|---|---|---|---|
| Control Groups | Site A | B | | V1 silent | | V2 silent | V3 silent | | V3 silent |
| | Site B | B | | V1 silent | | V2 silent | V3 silent | | V3 silent |
| Intervention Group | Site A | B | | V1 active | | V2 active | V3 active | | V3 silent |
| | Site B | B | | V1 active | | V2 active | V3 active | | V3 silent |
| B = baseline data; none = no intervention; silent = CONCERN App will function but will not display to clinician, active = CONCERN App will display to clinician. V1=version 1; V2=version 2 refined based on continuous monitoring of data | | | | | | | | | |

*CONCERN intervention trial data collection and analysis* includes collection of pre and post-intervention data during the 6 months before the intervention and 12 months after the intervention (see **Error! Reference source not found.** for timeline). Prior to conducting hypotheses tests, descriptive statistics will be used to describe outcome variables and key confounding variables. We propose a generalized linear mixed model to examine the impact of the CONCERN system on each of the two primary outcomes: in-hospital mortality and length of stay. This model is used to deal with combined data from multiple sites and can account for changes over time. This model allows different baselines and trajectories for different ICUs and non-ICU settings and can include both patient level and unit level covariates. We will also use a generalized linear mixed model for an interrupted time series analysis for unit level analysis. We will include a variable for closed versus open units in our analysis. We estimated statistical power for the comparison of mortality rates between the intervention and non-intervention periods and between silent and active model periods. All power calculations were based on 2-sided tests with alpha = 0.05. Using hospital patients' statistics, we expected at least 2,000 total admissions per month (ranging from 38 to 270 admissions in different units) with a mean mortality rates of 37.5 deaths per 10,000 inpatient days (ranging from 11.9 to 48.8), see Table 1. Using a very conservative number of total 50,000 inpatient days in each intervention period, we will have at least 80% statistical power to detect a difference of less than 1% relative difference in mortality rates. Because the 1% change in mortality are smaller than a clinically meaningful difference, we should have sufficient sample size When examined by different campuses, using a very conservative value of inpatient days in one campus of 6000 inpatient days in each intervention period, we will have at least 80% statistical power to detect a difference of less than 2% relative difference in mortality rates. There is no consensus regarding the best method for analyzing length of stay. Length of stay has been analyzed using both Poisson models (or NB, or other related models such as Zero-truncated Poisson models) and survival models (such as Cox PH models).[119] Both approaches will be applied to length of stay and the better performing model will be retained. We will use the logit link function for 30-day hospitalization outcomes. We will calculate the Number Needed to Treat during the months when the CONCERN system is on silent mode and in active mode for the non-ICU versus ICU and at each site for the

prevention of each of the following outcomes: length of stay, and 30-day hospital readmission rates. Additional secondary outcomes include 30-day hospital readmission, cardiac arrest, and unanticipated transfers to the ICU as well as analytics of CONCERN system log-files for clinician usage metrics. The following statistical tests will assess evaluate the reliability and validity of the results and effects of the CONCERN intervention: mutual information, association statistics including t-test and regression analysis, sub-sampling, and cross-validation and control of confounders (e.g., patient acuity with Charlson's Comorbidity Index, Dr. Alber's inpatient acuity calculation[118], and other validated acuity tools).[3,45,57]

*References from Original Protocol and Statistical Analysis Plan (NINR 1R01NR016941)*

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