

Improving Providers' Decision-Making and Reducing Information Overload Using Information Visualization in EHRs

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Master Protocol Document

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I have read, understood, and approved this version of the protocol.

Principal Investigator:



Date: 3/21/2026

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Date: 3/21/2026

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Table of Version Changes

Previous Version No.	Affected Sections	Summary of the Changes to the Protocol	Reason for Changes
0.0	1, 12	REMOVED AN OUTCOME MEASURE “NUMBER OF SCREENS” FROM AIM2 STUDY	Preliminary findings indicate that “number of screens” lacks significant value for the study’s objectives. Eliminating this measure avoids approximately 200 hours manual labor, ensuring the team can focus on more impactful data.

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Statement of Compliance

This study will be conducted as specified in the protocol and in accordance with the *International Conference on Harmonisation Guidelines for Good Clinical Practice* (ICH E6) and the *Code of Federal Regulations on the Protection of Human Subjects* (45 CFR Part 46).

The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the *Institutional Review Board* (IRB) for review and approval. Approval of both the protocol and the consent form must be obtained before any participant is enrolled. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. In addition, all changes to the consent form will be IRB-approved; a determination will be made regarding whether a new consent needs to be obtained from participants who provided consent, using a previously approved consent form.

If required by the IRB, the master protocol document, informed consent form(s), recruitment materials, and all participant materials will be submitted to the *Scientific Review Committee* (SRC) prior to IRB review (research.unc.edu/clinical-trials/src).

The statistical analysis plans will be consistent with guidance in CONSORT Statement [1] or STROBE Statement [2], ICMJE recommendations [3], the 2016 and 2019 statements of the American Statistical Association [4,5], and recommendations in Nature [6,7].*

All personnel involved in the conduct of this study have completed human subjects protection training.

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- * [1] www.consort-statement.org
[2] www.strobe-statement.org
[3] www.icmje.org
[4] Wasserstein RL, et al. (2016), The ASA's Statement on p-Values, *The American Statistician*, 70:2, 129-133
[5] Wasserstein RL, et al. (2019), Moving to a World Beyond $p < 0.05$, *The American Statistician*, 73:sup1, 1-19
[6] Amrhein, et al. (2019) Scientists rise up against statistical significance, *Nature* 567, 305-307
[7] Editorial (2019) It's time to talk about ditching statistical significance: Looking beyond a much used and abused measure would make science harder, but better. *Nature* 567, 283-283.

Table of Abbreviations

AE / SAE	adverse event / serious adverse event
CFR	U.S. Code of Federal Regulations (www.eCFR.gov)
CI	confidence interval
CIOMS	Council for International Organizations of Medical Sciences (cioms.ch)
CoC	certificate of confidentiality
CONSORT	Consolidated Standards of Reporting Trials (www.consort-statement.org)
CRF	case report form
CRO	contract research organization
CSCC	UNC Collaborative Studies Coordinating Center (sites.csc.unc.edu/csc)
CT.gov	ClinicalTrials.gov website
DCC	data coordinating center
DSMB	data and safety monitoring board
eCRF	electronic case report form
eCTD	electronic common technical document
DOH!	I need to delete this example term (and others not used in this protocol) from this table
FDA	U.S. Food and Drug Administration (www.fda.gov)
GCP	good clinical practice
HIPAA	U.S. Health Insurance Portability and Accountability Act (www.hhs.gov/hipaa)
ICF	informed consent form
ICH	International Council for Harmonization (www.ich.org)
ICMJE	International Committee of Medical Journal Editors (www.icmje.org)
IDE	investigational device exemption
IDS	UNC Investigational Drug Services (uncids.web.unc.edu)
IND	investigational new drug application
IRB	institutional review board
MAR	missing at random criterion
MCAR	missing completely at random criterion
MNAR	missing not at random criterion
MICE	multiple imputation by chained equations
MOP	manual of procedures
MPD	master protocol document
N	number of enrolled participants
NDA	new drug application
OCT	UNC Office of Clinical Trials (research.unc.edu/clinical-trials)
OHRP	Office for Human Research Protections
PHI	protected health information
PI	principal investigator
PRC	UNC Oncology Protocol Review Committee (UNCleneberger.org/protocolreview)
QA	quality assurance
RCT	randomized controlled trial
REDCap	Research Electronic Data Capture system
SD	standard deviation
SE	standard error
SOP	standard operating procedures
SRC	UNC Scientific Review Committee (research.unc.edu/clinical-trials/src)
STROBE	Strengthening Reporting of Observational Studies in Epidemiology (www.strobe-statement.org)
TraCS	N.C. Translational and Clinical Sciences Institute (tracs.unc.edu)
UNC	The University of North Carolina
UNCH	UNC Hospitals

1. Protocol Synopsis

Title	Improving Providers' Decision-Making and Reducing Information Overload Using Information Visualization in EHRs
Study Description	<p>Electronic Health Records (EHRs) are a major source of data for ICU clinicians. Synthesizing complex, electronic patient data is key to effective care delivery. EHRs contain both a record of past medical data and present continuous flows of new clinical data from various sources such as physiological inputs, laboratory results, imaging studies, and clinician notes. This complex, continuous stream of patient data can contribute to information overload, which can create barriers to the key cognitive tasks of data identification, extraction, and interpretation. Intensive Care Unit (ICU) providers must quickly synthesize data from more than 200 variables during critical care rounds, with critically ill patients generating a median of 1348 individual data points per day. Information overload has been identified as a key factor in the misinterpretation of data, leading to medical errors such as misdiagnoses. Improving our understanding of information overload—and investigations into new efforts to minimize it—can improve clinician workflow and productivity as well as patient safety. The objective of this study is to explore the impact of current data representation in the EHR on ICU clinicians' cognitive workload, performance, and satisfaction. The research design uses a mixed methods approach, including eye-tracking assessment and surveys, to assess the efficacy of current EHR interfaces for ICU clinicians in live and simulated environments.</p>
Specific Aims (objectives)	<p>Aim 1. Characterize the effect of EHR information overload on the quality of care by measuring prescribing providers' performance, information seeking load, and information processing load using real-time patient data in institutional Epic® and Cerner® EHR in a laboratory setting.</p> <p>Aim 2. Evaluate the effect of information visualization on providers' decision making, performance, efficiency, fatigue, workload, and satisfaction using real patient data in a randomized controlled trial.</p> <p>Aim 3. Determine the acceptability, ease of use, and barriers to implementing information visualization dashboards into practice in an ICU setting, using guided interviews with ICU providers.</p>
Target Population	<p>Eligibility Criteria</p> <p>Aim 1: Inclusion criteria: Must be an ICU physician or advanced practice provider (APP), be in active full time ICU service, use an institutional EHR (Epic or Cerner) to deliver care, and read/speak English.</p> <p>Aim2: Inclusion criteria: Must be an ICU physician or APP, be in active full time ICU service, use an institutional EHR (Epic or Cerner) to deliver care, and read/speak English.</p> <p>Aim3:</p>

	Inclusion criteria: Must be an ICU physician or APP, be in active full time ICU service, use an institutional EHR (Epic or Cerner) to deliver care, organizational IT leaders, and read/speak English.
Numbers of Enrollees	A total of N = 280 eligible individuals will be enrolled in the study.
Interventions and Exposures/Conditions	<p>Study Design for Aim 1 We will conduct a multi-site, cross-sectional usability assessment of information overload in two leading EHRs (Epic and Cerner) at four sites among ICU providers (20 per site, total n=80). The eye-tracking hardware (Tobii pro eye tracker) will be mounted on the computer monitor. We will use 4 ICU patient profiles (i.e., vignettes) with 2 typical (“standard”) ICU patient profiles and 2 high-risk (“complex”) profiles. At the start of the study, participants (N=80) will log into their institution’s EHR system (Epic or Cerner) and answer a series of questions in response to the 4 patient profiles, which will be presented in random order. Upon completion of the study protocol, each participant will receive a \$100 gift card.</p> <p>Study Design for Aim 2. Using the same recruitment methods from Aim 1, we will randomize consented participants into two groups: control (EHR) group (n=15) and intervention (AWARE) group (n=15). Providers in each group will review four patient profiles and will perform the same rating tasks and complete survey instruments (30 per site, total n =120). Providers in the control groups will review the patient cases in their institution EHR (Epic or Cerner), and providers in the intervention group will review the same patient cases but in AWARE. The control group will navigate through the EHR as per their usual routine in the ICU, with no added training sessions before the study. The intervention group will receive a short training presentation by the PI, explaining the functionality and design of AWARE. Each participant will be compensated with a \$100 gift card.</p> <p>Study Design for Aim 3. A qualitative study will be conducted at all four study sites with participants from Aim 2 (20 per site, total n=80) to determine their overall experience with the institutional EHR and/or AWARE, challenges in both environments, and possible solutions. All interviews will take place in a private room in a laboratory setting directly following Aim 2. We developed an in-depth, semi-structured interview guide to elicit provider perceptions on locating information in the EHR and in AWARE and the benefits and barriers of features in the EHR compared to AWARE. Interview participants will be offered \$50 gift card as compensation for their time.</p>
Outcome Measures	<p>For Aim 1. Primary outcomes are the number of correct decisions, time to make a decision, number and severity of errors, the number of eye fixations during each task. Secondary outcome will be EHR workload and usability using NASA-TLX, SUS, NFCC, and POMS respectively.</p> <p>For Aim 2. Primary outcomes will be number of correct responses, time to making decisions, time to case completion, number of clicks per case,</p>

	<p>total pupil constriction per case, and per question. Secondary outcomes are perceived workload, cognitive closure, and satisfaction.</p> <p>For Aim 3. We will look for themes around the acceptability of using information visualization, and challenges in learning how to use and integrate visualization tools.</p>
<p>Statistical Analysis Plans for Each Aim</p> <p>Yellow highlights potentially to be deleted</p>	<p>Aim 1 Plans. Each participant will receive a single score for each question determined by the domain expert (0: incorrect, 0.5: partial, 1: correct). Correct decisions are the aggregate of the correct answers, and errors are the aggregate of the incorrect answers. For each participant, we will compute a score for each patient case and a total score for all the patient cases. Case scores will depend on the number of tasks, such that if a case has ten tasks to be completed, the total score of this case will be equivalent to the highest possible points (10).</p> <p>Eye-tracking data gives the frequency and duration of fixations for each participant. We will calculate participants' fixation points based on 1) total fixations for the study, 2) total fixations per patient case, and 3) total fixations per EHR screen visited. We will compute descriptive statistics for patient and case characteristics, employing Chi-square tests, t-tests, and ANOVAs to examine between-group differences, where appropriate. We will examine differences between provider types (physicians and APPs), as well as between sites (Epic and Cerner). Given the nested nature of the data (i.e., repeated case assessments nested within providers), we will use multilevel modeling as the primary analytic approach. Each patient case will be coded based on the days of ICU stay and the presence or absence of key characteristics such as vent settings and inputs/outputs, to determine the level of complexity. Case variables will be entered into the model as case-level (Level 1) predictors. Models will also account for person-level (Level 2) factors such as participant gender, age, clinical role, site, and years of EHR experience. Person mean centering of Level 1 variables will be used to disentangle within- vs. between-person effects and group mean centering of Level 2 effects will be used to facilitate model convergence and interpretation. For each outcome, we will first examine an intercept-only model and compute the intraclass correlation (ICC) to characterize Level 2 variability. Next, we will examine each person level and case level variable in a separate unadjusted model, treating the intercept as a random effect. We will then compute a combined effects model that will include significant univariate predictors ($p < .05$) and a set of key covariates selected a priori (e.g., gender, clinical role). Chi-square difference testing and the Bayesian information criterion (BIC) will inform the selection of each final combined effects model. We will use SAS 9.4 using PROC MIXED for continuous outcomes and SAS PROC GLIMMIX for binary and count outcomes.</p> <p>Aim 2 Plans. As in Aim 1, we will examine descriptive statistics for both the case and participant characteristics and use multilevel modeling to assess the effect of case-level (e.g., complexity) and person-level (e.g., gender, professional roles, site) factors on the outcomes of interest</p>

	<p>(decision accuracy, usability, fatigue, clicks, time). Exploratory interaction testing between the intervention variable and key case level variables will also be tested. The same bottom-up building approach with comparative model fit testing and variable centering as used in Aim 1 will be used. A focus in the models will be the effect of the intervention (AWARE) versus control (EPIC or Cerner). We will use SAS 9.4 using PROC MIXED for continuous outcomes and SAS PROC GLIMMIX for binary and count outcomes.</p> <p>Aim 3 Plans. Our analysis will follow an inductive approach, with the individual interview participant as the unit of analysis. Eighty interviews will be transcribed by a transcription service using a qualitative management tool. All interviews will be coded independently by two coders supervised by a qualitative research expert from the UNC Odum Institute, using a standard codebook derived from the data by the qualitative expert. The codebook will be developed based on the research questions, topics from the interview guide, and initial readings of transcripts by the research team. The two coders will pilot-test the initial codebook by independently coding two provider transcripts and then comparing their results to fine-tune the codebook. Concept definitions and decision rules may be revised as needed, and the enhanced version of the codebook applied to the remaining transcripts. Coding discrepancies will be reconciled by discussion and consensus.</p>
Study Duration	~ 4 years
Participation Duration	~1 month
Enrollment Duration	~3 months

2. Introduction

2.1. Background Information

Purpose

To investigate the efficacy of novel information visualization methods to improve ICU providers' decision-making, efficiency, and satisfaction.

Participants

Physicians and advanced practice providers (APPs) working in the intensive care unit (ICU).

Procedures (methods)

We will recruit ICU providers from four academic medical centers: two Epic® sites (UNC, Mayo Clinic) and two Cerner® sites (MedStar, University of Pittsburgh). The first study will aim to characterize the effect of current EHR information overload on providers' information processing abilities. Second, we will test the efficacy of using an information visualization dashboard to improve ICU provider decision-making, efficiency, and performance as compared to their current EHR system. Third, we will conduct guided interviews to understand providers' perceptions around the implementation and use of visualization dashboard in real-world ICU settings.

Specific aims

- (1) Characterize the effect of EHR information overload on the quality of care by measuring prescribing providers' performance, information seeking load, information processing load using real-time patient data in institutional Epic® and Cerner® EHR in a laboratory setting.
- (2) Evaluate the effect of information visualization on providers' decision making, performance, efficiency, fatigue, workload, and satisfaction through real patient data in a randomized controlled trial.
- (3) Determine the acceptability, ease of use, and barriers to implementing information visualization dashboards into practice in an ICU setting, using guided interviews with ICU providers.

Background

Multiple studies indicate that the sheer volume of information that medical care providers must sift through within the typical EHR system can result in "information overload", which is when an individual becomes so overwhelmed with the sheer volume of information that they are unable to optimally absorb and synthesize the data provided. Overload in the context of the EHR system appreciably affects both provider well-being and patient care by causing delays in care, medical errors, and unanticipated patient safety events, especially in high-risk environments. Although, it is evident that information overload has very real negative consequences, there is currently a paucity of information on the mechanism of action between EHR system interfaces and information overload. In this study, we will employ novel eye-tracking methods to understand the effect of the current EHR system design and visualization dashboard on providers' cognition, performance, and fatigue. Eye-tracking (the study of eye movement) and pupillometry (the measurement of pupil size) have been used to study information processing in many non-clinical domains. In biomedicine, eye-tracking has been used to understand factors associated with the interpretation of radiological studies, identification of medication allergy, reading EHR progress notes, and physician attention during surgery. We propose to characterize information overload using eye-tracking as an innovation of this study. Also, studying information seeking and decision-making across two groups of prescribers (physicians and APPs) adds a new body of knowledge around differences in information needs between groups.

2.2. Scientific Rationale

Information overload and EHR disorganization are common complaints from EHR users, and present significant challenges to ICU providers, especially regarding risks to patient safety. When a person experiences information overload, their cognitive load reaches its maximum capacity, and their performance degrades in an inverted U-shape. This phenomenon might explain a provider's inability to integrate information into the decision-making process and can lead to confusion, stress, and difficulty remembering prior information.

Providers report spending 44% of their time searching for information on computers, compared to 24% communicating with patients. In addition to limiting communication with patients and the ensuing emotional distress, inadequate EHR design, coupled with its inherent information overload, inflates the probability of medical errors. In ICUs, EHR use can disrupt clinical workflow and contribute to an increase in patient safety risks. A current weakness in EHRs is the number of variables presented to providers; moreover, the way data is represented through the EHR interface leads to information overload, suggesting the need for improved EHR information representation. Aim 1, an observation of the current opinions and functionality of the EHR, will be used to prepare for a full-scale RCT in aim two where we will compare the current EHR interface to a new visualization dashboard. In aim 2, we will recruit full-time ICU providers so that they are clinically trained and competent.

3. Specific Aims

3.1. Aim 1

Aim 1: Characterize the relationship between EHR information overload on the quality of care by measuring prescribing providers' performance, information seeking load, information processing load using real-time patient data in institutional Epic® and Cerner® EHR in a laboratory setting.

3.2. Aim 2

Aim 2: Evaluate effect of information visualization on providers' decision making, performance, efficiency, fatigue, workload (NASA-Task Load Index), and satisfaction (Computer System Usability Questionnaire) using real patient data in a laboratory setting in a RCT comparing usual EHR to visualization dashboard.

3.3. Aim 3

Aim 3: Understand the acceptability, ease of use, and barriers to implementing information visualization dashboards into practice in an ICU setting using guided interviews with ICU providers and leadership.

4. Study Design

Study Design for Aim 1

We will conduct a multi-site, cross-sectional usability assessment of information overload in two leading EHR systems (Epic and Cerner) at four sites among ICU providers. After obtaining informed consent, we will recruit providers (20 per site, total n=80) for a one-hour individual session conducted in each institution's labs for simulation-based studies (e.g., UNC School of Nursing Biobehavioral Laboratory; BBL). We will use the standard computer screen used in each practice setting, with ICU-like ergonomic placement, ambient lighting, and seating. The eye tracking device (Tobii pro eye tracker) will be mounted on the computer monitor. We will use 4 real-time ICU patient profiles based on 2 typical ("standard") ICU patient records and 2 high-risk ("complex") ICU patient records. These high-fidelity patient cases will be developed by a critical care physician domain expert in collaboration with the study team. We will ask each participant a series of standard questions during and after their review of the patients. Before each session, site PIs will explain the study and consent forms to providers, assuring them that the study aims to assess EHR usability rather than a provider's clinical knowledge. Each provider will log into their institution's EHR environment in which the 4 ICU patient records are presented in random order to eliminate potential order effects resulting from specific case content. Participants will review one patient chart at a time and upon completion of chart reviewing, the research assistant (RA) will begin a series of Q&A for the participants to provide their assessment on the case. Participants will then move on to the next patient record, surveys will be distributed at the end of the four cases to avoid disruption. Upon completion of the study protocol, participants will receive a \$100 gift card. To identify and address possible issues with the study protocol, UNC will be the first study site.

Study Design for Aim 2. After completing the recruitment procedures, we will randomize consented participants (30 per site, total n=120) into two groups: control (EHR) group and intervention (AWARE) group. During the RCT, participants in each group will review the same patient records, perform the same tasks and complete the same survey instruments. Participants in the control group will review the patient cases in their institution EHR (Epic or Cerner), and providers in the intervention group will review the same patient cases but in AWARE. Participants in the control group will navigate through the EHR as per their usual routine in the ICU, with no added training sessions before the study. The day before each intervention session, the RA will send an email to the participants with a short demonstration video of AWARE to introduce them to the tool. The day of their session, intervention participants will receive a short training presentation that further explains the functionality and design of AWARE. The study will be conducted in simulation or biobehavioral labs at each site. We will follow the same study protocol as Aim 1. The PI will explain the study procedure and obtain consent. During the session, participants will review 4 patient cases in a training environment of either the institutional EHR or AWARE. Cases will be presented in random order for each participant to avoid selection or order bias. After usability testing, we will ask the participant to fill out the NASA-TLX survey, Profile of Mood States (POMS), and the Computer System Usability Questionnaire (CSUQ). After completing the study, each participant will be compensated with a \$100 gift card.

Study Design for Aim 3. participants from Aim 2 (20 per site, total n=80) will be recruited to participate in a qualitative interview to determine their overall experience with the institutional EHR and/or AWARE, challenges in both environments, and possible solutions. All interviews will take place in a private room in a laboratory setting directly following Aim 2. We developed an in-depth, semi-structured interview guide to elicit provider perceptions on locating information in the EHR and in AWARE and the benefits and barriers of features in the EHR compared to AWARE. The PI, who has training in interviewing, will conduct in-person, audio-recorded interviews, lasting approximately 30-60 minutes. One RA will be present during the interviews for notetaking. Interview participants will be offered \$50 gift card as compensation for their time. Interviews will be transcribed verbatim using a transcription service, and the PI will review transcripts for accuracy.

4.1. Treatment Design

In aim 2, we will randomly assign providers to either the control group (traditional EHR) or the experimental group (visualization dashboard). This is a controlled, cross-sectional, randomized study.

Aim one and three will be observational – we will use aim one as a quantitative basis for aim two; and aim three for a qualitative response after people have participated in aim two. Data will be collected prospectively, it is cross-sectional, and descriptive.

4.2. Experimental Design

Aims 1 and 3 are observational studies.

Only applicable for aim 2 – participants will be randomly assigned to the control vs the experimental group. All other aims are not interventional.

4.3. Measurement Design

Table 1. Variables of interest: their occasions of evaluation, their uses for the aims, their roles in the study

Variables within Domains	Scale ¹	Occasions ²	Aims ³	Main Roles
Identifiers				
Participant's unique ID	nominal	all	all	identifier
Treatment Regimen (AB or BA)	binary	E	all	identifier
Provider Characteristic				
Age	decimal yrs	0	all	Stratification
Sex	categorical	0	all	Screening/ Stratification
Specialty	binary	0	all	Screening / stratification
Professional role	categorical	0	all	stratification
Topic experience	Years	0	all	Stratification
Topic use	hours	0	all	stratification
Eye-Tracking				
Fixation Points	Continuous	-	Aim 1,2	Observational / interventional uses
Pupil Size	Continuous		Aim 1,2	Observational / interventional uses
Decision-Making				
Correct Responses	Continuous		Aim 1,2	Observational / interventional uses
Errors	Continuous		Aim 1,2	Observational / interventional uses
Usability				
Time to complete a task	Continuous		Aim 1,2	Observational / interventional uses
Mouse clicks	Continuous		Aim 1,2	Observational / interventional uses

Provider-Reported Outcomes				
NASA TLX	ordinal		Aim 1,2	exploratory uses
Computer System Usability Questionnaire (CSUQ)	ordinal 0-10		Aim 1,2	exploratory uses
Profile of Mood States (POMS)	ordinal 0-4		Aim 1,2	

¹ Units of measurement or the scale.

² Occasions of evaluation or retrieval:

³ The specific aims in which the variable will play a role in data analyses.

⁴ Uses: assess visualization effect, and exploratory analyses

In Table 1, the treatment regimens are:

A = visualization dashboard,

B = placebo.

Recruitment and randomization will be stratified by smoking status.

5. Study Participants

5.1. Numbers of Participants

5.1.1. Number to be screened: 500

5.1.2. Number to be enrolled: N = 280

The number to be enrolled is ~280. Participants who drop-out or have missing data will not be replaced.

We will be recruiting providers from the MICU. The study will only take one hour of their time, we are not expecting many people to drop out during that time.

Aim 2 involves an intervention, 15 will get control, 15 will get random.

5.2. Eligibility Criteria

Aim 1:

Inclusion criteria: ICU physicians and APPs, active full time ICU service, use an institutional EHR (Epic or Cerner) to deliver care, and reads and speaks English.

Exclusion criteria: Use of prescription glasses during the study session.

Additionally, the recruitment email states that participants must be able to view Epic without the use of prescription glasses. Contact lenses are acceptable, or participants may use the prescription lenses associated with the eye-tracker.

Aim2:

Inclusion criteria: ICU physicians and APPs, active full time ICU service, use an institutional EHR (Epic or Cerner) to deliver care, and reads and speaks English.

Exclusion criteria: Use of prescription glasses during the study session.

Additionally, the recruitment email states that participants must be able to view Epic without the use of prescription glasses. Contact lenses are acceptable, or participants may use the prescription lenses associated with the eye-tracker.

The exclusion criteria will be listed in the recruitment material.

Aim3:

Inclusion criteria: ICU physicians and APPs, active full time ICU service who use an institutional EHR (Epic or Cerner) to deliver care, organizational leaders, and reads and speaks English.

5.3. Enrollment/Selection Strategies

5.3.1. Prospective Recruitment -or- Retrospective Selection

Prospective recruitment

5.3.2. Screen Failures

Screen failures will simply not move forward with scheduling. We do not expect ineligible people to apply to the study, as the group we are looking for is very specific.

5.4.Strategies for Retention

The study will only take ~1 hour per individual, and they will only be assessed once (unless they reapply for a second aim). The offer of the \$100 gift card will hopefully encourage people to maintain their participation in the study. Aim 2 and 3 will be conducted as part of the same study session to maximize recruitment and retention for Aim 3.

5.5. Matching and Stratification

There will be no matching or stratification of participants per cohort.

5.6. Randomization and Concealment

For Aim 2, each study site team will be responsible to randomize participants into either a control or intervention group. Prior to data collection, a participant randomization list will be generated using an online random number generator that derives its randomness from atmospheric noise (random.org). At the time of enrollment, a participant will be assigned to participate in whatever condition assignment is provided next in the list of randomly ordered condition assignments.

5.7. Blinding

Participants will be blinded to the study arms they are assigned to. In addition, post-experiment debrief with participants will be delayed until data collection is completed to reduce the possibility of study assignment contamination (i.e., past participants discussing details of the study with potential future participants).

6. Treatment Design: Procedures

Description

Aim one – survey of a cohort / comparisons between sites

Aim two – randomized experimental design

Aim three - survey of a cohort / comparisons between sites

Storage All data will be stored securely on our UNC approved OneDrive or on physical hard drives that will be kept in a locked location.

7. Schedule of Activities and Procedures

7.1. Table of Events

Table 3. Schedule of activities and procedures for a randomized clinical trial (Aim 2)

Procedure		Visit 0 Screening (prior to all aims)	Visit 1 (aim one)
Recruit a Sample of Patients	Informed consent	X	X
	Eligibility assessments	X	
	Enrollment and randomization	X	
Intervention	Administer regimens		X
Provider Reported Outcomes	Quantitative response		X
	Survey responses		X

7.2. Screening

Participant screening is anticipated to begin within 28 days of the study beginning at each site. For each potential participant we will use the eligibility criteria to determine if they are a provider within a MICU and otherwise fit study inclusion criteria. If they meet all screening criteria, we will follow up to schedule a study visit.

7.3. Enrollment

Once general eligibility is confirmed, and the eligible participant agrees to participate, we will confirm MICU employment via web search or via the individual's home institution.

7.4. Study Visits

There will be two visits for data collection to each site (one per aim). Each participant will only be seen once. During each visit (for aim one and two) we will consent the participants, affirm they meet inclusion criteria, go through the case files, record qualitative data, have the participants take a survey, and then debrief. Departmental flyers and emails will be sent to providers with a link to a short eligibility survey. Only eligible individuals will be contacted by the RA for recruitment into the study. Then, the provider will indicate to the RA possible good times for a one-hour session. When the participant arrives at the lab, the TR will consent the participant. Then, the RA will take baseline measurements of the participant's pupil size. Afterwards, the participant will complete 4 patient cases and then complete a usability survey. Participant institutional emails will be recorded to avoid recruiting the same participants from aim 1 for aim 2.

Aim three will require an additional interview directly (or shortly) following aim two, during the same visit.

7.5. Final Visit

The final visit will be the last visit described above under study visit, this will take place in 2023.

7.6. Phone Contacts

No phone contacts will be collected, we will be recruiting via survey and then following up via email (which will be provided on the survey).

7.7. Follow-Up Contact

Not applicable

7.8. Early Discontinuations

Data to be Collected The data collected during any/all interactions will be recorded. No data outside of this study will be collected.

Criteria for Intervention Discontinuation The intervention would only be discontinued at the participants' choice or if they no longer met the inclusion criteria by time of data collection (which should not happen in the small window between recruitment and data collection).

7.9. Enrollees May Drop Out

Participants may voluntarily withdraw from participation at any time, for any reason, with no penalty or loss of rights. The reasons for drop-out and missing data will be documented and recorded. We will not likely follow up with those who discontinue participation, as this study only involves one session per participant.

8. Statistical Analysis Plans

8.1. Strategies that Apply to all the Aims

- To help ensure replicability of the research, the analysis plans will be reviewed and finalized prior to collection of data (a priori). For each specific aim, the analysis plans specify detailed steps for obtaining estimates of the population parameters of interest and for making inferences.
- Human studies are prone to drop-out, missing data, and interval-censored values. Best practices for dealing with incomplete data will depend on the documented causes of those occurrences. In the analysis plans established a priori, the strategies for coping with incomplete data will be based on anticipated causes. Alternative methods for dealing with incomplete data will play important roles in the sensitivity analyses.
- The analyses for aim 1 and 2 will focus on the magnitude and direction of point- and interval-estimates of the population parameters of interest. To indicate precision, all statistical estimates of population parameters will be tabulated along with corresponding 95% confidence intervals (CI). The CI will be interpreted as the set of potential values of the population parameter that are most compatible with the observed data.
- All hypothesis tests yielding large p-values will be reported as being inconclusive. For all sample sizes, all hypothesis test procedures are (by design) incapable of establishing that the null hypothesis is true.
- If p-values are computed they should be reported to several decimal places without categorizing or dichotomizing the p-value; that is, the words "significant" and "non-significant" will be avoided. The p value will be reported and interpreted as a continuous measure indicating the availability of information

against the (null) hypothesis being tested. The available amount of information against the null hypothesis is equal to the Shannon Information S-value, and the p-value = ($\frac{1}{2}$) S-value. Smaller p values (larger S values) indicate greater amounts of available information. Larger p values indicate a lack of information (e.g., if $p = 1$ then the $S = 0$. If $p = 0.03125$ then $S = 5$, which indicates a result that is as-surprising-as observing 5 ‘heads’ in a row when flipping a coin 5 times to test whether it is a fair coin). Due to lack of information, large p-values cannot be used to draw any conclusions as to whether the tested null hypothesis is true or false. Lack of availability of evidence of an effect is not evidence of a lack of effect.

- The proposed statistical analysis strategy acknowledges that no p-value can reveal the plausibility, presence, truth, or importance of an association or effect, which is consistent with the statements of the American Statistical Association [4,5], recommendations in the scientific journal *Nature* [6,7], and scientific reporting guidelines, such as the CONSORT Statement [1], STROBE Statement [2], and ICMJE guidance [3].
- The analysis plans will include outcome-dependent exploratory analyses to generate new hypotheses.
- Graphical methods such as forest plots will be used to visualize the analysis results.

8.2. Sample Description

Descriptive statistical methods will be used to describe the sample of individuals studied; they include graphical figures, counts, frequencies, sample means, sample standard deviations, percentiles, min, max, and standardized differences.

In aim 2, comparisons of treatment arms on baseline/pre-treatment characteristics will rely on standardized differences; use of p-values is highly inappropriate and should be avoided.

In aim 1, comparisons of cohorts on initial/baseline characteristics will rely on standardized differences; use of p-values is not useful for identifying confounders and should be avoided.

8.3. Aim-Specific Plans

Aim 1

Given the nested nature of the data (i.e., repeated case assessments nested within providers), we will use multilevel modeling as the primary analytic approach. Each patient case will be coded based on the days of ICU stay and the presence or absence of key characteristics such as vent settings and inputs/outputs, to determine the level of complexity. Case variables will be entered into the model as case-level (Level 1) predictors. Models will also account for person-level (Level 2) factors such as participant gender, age, clinical role, site, and years of EHR experience.

For each outcome, we will first examine an intercept-only model and compute the intraclass correlation (ICC) to characterize Level 2 variability. Next, we will examine each person level and case level variable in a separate unadjusted model, treating the intercept as a random effect. We will then compute a combined effects model that will include significant univariate predictors ($p < .05$) and a set of key covariates selected a priori (e.g., gender, clinical role). Chi-square difference testing and the Bayesian information criterion (BIC) will inform the selection of each final combined effects model.

Aim 2

Exploratory interaction testing between the intervention variable and key case level variables will also be tested. The same bottom-up building approach with comparative model fit testing and variable centering as used in Aim 1 will be used. A focus in the models will be the effect of the intervention (AWARE) versus control (EPIC or Cerner).

Aim 3

All interviews will be coded independently by two coders supervised by a qualitative research expert from the UNC Odum Institute, using a standard codebook derived from the data by the qualitative expert. The codebook will be developed based on the research questions, topics from the interview guide, and initial readings of transcripts by the research team. The two coders will pilot-test the initial codebook by independently coding two provider transcripts and then comparing their results to fine-tune the codebook. Concept definitions and decision rules may be revised as needed, and the enhanced version of the codebook applied to the remaining transcripts. Coding discrepancies will be reconciled by discussion and consensus.

8.4. Planned Interim Analyses

No interim analyses will be performed.

9. Sample Size Rationale

Aim 1, Statistical Power: The design effect arising from the clustering within-person inherent to the study's design is estimated using the following formula: $D_{eff}=1+(m-1)$, where m =average cluster size (4 cases) and p =ICC.

Assuming an ICC of .6 (a common ICC for similar intensive repeated measures designs), the application of this equation results in D_{eff} of 1.09, for an effective sample size of 294 ($320/2.8$). In a multivariable linear regression context assuming $N=114$, 5 person-level effects, 3 case level effects, a two-tailed critical $p = .05$, and 80% power, the minimum detectable effect size is Cohen's $f^2 = 0.10$, which is considered a small effect. In a multiple logistic regression with two tailed critical $p = .05$ and 80% power, the minimum detectable odds ratio is 3.23, which is considered a medium-sized effect.

Aim 2, Statistical Power: Assuming an ICC of .6 and 4 cases per participant, the design effect equation results in D_{eff} of 2.80, for an effective sample size of 171 ($480/2.80$). In a multivariable linear regression context assuming $N=171$, 6 person-level effects, 3 case level effects, a two tailed critical $p = .05$, and 80% power, the minimum detectable effect size is Cohen's $f^2 = 0.05$, which is considered a small effect. In a multiple logistic regression with two tailed critical $p = .05$ and 80% power, the minimum detectable odds ratio is 2.63, which is considered a small effect.

Aim 3 is qualitative research that requires no power analysis.

10. Data Capture and Database Management

10.1. Software for Data Capture

The study data will be entered into a REDCap database developed by the study personnel. REDCap is a 21 CFR Part 11-compliant data capture system provided by the NC TraCS Institute at UNC. The data system includes password protection and internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate. Study data will be entered directly from the source documents.

10.2. Responsibilities for Data Capture and Database Management

Data collection is the responsibility of the UNC team that will travel to each site to collect data. The investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.

All source documents should be completed in a neat, legible manner to ensure accurate interpretation of data. Hardcopies of the study visit worksheets will be provided for use as source document worksheets for recording data for each participant enrolled in the study. Data recorded in the electronic case report form (eCRF) derived from source documents should be consistent with the data recorded on the source documents.

The data system includes password protection and internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate.

10.3. Study Records Retention

All records will be kept until completion of data analysis and manuscript preparation (or after three years, whichever is sooner), they will then be destroyed.

11. Collection and Management of Tissue Specimens

11.1. Use in Current and Future Studies

Not applicable

11.2. Sample Preparation

Not applicable

11.3. Record Keeping and Monitoring

Not applicable

11.4. Storage and Security

Not applicable

12. Safety Monitoring and Management

12.1. Risk / Benefit Assessment

Potential Risks: The only risk is the potential breach of confidentiality, which is a very rare and mild risk. Data stored will not include PHI. We will only record and store provider-level data (such as time to complete a task, mouse clicks), as well as survey responses. The study does not use real patient records (no PHI) and therefore, the risks are not greater than minimal risks. Nevertheless, all study data will be stored and monitored by the PI and the study team. Data will be stored on a secure and HIPAA compliant UNC server (OneDrive) with access permissions to authorized personnel.

Potential Benefits: We anticipate that completion of this study will yield the following outcomes: 1) to add new knowledge around information overload-related patient safety risks in current EHRs; 2) to determine the efficacy of a visualization tool compared to prominent EHR interfaces Epic® and Cerner®; and 3) to create new knowledge around visualization implementation guidelines and usability best-practices. Because the visualization tool may improve the decision-making process for providers, we expect its use will increase patient safety and decrease the number of medical errors.

Participants will also receive compensation for their participation.

12.2. Assessment of Safety

Participants safety is our utmost priority. There is minimal to no risk to the participant during this study. They will be able to stop at anytime, for any reason. This is not a vulnerable population.

12.3. Unanticipated Problems, Adverse Events, Serious Adverse Events

Unanticipated Problems:

An unanticipated problem is any incident, experience or outcome that meets all three OHRP criteria (1) unexpected (in severity, specificity, frequency, or nature), (2) related or possibly related to the research, and (3) suggests the research places participants or others at greater risk than previously known or recognized.

Only a subset of adverse events will meet criteria for unanticipated problems. See: <https://ohresop.web.unc.edu/files/2018/04/1401-Reporting-New-Safety-Information.pdf> for current UNC IRB policies regarding identification, assessment, and reporting of adverse events.]

Adverse Event (AE) Definitions:

We do not expect any injuries as a result of participating in this study. In the case that there is, an adverse event form will be created to meet the goals of this data safety and monitoring plan and will be used by the study staff to report injuries or other adverse events that occur as a result of the intervention. The Data Monitoring Officer will review, collate, and evaluate all adverse and serious adverse events in real time. Any adverse events reported to the UNC IRB will also be reported to the NIH funding institute. All adverse events will be evaluated by the Data Monitoring Officer and the Principal Investigator within 72 hours; serious adverse events within 24 hours. Any study-related serious adverse event will be reported to the NIH funding institute within 2 weeks; all others will be included in the annual report to the NIH funding institute and the IRB. A safety report containing adverse events and event rates will be generated by the Principal Investigator every 6 months and reviewed by the Data Monitoring Officer at that time

12.4. Safety Monitoring

The intervention and measurement protocols pose minimal risk to participants. Because of this low risk status, the Data Safety Monitoring Plan (DSMP) for this trial includes monitoring by the principal investigator (PI), and prompt reporting of excessive adverse events and any serious adverse events to the NIH and to the IRB at the University of North Carolina- Chapel Hill.

The Data Monitoring Officer for the randomized trial will be Drs. Saif Khairat (PI) and Shannon Carson, a Professor and Chief of Critical Care and Pulmonary Medicine at the University of North Carolina- Chapel Hill. Dr. Carson is an MD and critical care physician with experience running randomized clinical trials. As Safety Officers, Drs. Khairat and Carson will review the reports sent by the PI (at the frequency outlined above) and will use a checklist to determine whether there is need for a corrective action that should be communicated to the study investigator, the University of North Carolina IRB, and the NIH funding institute.

12.5. Study Suspension / Early Termination of the Study

There are no foreseeable risks to participants from taking part in the study for the possibility of an early termination. The proposed study is a health promotion intervention study. Improving EHR information overload through understanding ways to redesign EHR interfaces has no potential negative health consequences. In this minimal risk study, it is very unlikely that an event would occur that would require stopping the trial. However, as previously described, we will monitor injury rates of all participants, and the Data Monitoring Officer, together with the study investigators will alert the university IRB and NIH funding institute if a larger than reasonably expected injury rate should occur among participants.













13. Regulatory, Ethical, and Study Oversight Specifications

13.1. Informed Consent Process

This study will comply with the regulatory requirements. Study consent will be provided prior to conducting study screening procedures and signed prior to beginning of the trial.

13.1.1. Consent/Assent and Documents Provided to Participants

Consent forms describing in detail the study intervention, study procedures, and risks are given to the participant and written documentation of informed consent is required prior to starting intervention/administering study intervention. The following consent materials are submitted with this protocol:

File Name	Document Type
 <u>Adult Consent Form aim 1 12.4.docx</u> Uploaded by: Saif Khairat On: 12/04/2020 At: 01:29:07 AM Included with the IRB Approval dated 08/18/2022	Adult Consent Form
 <u>Adult Consent Form aim 2 12.4.docx</u> Uploaded by: Saif Khairat On: 12/04/2020 At: 01:29:30 AM Included with the IRB Approval dated 08/18/2022	Adult Consent Form
 <u>Adult Consent Form aim 3 12.4.docx</u> Uploaded by: Saif Khairat On: 12/04/2020 At: 01:31:11 AM Included with the IRB Approval dated 08/18/2022	Other Consent Materials
File Name	Document Type
MedStar Health Research Institute	
 <u>Adult Consent Form aim 1 MedStar-- UNC IRB Required Revisions 05032022 Clean.docx</u> Uploaded by: Hannah Burgess On: 08/17/2022 At: 03:56:03 PM Included with the IRB Approval dated 08/18/2022	Local Consent Forms
 <u>Adult Consent Form aim 2 MedStar-- UNC IRB Required Revisions 05032022 Clean.docx</u> Uploaded by: Celeste Cantrell On: 08/12/2022 At: 09:28:45 AM Included with the IRB Approval dated 08/18/2022	Local Consent Forms
 <u>Adult Consent Form aim 3 MedStar-- UNC IRB Required Revisions 05032022 Clean.docx</u> Uploaded by: Celeste Cantrell On: 08/12/2022 At: 09:28:56 AM Included with the IRB Approval dated 08/18/2022	Local Consent Forms
University of Pittsburgh	
 <u>Adult Consent Form aim 1 UPMC Pitt HRP Reviewed-- UNC IRB Required Revisions 0081122.docx</u> Uploaded by: Celeste Cantrell On: 08/12/2022 At: 09:26:21 AM Included with the IRB Approval dated 08/18/2022	Local Consent Forms
 <u>Adult Consent Form aim 2 UPMC Pitt HRP Reviewed-- UNC IRB Required Revisions 0081122.docx</u> Uploaded by: Celeste Cantrell On: 08/12/2022 At: 09:26:30 AM Included with the IRB Approval dated 08/18/2022	Local Consent Forms
 <u>Adult Consent Form aim 3 UPMC Pitt HRP Reviewed-- UNC IRB Required Revisions 0081122.docx</u> Uploaded by: Celeste Cantrell On: 08/12/2022 At: 09:26:37 AM Included with the IRB Approval dated 08/18/2022	Local Consent Forms
Mayo Clinic	
 <u>Aim 1 consent form- Mayo Clinic.doc</u> Uploaded by: Hannah Burgess On: 08/17/2022 At: 03:53:30 PM Included with the IRB Approval dated 08/18/2022	Local Consent Forms
 <u>Aim 2 consent form- Mayo Clinic.doc</u> Uploaded by: Hannah Burgess On: 08/17/2022 At: 03:53:42 PM Included with the IRB Approval dated 08/18/2022	Local Consent Forms
 <u>Aim 3 consent form- Mayo Clinic.doc</u> Uploaded by: Hannah Burgess On: 08/17/2022 At: 03:54:12 PM Included with the IRB Approval dated 08/18/2022	Local Consent Forms

13.1.2. Consent Procedures and Documentation

Informed consent is a process that is initiated prior to the individual's agreeing to participate in the study and continues throughout the individual's study participation. Consent forms will be Institutional Review Board (IRB)-

approved and the participant will be asked to read and review the document. The investigator will explain the research study to the participant and answer any questions that may arise. A verbal explanation will be provided in terms suited to the participant's comprehension of the purposes, procedures, and potential risks of the study and of their rights as research participants. Participants will have the opportunity to carefully review the written consent form and ask questions prior to signing. The participants should have the opportunity to discuss the study with their family or surrogates or think about it prior to agreeing to participate. The participant will sign the informed consent document prior to any procedures being done specifically for the study. Participants must be informed that participation is voluntary and that they may withdraw from the study at any time, without prejudice. A copy of the informed consent document will be given to the participants for their records. The informed consent process will be conducted and documented in the source document (including the date), and the form signed, before the participant undergoes any study-specific procedures. The rights and welfare of the participants will be protected by emphasizing to them that the quality of their medical care will not be adversely affected if they decline to participate in this study.

13.2. Study Discontinuation and Closure

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to study participants, investigators, and the funding agency.

If the study is prematurely terminated or suspended, the Principal Investigator (PI) will promptly inform study participants, the Institutional Review Board (IRB), and sponsor and will provide the reason(s) for the termination or suspension. Study participants will be contacted, as applicable, and be informed of changes to study visit schedule.

Examples of circumstances that may warrant termination or suspension of the study include:

Criteria established in the MPD for early termination of the study have been satisfied

Detection of an unexpected unacceptable level of risk to participants

In preparatory (pilot) studies, futility due to insufficient adherence to protocol requirements

Unexpected inability to recruit participants

Study may resume once concerns about safety, protocol compliance, and data quality are addressed, and satisfy the regulatory oversight (e.g., DSMB, sponsor, IRB, FDA.)

13.3. Confidentiality and Privacy

Participant confidentiality and privacy is strictly held in trust by the participating investigators, their staff, and the sponsor(s) and their interventions. This confidentiality is extended to cover clinical information relating to participants. Therefore, the study protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party without prior written approval of the sponsor.

All research activities will be conducted in as private a setting as possible.

The study monitor, other authorized representatives of the sponsor, representatives of the Institutional Review Board (IRB), regulatory agencies may inspect all documents and records required to be maintained by the investigator. The clinical study site will permit access to such records.

The study participant's contact information will be securely stored at each clinical site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by the reviewing IRB, Institutional policies, or sponsor requirements.

Study participant research data, which is for purposes of statistical analysis and scientific reporting, will be transmitted to and stored at UNC. This will not include the participant's contact or identifying information. Rather, individual participants and their research data will be identified by a unique study identification number. The study data entry and study management systems used by clinical sites and by UNC will be secured and password protected. At the end of the study, all study databases will be de-identified and archived at UNC.

13.3.1. Certificate of Confidentiality

Not applicable

13.4. Future Use of Stored Specimens and Data

Data collected for this study will be analyzed and stored at UNC.

13.5. Key Roles and Study Governance

Principal Investigator	Medical Monitor
Saif Khairat, PhD, MPH, FAMIA , Associate Professor	Name, degree, title
UNC, School of Nursing	Institution Name
428 Carrington Hall, Campus Box 7460, Chapel Hill, NC 27599	Address
919-843-5416	Phone Number
Saif@unc.edu	Email

13.6. Safety Oversight

Safety oversight will be under the direction of a Data and Safety Monitoring Board (DSMB) composed of individuals with the appropriate expertise, including informatics and data science. Members of the DSMB should be independent from the study conduct and free of conflict of interest, or measures should be in place to minimize perceived conflict of interest. The DSMB will meet at least semiannually to assess safety and efficacy data on each arm of the study. The DSMB will operate under the rules of an approved charter that will be written and reviewed at the organizational meeting of the DSMB. At this time, each data element that the DSMB needs to assess will be clearly defined. The DSMB will provide its input to the institutional review board, and NLM program officer.

13.7. Clinical Monitoring Plan (CMP)

Clinical site monitoring is conducted to ensure that the rights and well-being of trial participants are protected, that the reported trial data are accurate, complete, and verifiable, and that the conduct of the trial is in compliance with the currently approved protocol/amendment(s), with International Conference on Harmonisation Good Clinical Practice (ICH GCP), and with applicable regulatory requirement(s).

- The Data Monitoring Officer for the randomized trial will be Drs. Saif Khairat (PI) and Shannon Carson, a Professor and Chief of Critical Care and Pulmonary Medicine at the University of North Carolina- Chapel Hill. Dr. Carson is an MD and critical care physician with experience running randomized clinical trials. As Safety Officers, Drs. Khairat and Carson will review the reports sent by the PI (at the frequency outlined above) and will use a checklist to determine whether there is need for a corrective action that should be

communicated to the study investigator, the University of North Carolina IRB, and the NIH funding institute.

- Independent audits will not be conducted.

13.8. Quality Assurance and Quality Control

Each clinical site will perform internal quality management of study conduct, data collection, documentation and completion. An individualized quality management plan will be developed to describe a site's quality management.

Quality control (QC) procedures will be implemented beginning with the data entry system and data QC checks that will be run on the database will be generated. Any missing data or data anomalies will be communicated to the site(s) for clarification/resolution.

Following written Standard Operating Procedures (SOPs), the monitors will verify that the clinical trial is conducted and data are generated and biological specimens are collected, documented (recorded), and reported in compliance with the protocol, International Conference on Harmonisation Good Clinical Practice (ICH GCP), and applicable regulatory requirements (e.g., Good Laboratory Practices (GLP), Good Manufacturing Practices (GMP)).

The investigational site will provide direct access to all trial related sites, source data/documents, and reports for the purpose of monitoring and auditing by the sponsor, and inspection by local and regulatory authorities.

13.9. Protocol Deviations

A protocol deviation is any noncompliance with the clinical trial protocol, International Conference on Harmonisation Good Clinical Practice (ICH GCP), or Manual of Procedures (MOP) requirements. The noncompliance may be either on the part of the participant, the investigator, or the study site staff. As a result of deviations, corrective actions are to be developed by the site and implemented promptly.

These practices are consistent with ICH GCP:

- 4.5 Compliance with Protocol, sections 4.5.1, 4.5.2, and 4.5.3
- 5.1 Quality Assurance and Quality Control, section 5.1.1
- 5.20 Noncompliance, sections 5.20.1, and 5.20.2.

It is the responsibility of the site investigator to use continuous vigilance to identify and report deviations within 90 working days of identification of the protocol deviation, or within 90 working days of the scheduled protocol-required activity. All deviations must be addressed in study source documents, reported to NIH National Library of Medicine Program Official and the Institutional Review Board at the University of North Carolina at Chapel Hill. Protocol deviations must be sent to the reviewing Institutional Review Board (IRB) per their policies. The site investigator is responsible for knowing and adhering to the reviewing IRB requirements. Further details about the handling of protocol deviations will be included in the MOP.

13.10. Publication and Data Sharing Policy

This study will be conducted in accordance with the following publication and data sharing policies and regulations:

National Institutes of Health (NIH) Public Access Policy, which ensures that the public has access to the published results of NIH funded research. It requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive PubMed Central upon acceptance for publication.

This study will comply with the NIH Data Sharing Policy and Policy on the Dissemination of NIH-Funded Clinical Trial Information and the Clinical Trials Registration and Results Information Submission rule. As such, this trial will be registered at ClinicalTrials.gov, and results information from this trial will be submitted to ClinicalTrials.gov. In addition, every attempt will be made to publish results in peer-reviewed journals. Data from this study may be

requested from other researchers 5 years after the completion of the primary endpoint by contacting the University of North Carolina at Chapel Hill .

In addition, this study will comply with the NIH Genomic Data Sharing Policy, which applies to all NIH-funded research that generates large-scale human or non-human genomic data, as well as the use of these data for subsequent research. Large-scale data include genome-wide association studies (GWAS), single nucleotide polymorphisms (SNP) arrays, and genome sequence, transcriptomic, epigenetic, and gene expression data.]

13.11. Conflict of Interest Policy

The independence of this study from any actual or perceived influence, such as by the pharmaceutical industry, is critical. Therefore, any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication, or any aspect of this trial will be disclosed and managed. Furthermore, persons who have a perceived conflict of interest will be required to have such conflicts managed in a way that is appropriate to their participation in the design and conduct of this trial. The study leadership in conjunction with the NIH National Library of Medicine has established policies and procedures for all study group members to disclose all conflicts of interest and will establish a mechanism for the management of all reported dualities of interest.

14. Additional Considerations

<insert text>

[This section should include a description of any additional considerations not currently covered in this protocol template, such as particular institutional or IRB-related requirements.]

15. References

<insert text>

[Include a list of relevant literature and citations for all publications referenced in the text of the protocol. Choose a consistent, standard, modern format. The choice might be dependent upon the required format for the anticipated journal for publication (e.g., N Engl J Med, JAMA, etc.).

The preferred format is International Committee of Medical Journal Editors (ICMJE).

Include citations to product information such as manufacturer's IB, package insert, and device labeling.]

[Example formats:

- **Journal citation**
Veronesi U, Maisonneuve P, Decensi A. Tamoxifen: an enduring star. J Natl Cancer Inst. 2007 Feb 21;99(4):258-60.
- **Whole book citation**
Belitz HD, Grosch W, Schieberle P. Food chemistry. 3rd rev. ed. Burghagen MM, translator. Berlin: Springer; 2004. 1070 p.
- **Chapter in a book citation**
Riffenburgh RH. Statistics in medicine. 2nd ed. Amsterdam (Netherlands): Elsevier Academic Press; c2006. Chapter 24, Regression and correlation methods; p. 447-86.
- **Web Site citation**
Complementary/Integrative Medicine [Internet]. Houston: University of Texas, M.D. Anderson Cancer Center; c2007 [cited 2007 Feb 21]. Available from: <http://www.manderson.org/departments/CIMER/>.
- **Electronic Mail citation**
Backus, Joyce. Physician Internet search behavior: detailed study [Internet]. Message to: Karen Patrias. 2007 Mar 27 [cited 2007 Mar 28]. [2 paragraphs]
- **References to package insert, device labeling or investigational brochure**
Cite date accessed, version number, and source of product information.]