MAYO CLINIC

General Study Information

Principal Investigator: Erin Barreto

Study Title: AKI in Care Transitions (ACT) Trial

Protocol version number and date: Version 1 and 12-21-2021

Research Question and Aims

Aim 1: Evaluate the feasibility and acceptability of the AKI in Care Transitions pilot and iteratively refine the intervention. Feasibility of the pilot will be quantified by the percentage of randomized AKI survivors who receive the full ACT intervention (nurse education visit, laboratory testing, pharmacist visit, primary care provider visit). Using encounter video recordings, and qualitative interviews with patients and clinicians, we will assess user interactions with the pilot intervention, tool fidelity, and acceptability of the intervention for patients and clinicians. Based on identified barriers and facilitators, the intervention will be iteratively refined for scaling and testing in a larger prospective clinical trial.

Aim 2: Generate preliminary estimates of the ACT intervention on clinical and patient-reported outcomes. We will conduct a pilot clinical trial in 50 patients over 18-months. Patients with severe AKI will be randomized 1:1 (25 per group) to either the control group (usual care) or the intervention group (ACT). In the intention-to-treat population, we will assess change in AKI knowledge from baseline to 30-days using a validated scale. Differences in other patient-reported and clinical outcomes will be characterized. The use of nephrotoxins will be quantified from reconciled medication lists. We *hypothesize* that the intervention group will experience improved AKI-related knowledge, processes of care, and outcomes compared to control patients.

Background and Significance

Significance

AKI affects approximately 1 in 5 hospitalized patients, with the risk much higher in patients with sepsis, shock, major surgery, or in the developing world[1,2]. In the hospital, AKI contributes to a 6.5-fold higher mortality, a 3.5-day longer length of stay, and $5 billion in hospital costs annually in the United States[1,3]. In the 80-90% of individuals who survive an AKI episode, the risk of chronic kidney disease (CKD) is 1.5-2.5-fold higher[4]. Even in those who have seemingly 'recovered' after AKI, 15% develop new stage 3 CKD 2.5 years after the event. This corresponds to a 3.8-5.9-fold higher risk than in patients without AKI[5,6]. Cardiovascular disease is also a frequent AKI complication. The pooled risk of major acute cardiovascular events was 1.4-fold higher in those with AKI than those without[7]. In addition to long-term, potentially irreversible CKD or cardiovascular disease, 49% of patients are rehospitalized within one year[8], a major contributor to poorer quality of life. In studies where a health utility indicator of 0 is consistent with death and 1 is perfect health, mean health utility scores in AKI survivors 2-6 months after the episode are between 0.4 and 0.68, significantly worse than age- and sex-matched controls in the general population[9–12].

AKI survivors at care transitions experience gaps in kidney-focused care that may affect long-term outcomes. Interventions that modify the transition conditions and provide a structured framework for post-AKI care can close gaps in quality. In patients with complex care needs, we and others have instituted care transitions programs that successfully limit deleterious outcomes. Generally, these programs include interventions that begin in the hospital and continue for 1-3 months after discharge. Efforts are targeted at medication self-

management, use of a patient-centered health record to facilitate care continuity, completion of timely follow-up with primary or specialty care, and knowledge of "red flag" symptoms and how to respond[13]. Care transition models like these, including those described by our team[14], have reduced emergency department visits, rehospitalizations, costs, and improved quality of life and self-rated health[13,15–17]. These cost-effective team-based strategies could be successfully leveraged to deliver better care for AKI survivors.

Preliminary data

Using data from the Rochester Epidemiology Project, we demonstrated that 30% of AKI Survivors (stage II or III, moderate or severe, respectively) failed to have a serum creatinine assessment and a healthcare visit in the 30-day interval after discharge. These would be considered basic elements of kidney health follow-up. Nephrology visits occurred in less than one-fourth of individuals, even when the time horizon was extended to one year or high-risk patients were considered (i.e., CKD, diabetes) (Manuscript in press at *Am J Nephrol*). Nephrotoxins are also a particular area of concern in AKI survivors, given they are one of few potentially modifiable determinants of long-term complications. We demonstrated that 87% of AKI survivors receive at least one potentially nephrotoxic medication in the 3-years after discharge. Each additional nephrotoxin was associated with a 1.3-fold higher risk of new or progressive CKD within 3-years (Manuscript under review at *Am J Nephrol*).

To address this unmet need for AKI survivor care, we developed the **A**KI in **C**are **T**ransitions (ACT) intervention with feedback from stakeholders in Nephrology, Pharmacy, Primary Care, Nursing, Informatics, and Administration. The focus is on the delivery of post-AKI care in the patient's medical home, primary care. This multicomponent strategy includes 1) use of an electronic health record (EHR) indicator to identify high-risk AKI survivors based on biochemical markers (serum creatinine increase, urine output decline), 2) Education about kidney health before discharge by nephrology nurses, 3) kidney function testing in the 7-14-days after discharge, 4) a post-hospital visit by a pharmacist within 7-14-days after discharge, and a 5) post-hospital visit by a primary care provider within 7-14 days after discharge (may be combined with the pharmacist visit). Specialty nephrology follow-up is at the discretion of the inpatient nephrologists or patient's PCP. The ACT intervention is a transitions of care support strategy where these bundle elements are recommended and made available to the care teams using electronic orders and clinical decision support, but ultimately at the discretion of the treating providers.

Pilot testing of each component of the ACT intervention began in April 2020 (IRB 20-004204). During the first phase of testing, the electronic health record indictor was optimized to identify candidate individuals for the ACT intervention. Alerts were manually validated and cross-referenced with clinical notes and nephrology service rosters. During the second phase of testing, the feasibility of the nurse education visit was evaluated. A nephrology nurse liaison successfully visited all 18 patients targeted for education. The nephrology consultation service, and by extension the nurse liaison, was not previously following 7 (39%) of these individuals. In the third testing phase, 11 individuals consented to participate and were placed on the AKI survivor care path. Of these individuals, one died before discharge, one was discharged on dialysis, and one did not receive education from the nurse liaisons before discharge. In the remaining eight patients, 100% completed an encounter with the PCP, a serum creatinine evaluation, and urinalysis within two weeks of discharge [median time to follow up 2 (IQR 1, 6) days]. Six (75%) completed an encounter with a pharmacist 5 (1, 10) days after discharge. Two (25%) patients consulted with an outpatient nephrologist on day one and day 22 after discharge, respectively. Over time, kidney health knowledge improved in the majority of patients. In the majority of patients who received education [from a nurse (phase 2) or a nurse + primary care provider +/- pharmacist (phase 3)], knowledge scores improved immediately after education delivery and remained improved for 2-4 weeks thereafter.

Study Design and Methods

Overall Design**:** We will conduct a single center randomized trial at the patient level comparing the ACT intervention to usual care in patients with Stage III AKI during a hospitalization. The study will assess the feasibility of the ACT intervention, and obtain preliminary estimates of its impact on kidney care quality metrics, patient-reported, and clinical outcomes. Also, as part of this trial, we will assess user interactions with the ACT intervention, tool fidelity, and acceptability of the intervention for patients and clinicians through direct observation and qualitative interviews. Data collection will include medical record review, interviews, and video/audio recording of the clinical encounters.

Setting: This pilot randomized clinical trial will occur at Mayo Clinic in Rochester, an academic medical center in Minnesota.

Sample, recruitment:

Clinicians: All clinicians responsible for caring for eligible patients will be considered for inclusion in the qualitative research. The research team has secured buy in from relevant stakeholder groups across the institution to pilot the ACT intervention. This includes support from leadership teams from hospital internal medicine, family medicine, subspecialty service lines (i.e., surgical services, cardiology), community internal medicine and primary care, nephrology, nursing, desk operations, and pharmacy, as well as relevant operational committees at the institutional level. Potential clinician candidates (e.g., nurse educators, physicians or advanced practice providers in primary care or nephrology, pharmacists) will be approached for participation before conducting an interview, direct observation, or recording an encounter with an ACT patient. Oral consent for participation will be obtained and only needs to occur one time per clinician (prior to the first study encounter they engage in). The clinician will have the option to consent to an interview, and/or direct observation or recordings (video/audio or audio only) of clinical encounters with enrolled patients. If the clinician agrees to recording of the clinical encounters at the time of oral consent, they may still decline at the time that the clinical encounter occurs. If the clinicians and patients agree to the recording, the study coordinator will start the recording before leaving the room. The participants can stop this recording (video, aimed at the desk, or audio when the video camera is aimed at the ceiling) at any time (the device has a large red start/stop button and an on/off indicator light). If the clinician declines to do the recording, they are still eligible for participation in other qualitative aspects of the study, including direct observations of the encounter with note taking by a qualitative analyst or a qualitative interview. Similarly, if the clinician declines to participate, the patient is still eligible for the study, but qualitative evaluations will be omitted. Clinicians will be informed that there is no monetary or other sort of reimbursement for participating in the trial and that participation will not affect their current or future employment or be shared with their supervisor.

Patients: Participants will be recruited from those identified by a developed electronic health record list of patients with AKI. Included individuals that populate the list are those with stage III AKI (severe) during a hospitalization based on serum creatinine rise or urine output decline[18] from Olmsted County. The EHR list which includes these criteria was developed, tested, and refined for accuracy and completeness as part of IRB 20-004204 (see above preliminary data). Screened individuals with dementia, those who are non-English speaking, or expected to dismiss to a skilled nursing facility at discharge will be excluded. Individuals who are expected to need dialysis at discharge or who are discharging on hospice will be excluded. If the patient is actively enrolled in the Primary Care Transitions Program at hospitalization they will be excluded. Recipients of any transplant, including solid organ, hematopoietic stem cell, or CAR-T, within 100-days of enrollment will also be excluded. Individuals may only be enrolled in the trial one time. Trained study team members will approach potential candidates during their hospitalization to obtain written informed consent. Individuals will be provided with information about the research, HIPAA Authorization, and IRB approved consent forms for review. Sufficient time will be allowed for discussion and patient questions. Patients will be informed that declining to participate in the study will not impact the care that they receive. Consent will be obtained in person where possible, but may be obtained via telephone call depending on the safest mode of contact due to

COVID-19. All consenting patients will be included in the clinical trial. No reimbursement or remuneration will be provided for participation.

Randomization: Should the patient consent to participate, the individual will randomly be assigned 1:1 to one of two groups, the ACT group (intervention) or usual care (control). Randomization will occur via sealed envelopes which will contain the randomization information. Based on our preliminary data, randomization will be stratified according to hospital service/source: hospital medicine/family medicine or other services. Individuals will be randomly allocated equally to the intervention or control groups within each stratum using a permuted block design with varying block sizes of between 2 and 4. The target sample size is 50 (25 per group). The study coordinator will disclose the group allocation to patients after completing standard informed consent for participation in clinical research including permission to use protected health information.

Intervention: The ACT intervention was approved by the Mayo Midwest Clinical Practice Committee and local discipline specific subcommittees (nephrology, primary care, pharmacy). The intervention workflow was developed and pilot tested as part of IRB 20-004204. A description of the intervention is undergoing peer-review for publication (Barreto, et al.). As outlined in the preliminary data, patients randomized to the ACT intervention receive a multicomponent transitional support bundle including 1) a consultation from nurse educators before discharge to deliver kidney health education using approved materials available for use by any Mayo Clinic provider or patient (http://intranet.mayo.edu/charlie/nephrology-hypertension-rst/education/patient/ , https://askmayoexpert.mayoclinic.org/topic/clinical-answers/cnt-20114555/sec-20114604), 2) coordinated appointments for post-discharge laboratory testing (serum creatinine and urinalysis with microscopy), a primary care provider visit, and a pharmacist visit within approximately two weeks of discharge. Each of these elements would be considered standard for an AKI survivor, but the ACT intervention aims to operationalize them more cohesively and consistently to facilitate the care transition. A note will be entered into the patient's EHR to communicate enrollment to the healthcare providers. As an example, a note that may be entered for an intervention patient could be as follows:

> "The patient has been enrolled in the ACT (**A**KI in **C**are **T**ransitions) trial because they were identified as having biomarker changes consistent with severe AKI (creatinine elevation or oliguria/anuria) and are not expected to leave the hospital on dialysis. They will receive kidney health education from a dedicated team nurse and the ACT team will prepare dismissal orders for a kidney function panel (extended electrolyte panel that includes serum creatinine), a urinalysis with microscopy, a visit with the primary care provider and a visit with an ambulatory care pharmacist for your consideration at dismissal summary signing. Please contact Erin Barreto 127-14124 if there are any questions or concerns."

A failsafe EHR clinical decision support tool exists to prompt these dismissal orders for care teams should they be discontinued. Individuals will also be enrolled in a 'care path.' This tool operates based on embedded rules in the EHR to deliver context appropriate prompts and resources for providers. The benefits of a 'care path' is that it is not affiliated with a specific encounter. It remains active for the patient regardless of setting (inpatient or outpatient) until the rule-based criteria are fulfilled (i.e., education delivered, visits ordered and scheduled, visits and tests completed). In the post-hospital primary care provider and pharmacist visits, a passive Epic 'best practice advisory' has been created to encourage care providers to address kidney function, education, medication management, blood pressure assessment and sick day counseling.[19] Institutional provider or patient resources on AKI survivor care are available for use in these visits (http://intranet.mayo.edu/charlie/nephrology-hypertension-rst/education/patient/ , https://askmayoexpert.mayoclinic.org/topic/clinical-answers/cnt-20114555/sec-20114604). A structured documentation template for visits has been developed. If deemed appropriate, nephrology referral will be coordinated by the PCP.

Control. Participants in the control group will receive no specific study-related intervention. AKI identification, patient education, and follow-up care will be at the discretion of the primary treating team. It is customary for these patients to receive some degree of laboratory monitoring and clinical follow-up in the post-

discharge period, but for this group, timing and components will not be standardized. Care providers have access to the same educational materials for providers and patients as in the intervention group. These are published on the Mayo Clinic intranet (http://intranet.mayo.edu/charlie/nephrology-hypertension-rst/education/patient/ , https://askmayoexpert.mayoclinic.org/topic/clinical-answers/cnt-20114555/sec-20114604).

Data collection

Individuals that consent to participate will be captured in the REDCap system. Those found to be ineligible or eligible but decline participation will be captured in a recruitment tracking log. Data sources for the study include medical record review, interviews, and direct observations or video/audio recordings of the clinical encounters. An overview of the data collection plan is outlined in **Table 1**.

Data will be abstracted from the EHR on patient demographics, comorbidities, attributes of the hospitalization, details about the episode of AKI and the degree of recovery by discharge, follow-up processes of care (laboratory assessments, visits), and clinical outcomes. Core data to be collected will include age, sex, height, weight, race/ethnicity, socioeconomic status, health literacy (using the Brief Health Literacy Screen), history of hypertension, diabetes, cardiovascular disease, chronic kidney disease, or other vascular diseases, hospital and intensive care unit length of stay, reason for admission (non-operative, operative), discharge disposition, whether nephrology was involved with the patient's care during the hospitalization, the severity of AKI, need for dialysis, and discharge kidney function. Select medication data will be collected at baseline (preadmission based on the documented medication list in the EHR), discharge, and 30-day follow-up. This will include the use of angiotensin converting enzyme inhibitors/angiotensin receptor blockers (ACEi/ARBs), sodium glucose co-transporter 2 inhibitors (SGLT2i), metformin, GLP-1 receptor antagonists, sulfonylureas, insulin, loop diuretics, thiazide diuretics, statins, aspirin, non-steroidal antiinflammatory drugs (NSAIDs). The total number of medications at discharge will be evaluated. Using previously described methods, EHR documentation for patients who complete a follow-up encounter with a health care provider (provider, pharmacist, or other), will be reviewed to identify medication discrepancies and drug therapy problems.[20] These will be catalogued for all medications and specifically nephrotoxic or renoprotective medications. Drug therapy problems will be categorized as pertaining to effectiveness, indication, safety, or adherence. Additional data elements may be abstracted from the electronic health record to support the study aims. Data will be collected in a secure REDCap database designed expressly for this study. REDCap (https://redcap.mayo.edu/redcap/index.php) is a secure, web-based application that is HIPA compliant and available 24 hours per day. Data will be managed by the trial statistician and the principal investigator.

Outcomes

Feasibility and acceptability: To assess the feasibility of the ACT intervention, we will evaluate the number of patients able to be successfully randomized during the study timeframe (intention to treat group). We will also determine the proportion of those randomized to the intervention group who complete the nurse education visit, laboratory testing, pharmacist visit, and primary care provider visit (per protocol group). For those who do not complete the full ACT intervention, we will characterize the attrition [i.e., change in goals of care/clinical status, inability to deliver education during hospitalization, inability to schedule post-dismissal visits, patient did not complete the post-dismissal visit(s)] Acceptability of the ACT intervention will be determined through the use of the "Was it worth it?" survey at follow-up[21], qualitative interviews with consenting clinicians and patients and an analysis of recordings (video/audio or audio) of the clinical encounter. Using a semi-structured interview guide, interviewees will be asked to describe their experiences with the structure and process of the ACT intervention and their sense of their outcomes. Interviews will be conducted in-person or over the phone. All interviews will be audio-recorded with permission and immediately transferred to secure and password-protected servers from which only authorized research personnel can conduct evaluations. Audio files will be transcribed verbatim by an approved Mayo Clinic transcription service.

The data will be held confidential and shared among the team members. Transcripts will then be reviewed by a trained qualitative analyst and codes will be assigned. Both deductive analysis (informed by theoretical frameworks) and inductive analysis (identification of emerging themes) will occur. Themes identified from patients and clinicians will be compared. The data will be used to refine the ACT intervention for future testing.

Study team members will review video/audio recordings to assess the impact of the ACT intervention on the encounter. Reviewer(s) will watch the video (if available) and read the transcripts for the clinical encounter. Based on the literature, encounters will be primarily evaluated for six elements of kidney health follow-up for AKI survivors: Kidney function, advocacy/education, medication reconciliation/review, blood pressure, sick day counseling, and a follow-up plan.[22,23] Twenty percent of the recorded encounters will be reviewed by two study team members independently and in duplicate. Concordance between individuals in assigned ratings of the six elements will be evaluated. If greater than 0.8, reviewers will be considered concordant and one study team member will evaluate the remaining encounters. If concordance is not met, an additional 20% of the included encounters will be evaluated in duplicate. The duration of time (minutes) spent on each element will be catalogued. Reviewers will record whether the clinician utilized the ACT 'best practice advisory' in the electronic health record, or any AKI or kidney health handouts or print or electronic materials during the clinical encounter. In primary care encounters, occasions where kidney health was discussed will be catalogued as clinician-initiated or patient-initiated.

Patient-reported outcomes: We will evaluate patient knowledge about AKI measured with an adaptation of the Kidney Knowledge Survey (modified KiKS; mKiKS). mKIKS assesses participants' objective knowledge about AKI causes, risk factors, and management.[25] Unanswered questions (missing data) on the mKiKS are assigned a score of 0, and the total score is used for comparisons. mKIKS will be evaluated at randomization and 30 +/- 7 days post-discharge in all patients. Quality of life will be assessed at randomization and 30 +/- 7 days post-discharge in all patients using the PROMIS Global 10 tool (v1.2). The aforementioned "Was it worth it?" survey will be performed at 30 +/- 7 days post-discharge.[21] Patient-reported outcomes will be collected in person or over the phone by a study team member (estimated time to complete in pilot testing is 15 minutes).

Clinical and process outcomes: Participants will be followed for 1 year post-discharge or until death or loss of follow-up within that timeframe. At 90-days, clinical outcomes to be assessed include Major Acute Kidney Event (MAKE) at 90-days, unplanned emergency department visit or rehospitalization. Incidence of de novo or progressive chronic kidney disease or death up to 12-months after discharge will be documented. Number of nephrotoxic medications, medication discrepancies, and drug therapy problems will be described. Process outcomes will include kidney laboratory assessments and their timing, clinician visits (e.g. with primary care provider, pharmacist, nephrologist), visit type (in-person vs telemedicine/virtual), and timing.

Table 1. Summary of study measures

Element	Source	Admission	Randomization	Discharge	Study follow-up visit (intervention patients only)	30-days	90-days	1-year
Sociodemographic factors, comorbidities	EHR	X						
Attributes of hospitalization and AKI episode	EHR			X				
Medication utilization	EHR	X		X		X		
Brief Health Literacy screen	Patient self-report		X					
mKiKS	Patient self-report		X			X		

PROMIS 10	Patient self-report		X			X		
Was it worth it?	Patient self-report					X[a]		
Encounter observation +/- video/audio recording	Direct observation				X[a]			
Qualitative interviews	Patient or clinician self report					X[a]		
MAKE, unplanned ED visit, rehospitalization	EHR						X	
CKD or death	EHR							X
Kidney laboratory assessments, outpatient clinician visits	EHR						X	
a: Intervention patients only								

Statistical analysis

Analysis plan: To describe the feasibility of ACT and generate preliminary estimates of the effect on patient reported and clinical outcomes, descriptive analyses will be conducted in three groups 1) the intention to treat population (anyone randomized), 2) the per protocol population (randomized patients who receive the assigned study intervention; in the case of ACT patients this would include completion of nurse education, laboratory testing, pharmacist visit, and primary care provider visit), and 3) the complete follow-up population (the per protocol population with follow-up patient reported outcomes at 30 +/- 7 days). Baseline characteristics will be described with means and standard deviations and counts and percentages and compared using t-tests and chi-squared tests, respectively. Any baseline imbalances ($p<0.05$) will be explored as a possible factor to adjust for when the outcome measures are analyzed. The CONSORT guidelines will be followed to transparently report study results.

AKI knowledge will be described between groups with the mean mKiKS score. In patients with incomplete follow-up, model imputation will be used to impute follow-up scores. Mean between-group differences in the total baseline and follow-up scores will be compared using the t-test or non-parametric Mann Whitney U test. An exploratory multivariable linear regression model will be fit with group assignment as the independent predictor of interest, mean follow-up knowledge scores as the dependent variable, and baseline scores as a covariate. Other variables to be considered will include age, sex, baseline health literacy, socioeconomic status, and baseline comorbidities, specifically CKD. Clinical outcomes up to 12-months will be compared with Cox proportional hazards models.

Sample Size: As a pilot clinical trial, we will include all eligible candidates during the enrollment period. Based on preliminary feasibility data, we estimate approximately 1-2 patients per week will be identified with the EHR trigger, of which 70% will be eligible, agree to participate in the trial, and have evaluable outcomes data. We, therefore, estimate enrollment of approximately 25 patients per group (50 total) during the 18-month study timeframe. A sample size of 25 participants per group would be sufficient to detect a mean difference of 2 points on the mKiKS score (12.5%), using a two-tailed alpha of 0.05 and 80% power, assuming a standard deviation of 15%. Results from this study will provide the necessary pilot data to inform future investigations.

Data safety monitoring plan

This study will employ a Data Safety and Monitoring Plan (DSMP) to guide our efforts to monitor participant safety, data completeness and adherence to study protocol. This study does not plan to employ a Data Safety Monitoring Board (DSMB). The decision not to establish a DSMB is based on the fact that: (1) this is not a Phase III clinical trial; (2) the study will not employ a high-risk intervention; (3) the study is not blinded (masked); and (4) the study does not involve vulnerable populations. The DSMP will monitor participant safety, data integrity, participant privacy, data confidentiality, and study documentation. The trial steering committee will review the plan during meetings (at least quarterly) until data collection and analysis are completed. Any potential adverse events will be entered into the study database and the Mayo Clinic IRB will be notified.

Protection of human subjects

This research could not practicably take place without the use of human subjects. Study launch, recruitment, participant consent, and data collection will be performed by study personnel with human subjects training and approvals. Study staff from Mayo Clinic will be responsible for coordinating human subjects research approvals and consent procedures for all participants.

The risks to participants are minimal. Study procedures include education, laboratory specimen collection and a healthcare visit consistent with routine clinical care. The ACT intervention aims to operationalize them more cohesively and consistently to facilitate the care transition. A potential risk to participants is a loss of confidentiality. This risk will be minimized by research procedures that outline consent requirements and processes, and data collection and data transfer systems that ensure secure storage and transmission and restrict access to approved members of the study team. This includes use of HIPAA compliant electronic data capture tool hosted by Mayo Clinic (Research Electronic Data Capture [REDCap]). Any research material outside of what is stored within this web-based interface will be maintained on a secure server beyond the Mayo Clinic firewall or in locked file cabinets All data collection and management will be obtained specifically for research purposes and only approved research personnel will have access to identifiable private information. Participants will be assigned a unique study number, which bears no relationship to personal identifiers including name, initials, address, telephone number, social security number, or patient number. This unique study ID will be used to identify participants in all computer files and analyses to maintain confidentiality. Completion of study questionnaires will be performed in private areas of the medical center either face-to-face or over the phone, to ensure the privacy of the research participant. Findings will be summarized and reported in aggregate without patient identifiers. Given the confidentiality measures outlined above and the measures proposed to protect against this risk, we believe the likelihood of a confidentiality risk to research subjects would be minimal.

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