Kidney Precision Medicine Project

Recruitment Site

Manual of Operations

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Contents

1. Introduction

1.1. KPMP Overview

The Kidney Precision Medicine Project (KPMP) is a prospective cohort study, whose goal is to use deep molecular phenotypes of kidney biopsies to develop new disease ontologies and treatments for acute kidney injury (AKI) and chronic kidney disease (CKD).

1.1.1. Objectives

Both AKI and CKD impose a significant global health burden. Yet, no effective therapies currently exist for AKI, and only a few are available for CKD. To address this need, KPMP will obtain kidney biopsy tissue from study participants with AKI or CKD. The network will utilize state-of-the-art methods to perform molecular interrogation of the tissue and to link the molecular data to kidney structure and clinical information in the form of a human kidney atlas. Molecular and imaging data derived from kidney tissue will be integrated with clinico-pathologic and genetic information, as well as other datasets derived from the analyses of fluid biospecimens, including peripheral blood and urine. Using advanced analytics to integrate the data, KPMP will aim to define kidney disease subgroups in molecular terms by identifying critical cells, pathways and targets for novel therapies.

1.1.2. Description

Participants with AKI or CKD will be recruited from recruitment sites during clinical care encounters (e.g. clinic visits for CKD patients, hospitalizations or emergency room visits for AKI patients) and from electronic resources (e.g. existing registries, electronic health records). Written informed consent will be obtained from study participants using a uniform informed consent document approved by the KPMP Single IRB at Washington University in St. Louis. For each participant, kidney tissue will be obtained for molecular phenotyping and clinical diagnosis. The diagnostic interpretation will be returned to the participant's caregiver to inform clinical care, but no treatment interventions will be prescribed by the KPMP. In addition to kidney biopsy, the study will involve collection of baseline (time of biopsy) and longitudinal biosamples (including urine, plasma, serum, and DNA) and demographic, clinical, and laboratory data. Participants will be followed through scheduled in-person and remote (telephone) study visits, as well as through periodic review of electronic health records (EHR). The KPMP biorepository at the University of Michigan will contain biospecimens collected at the biopsy and follow-up visits for future studies. As new RFAs are funded, the biorepository may also include reference kidney tissue obtained from allograft protocol implant biopsies or tumor-free nephrectomy specimens.

All biological samples, clinical datasets, biopsy slides, digital images and other relevant data will be deposited, harmonized, curated, and stored/tracked at the Central Biorepository at the University of Michigan. The Central Hub will manage and administer tissue distribution from the Recruitment Sites to the Tissue Interrogation Sites, where it will be interrogated using complementary, state-of-the-art platforms with rigorous quality control. Data generated at the Tissue Interrogation Sites will be transferred to the Central Hub, where they will be analyzed and visualized to further the scientific interests of the KPMP, including the building of a Kidney Atlas. Participant safety, satisfaction, participant reported outcomes, and the diagnostic yield of kidney biopsies will be systematically

assessed. Curated and validated data will be available to the scientific community via an online portal and public research databases. The KPMP will prioritize dissemination of study results to all relevant stakeholders, including study participants, patients, health care providers, researchers, and the broader scientific community.

1.2. KPMP Study Organization

The organizational structure of the KPMP consortium is summarized in Figure 1. The KPMP consortium consists of a cooperative agreement between the NIDDK/NIH, one Central Hub, six Recruitment Sites and five Tissue Interrogation Sites.

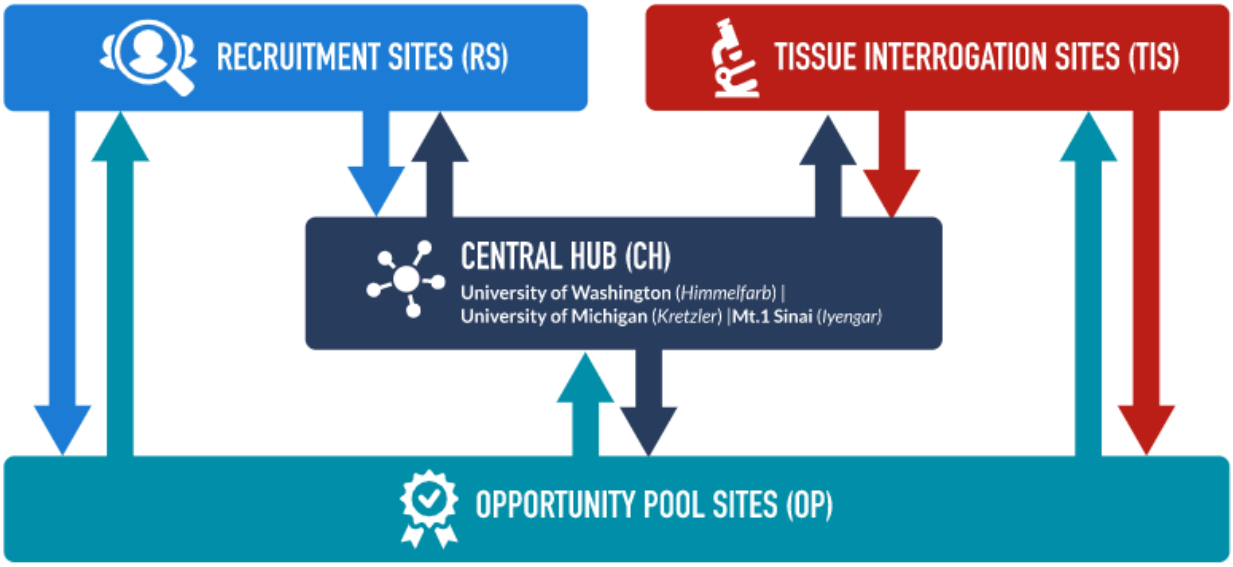


Figure 1: KPMP structure

1.2.1. Central Hub

The purpose of the Central Hub is to aggregate, analyze and visualize all data and samples, and provide scientific, infrastructure and administrative support for the entire KPMP. The Central Hub will collaborate with the KPMP Recruitment Sites and Tissue Interrogation Sites to obtain and evaluate kidney biopsies from study participants with AKI or CKD, create a kidney tissue atlas, define disease subgroups, and identify cells, pathways and targets for novel therapies. The Central Hub is led by a multi-PI plan to allow for synergistic interactions in different areas of expertise to accomplish common goals.

Central Hub Site (Joint-PI Plan)	Principal Investigator (PI)	Location
University of Washington	Jonathan Himmelfarb, MD	Seattle, WA
University of Michigan	Matthias Kretzler, MD	Ann Arbor, MI
Mount Sinai	Srinivas Iyengar, PhD	New York, New York

1.2.2. Recruitment Sites

The Recruitment Sites will recruit adult men and women with either AKI or CKD for longitudinal cohort studies that include a research kidney biopsy. The Recruitment Site will work collaboratively to capture demographic information, conduct longitudinal clinical phenotyping, and collect biological samples in a standardized manner.

Recruitment Site	Principal Investigator (PI)	Location
Cleveland Clinic (CKD)	Emilio Poggio, MD John Sedor, MD John O'Toole, MD	Cleveland, OH
Columbia University (AKI)	Krzysztof Kiryluk, MD Andrew Bomback, MD, MPH Jonathan Barasch, MD, PhD	New York, NY
Harvard University (CKD)	Sylvia Rosas, MD	Boston, MA
Boston University (CKD) Brigham and Women's Hospital (CKD)	Sushrut Waikar, MD, MPH	Boston, MA
University of Pittsburgh (AKI)	Paul Palevsky, MD Matthew Rosengart, MD, MPH	Pittsburgh, PA
University of Texas Southwestern, Dallas (CKD)	Miguel Vazquez, MD Robert Toto, MD	Dallas, TX
Johns Hopkins University (AKI)	Chirag Parikh, MD, PhD	Baltimore, MD
Yale University (AKI sub-site for JHU)	Francis Perry Wilson, MD, MS	New Haven CT

1.2.3. Tissue Interrogation Sites

Tissue Interrogation Sites will receive kidney biopsy tissue collected from participants at the Recruitment Sites. They will use this tissue to: 1) investigate kidney cell and disease heterogeneity in tissue sections and/or dissociated cells, 2) generate high-quality data and images for a kidney tissue atlas, 3) facilitate the structural, histologic and molecular assessment of cellular "states" associated with healthy function, activation, injury, recovery, and adaptive and maladaptive repair, 4) develop novel methods to distinguish diseased from non-diseased areas of kidney, and 5) identify robust structural, histologic and molecular signatures and pathways that can be used to accurately phenotype individuals with AKI or CKD to inform future diagnostic, prognostic or therapeutic selection schemes (subgroups).

Tissue Interrogation Site	Principal Investigator	Location
Indiana University	Pierre Dagher, MD Tarek Ashkar, MD	Indianapolis, IN
Ohio State University	Brad Rovin, MD	Columbus, OH

University of California, San Francisco	Zoltan Laszik, MD, PhD	San Francisco, CA
University of California, San Diego Washington University, St. Louis	Kun Zhang, PhD Sanjay Jain, MD, PhD	San Diego, CA St. Louis, MO
University of Michigan Princeton University Broad Institute	Jeff Hodgin, MD Olga Troyanskaya, PhD Nir Hacohen, PhD	Ann Arbor, MI Princeton, NJ Cambridge, MA
University of Texas Health San Antonio	Kumar Sharma, MD	San Antonio, TX

1.2.4. Additional Participating Laboratories and Centers

UMMS Central Biorepository
NCRC Building 60 G631
Ann Arbor, Michigan 48109

1.2.5. Funding

Funding for KPMP is provided by the National Institute of Diabetes, Digestive and Kidney diseases (NIDDK), a division of the National Institutes of Health (NIH), Department of Health and Human Services.

1.2.6. Project Cycle

The KPMP study is funded for 5 years at the Central Hub sites University of Washington, University of Michigan and Mount Sinai School of Medicine (September 2017 – June 2022). The KPMP study is funded for 2 years at all Recruitment Sites & Tissue Interrogation Sites (September 2017 – June 2019) with a subsequent three-year competitive renewal period (June 2019 – June 2022). The first year of KPMP focused on consensus building, organizing working groups & committees, protocol development, forms development, development of agreements & contracts and staff training. The recruitment phase begins in the third year of the study and continues through year five.

1.3. General Policy

1.3.1. General Protocol Policy

The first two years of the KPMP (2017-2019) will be devoted to establishing feasibility protocols for enrollment, tissue processing and technology development, identifying and implementing quality control procedures, and demonstrating feasibility and safety of the approach. Throughout the pilot phase, the protocol will be reviewed and revised to allow implementation of changes before recruitment accelerates starting in year three. Beyond year three, changes in the protocol will be considered only if they are required to ensure participant safety or will significantly enhance the scientific validity of the study. The objectives of the study are most likely to be achieved if the protocol does not require alteration beyond year three.

1.3.2. Initiating a Protocol Change

The Executive and Steering Committees must review and approve all protocol amendments or revisions. Proposed Protocol changes should be presented in writing to either the Chair of the Executive Committee or to the Data Coordinating Center (DCC). The DCC and/or Chair of the Executive Committee will present the proposed amendment to the Executive Committee and Steering Committee for review and discussion. Approved amendments must be submitted to the single IRB for approval and once approved, be incorporated into the protocol. IRB approval must occur prior to the implementation of an amendment. Amendments that include minor changes to the protocol may undergo expedited review if these changes fit into expedited approval criteria. All changes to the informed consent form must also be approved by the single IRB at Washington University.

2. Participant Recruitment

2.1. Overview of Recruitment

Recruitment Sites will use similar recruiting strategies, but site-specific approaches will optimize effectiveness and efficiency according to their local health care settings and target study population(s). Strategies will include both recruiting from clinical care encounters (e.g. clinic, emergency room or hospital visits) and recruiting based on electronic health information (e.g. existing registries and electronic health records - EHR). Local recruiting networks will be utilized whenever possible at both CKD and AKI Recruitment Sites. KPMP study candidates will be first asked by their clinicians to agree to an in-person or phone contact from the research team. According to local site-specific procedures and work practices, other modes of first contact, including direct outreach from the researchers to patients, may be considered for recruitment strategies. Research sites will follow local customs when approaching patients (i.e. some Recruitment Sites may require study staff to ask permission of a patient's clinician before approaching a potential participant).

An in-depth review and discussion of the KPMP will be conducted in the informed consent process for all participants with CKD or AKI. They will be afforded ample time to review the information and have all their questions fully answered. Written informed consent will be obtained from all KPMP participants before any study activities commence. Consent may be obtained from a legally authorized representative (LAR) for open biopsies at the Pittsburgh Recruitment Site. Details of the informed consent process are described in Section 3.4.

2.1.1. Approaching Potential CKD Participants

Recruitment of CKD patients will focus on the outpatient setting. Prospective participants will be identified in several ways, including registries, referrals, direct to patient outreach, or using EHR-based tools to screen for eligibility. Where possible, local CKD registries will be searched using the study entry criteria to find potential participants.

- KPMP study candidates will be first contacted by their clinicians, or other clinic staff.
- Clinician outreach to patients may include in-person discussion, telephone calls, letters, or clinic-approved forms of electronic communication.

- According to local site-specific procedures, other modes of outreach from the researchers to patients may also be used for recruitment.
- If potentially eligible study participants are interested in learning more about the KPMP, they may contact a Research Coordinator, or a Research Coordinator may contact them.
- Prospective participants will also meet in-person with a Research Coordinator and/or study investigator to review and discuss the study in detail.
- Informed consent process will be conducted by a physician and study coordinator team.
- Potential participants will be given information verbally and in print that clearly describes the kidney biopsy procedure, procedural risks, and utilization of samples in the KPMP.
- This study information will also be posted on the publicly available KPMP website.

2.1.2. Approaching Potential AKI Participants

Recruitment of AKI participants will be primarily in the inpatient setting. Some sites will utilize local EHR data to identify potential participants for enrollment. Sites will also screen for potentially eligible participants across nephology consultative services, emergency rooms, and intensive care units.

- Those who are eligible will be discussed with the nephrology attending physician or other care team members to determine if the patient is an appropriate candidate for KPMP.
- The primary clinician will first discuss the KPMP study with the potential participant or their LAR (for open biopsies at the Pittsburgh Recruitment Site).
- If potentially eligible study participants are interested in learning more, they will be informed that a Research Coordinator and/or study investigator will meet with them to discuss study participation.
- Informed consent process will be conducted by a physician and study coordinator team.
- Potential participants or their LAR will be given information verbally and in print that clearly describes the kidney biopsy procedure, procedural risks, and utilization of samples in the KPMP.
- This study information will also be posted on the publicly available KPMP website.

Recruitment of AKI participants for open kidney biopsy will include patients with established AKI as well as patients at high risk for AKI or in the earliest stages of AKI who undergo laparotomies for indications such as abscess, bowel perforation or infarction, or trauma. These potential participants will be identified through EHR alerts as well as by direct identification by hospital intensivists and surgeons. This population may be enrolled and consented by a LAR.

- The surgeon performing the laparotomy and kidney biopsy, accompanied by a KPMP Research Coordinator and/or study investigator, will discuss study procedures and risks with the participant.
- Potential participants and their LAR will be given information verbally and in print that clearly describes the kidney biopsy procedure, procedural risks, and utilization of samples in the KPMP.
- This study information will also be posted on the publicly available KPMP website.

2.2. Study Eligibility Criteria

Determining eligibility is a multiple step process involving the review of health records, interview of potential participants, and discussion with the potential participant's healthcare provider and the KPMP study PI. Information collected in the Screening Worksheet, prior to or at the Enrollment Visit represents the first step in determining a participant's eligibility based on available information. Recruitment Sites should consider the location of the participant to determine if they live close enough to the clinic to return for in-person follow-up visits.

2.2.1. CKD Participant Inclusion Criteria

2.2.1.1. Diabetic kidney disease (DKD)

Patients are eligible for the KPMP Study if they meet the two following diabetic CKD-specific criteria:

- Diagnosis of diabetes mellitus (type 1 or 2) established by at least one of the following criteria:
    - Hemoglobin A1C greater than or equal to 6.5%, confirmed with a repeat test *within the past year*
    - Fasting blood sugar greater than or equal to 126 mg/dL, confirmed with a repeat test *within the past year*
    - Use of glucose-lowering therapy (insulin or oral or other subcutaneous agents)

Medication Class	Examples
Biguanide	Metformin (Glucophage, Glumetza, Glycon),
Sulfonylurea	Glimepiride (Amaryl), Glipizide (Glucotrol), Gliclazide (Diamicron), Glyburide (Diabeta, Micronase, Glynase)
Meglitinides	Nateglinide (Starlix), Repaglinide (Prandin)
Thiazolidinedione	Pioglitazone (Actos), Rosiglitazone (Avandia)
DPP-4 Inhibitor	Alogliptin (Nesina), Linagliptin (Tradjenta), Saxagliptin (Onglyza), Sitagliptin (Januvia)
SGLT2 Inhibitor	Canagliflozin (Invokana), Dapagliflozin (Farxiga), Empagliflozin (Jardiance), Ertugliflozin (Steglatro)
GLP-1 Receptor Agonist	Dulaglutide (Trulicity), Exenatide (Byetta, Bydureon), Liraglutide (Saxenda, Victoza), Lixisenatide (Adlyxin), Semaglutide (Ozempic)
Insulin	Aspart (Novolog, Fiasp), Degludec (Tresiba), Detemir (Levemir), Glargine (Lantus, Toujeo, Basaglar), Glulisine (Adipra), Lispro (Humalog, Admelog), NPH (Humulin N, Novolin N), Regular (Humulin, Novolin) Mix (Novolog or Humalog 70/30, Ryzodeg 70/30), Inhaled (Afrezza)

    - International Classification of Diseases (ICD) 9/10 diagnostic code for diabetes
- Evidence of persistent kidney damage, manifest as any of the following present on at least two clinic assessments prior to enrollment and at least 3 months apart and excluding subjects with acute medical illnesses and changing kidney function:

Must be present on at least two assessments (including the most recent) at least 3 months apart. Most recent measure	**AND**	**Must be present at least once (most recent available measurement):**

must be within the past year, first (older) assessment must be within the past 3 year.		
Estimated glomerular filtration rate 30-59 mL/min/1.73m2	**AND**	--
Urine albumin excretion greater than or equal to 30 mg/g (or mg/day creatinine) **-or-** Urine protein excretion greater than or equal to 150 mg/g creatinine (or 150 mg/day)	**AND**	**Estimated glomerular filtration rate greater than or equal to 60 mL/min/1.73m2**

Notes:

- The timing between qualifying eGRF/urine albumin/urine protein and date of biopsy is up to the discretion of the PI, but blood safety labs must be completed within 2 weeks of the biopsy.
- Urine albumin excretion is **not** the same as spot urine albumin.

2.2.1.2. Hypertension-associated CKD (H-CKD)

Patients are eligible for the KPMP Study if they meet the two following hypertensive CKD-specific criteria:

- Diagnosis of hypertension (HTN) established by at least one of the following criteria:
  - BP greater than 140/90 mmHg measured on three occasions over at least 1 month
  - Taking antihypertensive medication for blood pressure (BP) control

Medication Class	Examples
ACE-inhibitors	Benazepril (Lotensin), Captopril, Enalapril (Vasotec), Fosinopril (Monopril), Lisinopril (Prinivil, Zestril), Perindopril (Aceon), Quinapril (Accupril), Ramipril (Altace), Trandolapril (Mavik)
Angiotensin Receptor Blockers	Candesartan (Atacand), Irbesartan (Avapro), Losartan (Cozaar), Olmesartan (Benicar), Telmisartan (Micardis), Valsartan (Diovan)
Alpha-blockers	Doxazosin (Cardura), Prazosin (Minipress), Terazosin (Hytrin)
Combined alpha/beta block	Carvedilol (Coreg), Labetalol (Normodyne)
Beta-Blockers	Atenolol (Tenormin), Bisoprolol (Zebeta), Metoprolol (Lopressor, Toprol), Propranolol (Inderal)
Calcium Channel Blockers	Amlodipine (Norvasc, Lotrel), Diltiazem (Cardizem), Felodipine (Plendil), Nicardipine (Cardene), Nifedipine (Adalat, Procardia), Verapamil (Calan, Covera)
Central Agonists	Alpha Methyldopa (Aldomet), Clonidine (Catapress), Guanfacine (Tenex)
Thiazide Diuretics	Chlorthalidone, Hydrochlorothiazide, Indapamide (Lozide), Metolazone
Loop Diuretics	Bumetanide (Bumex), Ethacrynic Acid, Furosemide (Lasix), Torsemide (Demadex)
Potassium Sparing Diuretics	Amiloride, Eplerenone (Inspra), Spironolactone, Triamterene
Peripheral adrenergic inhib.	Reserpine (Serpasil)
Vasodilators	Hydralazine (Apresoline), Minoxidil (Loniten)

  - International Classification of Diseases (ICD) 9/10 diagnostic code for hypertension

- Evidence of persistent kidney damage, manifested as any of the following present on at least two assessments at least 3 months apart and excluding subjects with acute medical illnesses and changing kidney function (a*ssessed by outpatient labs):*

Must be present on at least two assessments (including the most recent) at least 3 months apart. Most recent measure must be within the past year, first (older) assessment must be within the past 3 year.	**AND**	**Must be present at least once (most recent available measurement from within the past year):**
Estimated glomerular filtration rate 30-59 mL/min/1.73m2	AND	albuminuria or proteinuria less than 2000 mg/d or 2000 mg/g creatinine.
Urine albumin excretion 30-2000 mg/g creatinine (or mg/day for 24-hour urine) **-or-** Urine protein excretion 150-2000 mg/g creatinine (or mg/day for 24-hour urine) within the past year	AND	Estimated glomerular filtration rate greater than or equal to 60 mL/min/1.73m2

Notes:

- The timing between qualifying eGRF/urine albumin/urine protein and date of biopsy is up to the discretion of the PI, but blood safety labs must be completed within 2 weeks of the biopsy.
- Albuminuria is the same as urine albumin excretion; proteinuria is the same as urine protein excretion.

2.2.2. AKI Participant Inclusion Criteria

AKI Percutaneous Biopsy Inclusion Criteria

Patients are eligible for the KPMP Study if they meet all three of the following AKI-specific criteria. **Bolded** terms defined below. Note that PI judgement determines whether to enroll and perform a biopsy for participants that meet eligibility criteria and then appear to be recovering.

- Baseline estimated glomerular filtration rate greater than 45 mL/min/1.73m^2. **Baseline serum creatinine** is defined by the median of the last three outpatient serum creatinine from days 7 to 365 prior to enrollment.
    - If only two measurements obtained within this window, the two eGFR results will be averaged.
    - If only one measurement was obtained within this window, this eGFR result will be used

- If baseline is missing the patient can be enrolled with an estimated **Baseline serum creatinine**, but only if there is no past medical history of chronic kidney disease (see Table 1).

Table 1. Estimated Baseline serum creatinine.

To be used only when no past medical history of CKD and no clinical signs of advanced CKD (serum phosphate < 5 mg/dl and plasma PTH < 70 pg/ml).[22]

Age (years)	Black Male mg/dl (lmol/l)	Other Male mg/dl (lmol/l)	Black Female mg/dl (lmol/l)	Other Female mg/dl (lmol/l)
20–24	1.5 (133)	1.3 (115)	1.2 (106)	1.0 (88)
25–29	1.5 (133)	1.2 (106)	1.1 (97)	1.0 (88)
30–39	1.4 (124)	1.2 (106)	1.1 (97)	0.9 (80)
40–54	1.3 (115)	1.1 (97)	1.0 (88)	0.9 (80)
55–65	1.3 (115)	1.1 (97)	1.0 (88)	0.8 (71)
>65	1.2 (106)	1.0 (88)	0.9 (80)	0.8 (71)

- **Elevated/Index serum creatinine** (greater than or equal to 1.5 times **Baseline sCr** as defined above).
- And at least ONE of the following:
  - A **Repeat serum creatinine** within 48 hours of **Elevated/Index serum creatinine**, showing a further increase of 0.3 mg/dL. *Once patient qualifies, they can still be enrolled if creatinine goes down. PI judgement determines whether to perform biopsy if patient is getting better.* ***Elevated/Index creatinine*** *does not have to be the* ***admission*** *value.*
  - Positive kidney injury urine biomarker, as defined by any of the following:
    - NGAL level greater than or equal to 150 ng/mL by ELISA or clinical analyzer
    - KIM1 level greater than or equal to 2.8 ng/mL by ELISA
    - TIMP2 x IGFBP7 greater than or equal to 2.0 by NephroCheck®
  - Urine microscopy suggestive of acute tubular necrosis defined as a urine microscopy score of greater than or equal to 2 (*Evaluated and documented by site investigator)*. [1]
    - greater than or equal to 1 Renal Tubular Epithelial cells (RTE) per high powered field (HPF) AND greater than or equal to 1 granular cast/ low powered field (LPF); or
    - greater than or equal to 5 Renal Tubular Epithelial cells (RTE) per high powered field (HPF); or
    - greater than or equal to 5 granular cast/ low powered field (LPF)

Creatinine Term Definitions:

- **"Baseline sCr"** = the value from days 7 to 365 prior to enrollment. Value is calculated based on 1-3 available sCr measurements or imputed based on age/race/gender
- **"Admission sCr"** = the value at time of admission
- **"Elevated/Index sCr"** = the value greater than or equal to 1.5 times Baseline sCr (also called "initial sCr")

- **"Repeat sCr"** = the value within 48 hours of Elevated/Index sCr, which should show further increase of at least 0.3 mg/dl

2.2.3. Special Populations

2.2.3.1. AKI Open Biopsy Inclusion Criteria

(**Bolded** terms defined above in the AKI Percutaneous biopsy inclusion criteria)

Patients undergoing open laparotomy/surgical biopsy are eligible for KPMP if they have AKI clinical indication with:

- **Baseline** estimated glomerular filtration rate greater than 45 mL/min/1.73m2 as defined above in Table 1 AND one of the following:
- **Elevated/Index serum creatinine** (greater than 1.5 times **Baseline sCr**) or increase in serum creatinine greater than or equal to 0.3 mg/dL within 48 hours, above **Admission serum creatinine**. *Once patient qualifies, they can still be enrolled if creatinine goes down. PI judgement determines whether to perform biopsy if patient is getting better. Baseline creatinine does not have to be the admission value. Fluid resuscitation is 1 liter or according to PI judgement.*
  OR
- High risk for acute kidney injury defined by TWO or more criteria:
    - Positive kidney injury urine biomarker measured at the Recruitment Site, as defined by any of the following:
        - NGAL level greater than or equal to 150 ng/mL by ELISA or clinical analyzer
        - KIM1 level greater than or equal to 2.8 ng/mL by ELISA
        - TIMP2 x IGFBP7 greater than or equal to 2.0 by NephroCheck®
    - Urine microscopy suggestive of acute tubular necrosis (*Evaluated and documented by site investigator)*.
        - Greater than or equal to 1 Renal Tubular Epithelial cells (RTE) per high powered field (HPF) AND greater than or equal to 1 granular cast/ low powered field (LPF); or
        - Greater than or equal to 5 Renal Tubular Epithelial cells (RTE) per high powered field (HPF); or
        - Greater than or equal to 5 granular cast/low powered field (LPF)
    - Oliguria (less than 0.3mL/kg/hr) at least 1 hour after fluid resuscitation *(1 liter or according to PI judgement)*.
    - One or more exposure(s) known to cause acute kidney injury (major surgery (not including index laparotomy), sepsis, nephrotoxic drugs, etc.).
      Nephrotoxic Medications:

Acyclovir	Gadoextate disodium*	Nafcillin

Ambisome	Gadopentetate dimeglumine*	Naproxen*
Amikacin	Ganciclovir	Pamidronate disodium**
Amphotericin B*	Gentamicin	Pentamidine*
Aspirin*	Ibuprofen	Piperacillin
Captopril	Ifosfamide	Piperacillin/ Tazobactam
Carboplatin	Indomethacin*	Sirolimus
Cefotaxime	Iodixanol*	Sulfasalazine
Ceftazidime	Iohexol*	Tacrolimus
Cefuroxime	Iopamidol*	Tenofovir*
Celecoxib	Iopromide*	Ticarcillin/ Clavulanic Acid
Cidofovir*	Ioversol*	Tobramycin
Cisplatin	Ioxaglate meglumine and ioxaglate sodium*	Topiramate
Colistimethate	Ioxilan*	Valacyclovir
Cyclosporine	Ketorolac	Valganciclovir
Dapsone	Lisinopril	Valsartan
Diatrizoate meglumine*	Lithium	Vancomycin
Diatrizoate sodium*	Losartan	Zoledronic acid
Enalapril	Mesalamine	Zonisamide
Enalaprilat	Methotrexate	
Foscarnet	Mitomycin	

* Medications counted for seven days after administration towards exposure

2.2.3.2. DKD Resilient Individuals Inclusion Criteria

DKD Resilient individuals, i.e. individuals with diabetes for >25 years that are free from nephropathy

- Type 1 diabetes for over 25 years
- Estimated glomerular filtration rate greater than or equal to 60 mL/min/1.73m^2
- Urine albumin excretion less than 30 mg/d (or mg/g creatinine)

2.2.4. Exclusion Criteria

Any potential participant meeting any one of the general or safety exclusion criteria will not be eligible for enrollment in the KPMP. It will be recorded in the follow-up data if a potential participant has developed any of the exclusion criteria.

Determined at time of Eligibility Assessment prior to consent:

- Non-English or Spanish language
- Less than 18 years of age
- Severe allergy to iodinated contrast
- Pregnancy
- Transplant recipient (kidney or non-kidney, including solid organ and bone marrow transplantation)
- Additional vulnerable individuals (incarcerated, institutionalized, or otherwise unable to participate in the study)
- Inability to provide informed consent (*includes advanced dementia or developmental delay).*
    - Consent from a legally authorized representative (LAR) is allowed for Pittsburgh surgical AKI biopsies. Participants will re-consent when they regain the capacity to do so, preferrable during the hospital stay. Participants must provide consent before the 3-month in-person visit.
- Clinical diagnosis of kidney disease from an autoimmune disease, dysproteinemia, viral disease or glomerular disease other than DKD or H-CKD
- Kidney infection, perirenal infection, or cutaneous infection that overlies the kidney (percutaneous biopsies only)
- Chronic anticoagulation
- Inability to withdraw aspirin, clopidogrel, cilostazol, or similar anti-platelet agents for at least 7 days prior to biopsy (unless bleeding time is normal before open surgical biopsy); clinical judgement will be used in the case of Nonsteroidal anti-inflammatory drugs (NSAID) exposure occurring less than 7 days before percutaneous biopsy (clinical judgement may be used to override this exclusion criteria for NSAIDs only, **not** aspirin).
- Blood pressure of more than 160 mmHg systolic or 100 mmHg diastolic
    - The target blood pressure is less than 140 mmHg systolic and less than 90 mmHg diastolic.
    - Peri-procedure blood pressure fluctuations between 140-160 mmHg systolic and 90-100 mmHg diastolic require management, ideally to target, based on clinician/investigator judgment.
- Ventilator-dependent patient (does not apply to AKI open biopsies or CKD biopsies)
- Hypotension or any pressor support requirement at screening or biopsy visit (does not apply to AKI open biopsies or CKD biopsies)
- Any other condition where in the judgement of the operator, biopsy cannot be performed safely.
- Unwilling to receive blood transfusion (if needed)

Determined by kidney ultrasound before the biopsy procedure (may be the same day as the biopsy procedure)

- Kidney depth more than 13 cm (as measured perpendicular from the skin) (percutaneous biopsies only)
- Kidney size less than 8 cm (percutaneous biopsies only)
- Solitary or single functioning kidney
- Evidence of urinary tract obstruction or hydronephrosis
- Multiple bilateral kidney cysts
- Any other imaging abnormality, which in the judgement of the operator, prevents biopsy being performed safely.

Determined by blood test within 2 weeks of CKD biopsy or 48 hours for AKI biopsy:

- International Normalized Ratios (INR) greater than 1.4
- Platelet count less than 100,000/uL
- Hemoglobin less than 9 g/dL

3. Participant Enrollment

3.1. Population and Recruitment

The diversity within the CKD and AKI Recruitment Sites will facilitate recruitment and enrollment of racial and ethnic minorities who are over-represented among patients with kidney diseases such as people of African ancestry, Hispanic ethnicity, or American Indians and Alaskan Natives. In addition, representation of women will correspond to the fraction of women in the population diagnosed with CKD and AKI. Participants will be drawn from a variety of primary kidney care and specialty care clinics in academic and community practices (e.g. nephrology, diabetes and general endocrinology, internal medicine, family medicine, cardiology, intensive care, surgery). Engagement of patients and clinicians by regular outreach and ongoing dissemination of study progress and results will enhance recruitment.

- The KPMP will track enrollment according to stage and clinical diagnosis of CKD or AKI in order to assure appropriate representation from target populations.
- Reasons for non-participation will be ascertained to mitigate selection bias and to optimize site recruiting practices.
- Race/ethnicity and sex/gender will be tracked to assure that KPMP achieves population-level demographics reflective of patients affected by the targeted causes of CKD or AKI.
- The KPMP will strive to enroll participants residing across a broad geography, inclusive of both rural and urban regions.
- KPMP will not exclude participants who are enrolled in other research studies.
- Participants who enroll in KPMP and have a biopsy that does not provide sufficient tissue for diagnostic or research analyses will be encouraged to participate in follow-up calls and visits for the full timeframe of the study (expected up to 10 years).

3.2. Eligibility assessment

A multi-pronged assessment of eligibility is required to maximize participant safety. First, a Research Coordinator(s) will assess each quantifiable eligibility criterion using a KPMP Screening Worksheet (see Appendix F). Second, a physician(s) will assess more detailed aspects of eligibility (e.g. risks of bleeding from kidney biopsy beyond standard KPMP eligibility criteria). The physician(s) will also quantify anticipated potential benefits and risks for the individual patient considering participation in order to facilitate informed consent and scientifically evaluate the value of KPMP kidney biopsies.

3.3. Approaching Potential Participants

- A study team physician will meet with each potential participant or their LAR to discuss the KPMP study and conduct the informed consent process during a clinic or hospital visit. Complete review of inclusion and exclusion criteria will be performed.
- The risks, benefits, and alternatives to the research study will be discussed in detail.
- Potential participants or their LAR will be afforded ample time to review the information and have all their questions fully answered at a single session or extended over several interactions with the study team.
- Site investigators will be available to answer any questions or provide additional information to those considering KPMP participation. The biopsy operator will be available to explain the biopsy procedure and safety risks.
- Written and video recruitment materials will be provided in either English or Spanish. Spanish-speaking participants who are enrolled must sign a Spanish-translated IRB-approved informed consent form.

3.4. Informed Consent

Reliance agreements will be established between the Washington University (St. Louis) Institutional Review Board (IRB), the single IRB for the KPMP, and the IRBs at the CKD and AKI Recruitment Sites. The Washington University IRB will review and approve the KPMP Informed Consent Form along with all participant-facing materials, the clinical protocol and any amendments or study changes. The KPMP study will comply with the Declaration of Helsinki.

The consent process can occur either in-person or via phone or video chat. The signed consent form must be received (via secure email, fax, regular mail, or any HIPAA-compliant procedure) by the RS before any study procedures, including questionnaires, can begin.

3.4.1. Obtaining Informed Consent from the Participant

The informed consent process is the cornerstone of ensuring safe and ethical implementation of the KPMP. Informed consent is the primary process through which KPMP procedures, risks, and benefits will be fully disclosed to potential participants and through which potential participants will choose whether to take part in the KPMP. This process will involve multiple exchanges of information between potential participants, study staff, clinicians, and other trusted advisors (such as individuals within their family, friend group, faith or other shared community, or patient advocate group), in the native language of the participant (either English or Spanish). Informed consent and screening will proceed in parallel, so that

information obtained through screening can be used to inform potential participants of their individual expected risks and benefits. The informed consent process may be completed during a single encounter, but more frequently will involve serial interactions over a period of time.

Throughout the process, potential participants will be encouraged to ask questions of study staff, clinicians, and trusted advisors. Contributors to the informed consent process and their roles include:

1. **The participant.** The potential participant is the focus of the informed consent process. Most potential participants will choose to include trusted advisors in their decision-making.
2. **Research coordinator**. A trained Research Coordinator(s) will be primarily responsible for providing a complete overview of the KPMP protocol. This overview will include all elements of the protocol relevant to the individual participant (e.g. CKD or AKI group), including but not limited to a general description of the kidney biopsy, the general risks and benefits associated with kidney biopsy, data and biosample collection, collection and use of genetic information, plans for long-term follow-up, and overall study risks and benefits. As part of this process, the Research Coordinator will review the entire written informed consent form with the potential participant.
3. **Physician.** A physician(s) with adequate knowledge of the potential participant's clinical status will evaluate the risks and benefits of a kidney biopsy and KPMP participation for each individual potential participant. This physician may be a clinician with adequate knowledge of the KPMP protocol or a KPMP physician who has adequate knowledge of the participant's clinical condition, or multiple physicians may confer to provide comprehensive evaluation and information to the potential participant. The physician(s) will assess the individual's potential risks (particularly those related to kidney biopsy) and benefits (particularly potential knowledge derived from the clinical pathology report). This report will include the clinical diagnosis for CKD or AKI, prognostic information regarding the expected future course of CKD or AKI, and/or clinical management. Risks and benefits will be thoroughly discussed with the potential participant, offering an opportunity for questions and discussion. If the physician feels that a kidney biopsy is unacceptably risky, the potential participant will not be offered enrollment in the KPMP.
4. **Participant advocates.** In some cases, KPMP sites may offer potential participants access to patients who know the KPMP protocol and have had an opportunity to reflect on the protocol from a patient perspective. Patient-to-patient contact may help potential participants understand how participating in the KPMP may affect their health and health care.

IRB-approved, written informed consent will be required of all KPMP study participants. Spanish-speaking participants must review and sign an IRB-approved Spanish-translated consent form. Only those who express interest in participation, meet all eligibility criteria, and provide written informed consent will be enrolled. They will sign and date the consent form indicating their understanding and willingness to participate. Study activities will commence only after written informed consent is obtained. Documentation of consent process activities and participant's understanding is recorded in the Consent Form in the REDCap Participant Management Program.

3.4.2. Obtaining Informed Consent from a LAR

KPMP allows LAR consent at the Pittsburgh Recruitment Site in the setting of AKI surgical/open biopsies.

When and where coordinators will approach the legally authorized representative

LARs can be contacted at bedside, in patient waiting areas, private area or via telephone. Consent conversation can take place with a LAR anywhere that they are comfortable. However, patient's LAR must be present to sign consent. Consent criteria for a LAR is the same as if they are a patient. Consent must be reviewed in its entirety. The Physician-Investigator must be the individual to complete the informed consent with the LAR (noting that the physician-investigator who works with the LAR to complete the consent will not be the same person who performs the surgery).

Talking points for introducing the study

Introduction process is the same for LAR as it is for a Patient. The study team must first be introduced by a clinical staff member who can confirm that the LAR is willing to speak/hear about research. After LAR is willing to speak to research, it is best to start with the Who, What, When, Where, and Why of the study as an introduction (Essentially everything covered on first 1-3 pages of Consent); who we are, what we are researching, why we are approaching LAR on behalf of the patient, where the research will be done, and when and for how long the research will occur. If LAR is still interested, the Physician-Investigator will join the conversation to answer any questions and review full consent (noting that the physician- investigator who works with the LAR to complete the consent process will not be the same person who performs the surgery). The physician investigator will review the informed consent form section by section making sure LAR understands each section and encourage LAR to ask questions. The LAR will sign consent as they would if they were the patient. Remind the LAR that the patient will be asked to sign the consent after they regain the ability to do so.

A general outline of how coordinators will explain the study

The script is the consent itself (a summary of the study). For LAR consent, the informed consent form will be reviewed section by section in its entirety because it goes through everything the LAR needs to know from why they are being approached to what is being asked of them on behalf of the patient; and then other aspects of how the study will affect the patient (e.g., potential payments, risks, benefits, contact information for the study, ability to withdraw and how to do so, etc.). The informed consent form is written in a format that is easy to understand. The study team is required to go section by section reviewing the entire consent. Ask questions to ensure the LAR understands what was discussed and ask them to return the information (to confirm they understand); Encourage the LAR to ask any and as many questions as they have about the study and process.

Explain that when a patient (who had LAR consent signed for them) regains capacity to consent on their own, a study coordinator or investigator will re-approach the patient, explain the study and what has been done up until that point, and determine if the patient wants to continue to be in the study (note once again that the physician-investigator who works with the patient to complete the consent will not be the same person who does the surgery). If the patient should decide to decline, we cannot undo a biopsy or return labs that have already been collected, thus in most situations we will maintain the samples that have already been collected to use for the study but will not have any more follow up with patient, aside from potential safety monitoring post biopsy for 28-days.

Assigning a LAR and describing their role

A Legally Authorized Representative is legally allowed to consent for a patient when the patient temporarily or permanently lacks the capacity to consent on their own.

For the Pittsburgh site, only family members are allowed to sign consent as a LAR, unless there is power of attorney or guardianship. Pennsylvania state law provides hierarchy on who the appropriate LAR would be if multiple family members are present.

If the patient is incapable of consenting for themselves, then approach an authorized representative regarding enrollment. The authorized representative is often the next of kin unless the patient has a pre-existing legal document specifying another individual is responsible for medical decision making for them. The preferred order for legal authorized representative is as follows:

1. spouse, unless an action for divorce is pending, and the adult children of the principal are not the children of the spouse
2. adult child
3. a parent (natural or adoptive)
4. adult brother or sister
5. adult grandchild
6. an adult who has knowledge of the principal's preferences and values, including, but not limited to, religious and moral beliefs, to assess how the principal would make health care decisions

The LAR will be given ample time to review the consent document prior to speaking with the physician-investigator. The study will be described in lay terminology, explaining the risks and emphasizing that the decision to participate (or not) in the investigation will have no effect on routine medical care. The listed Physician-Investigator obtaining consent will provide their name and phone number and suggest that the LAR call if they have further questions or wish to withdraw from the study at any time. The listed investigator obtaining the consent will also provide the participant or their representative with a written copy of the consent form and ample time to have questions answered prior to enrollment. (Again, note that the physician- investigator who completes the consent process will not be the same person who performs the surgery.)

Additional information added for LAR consent explains that participants who are enrolled when cognitively impaired will be given the opportunity to consent to further participation (or to withdraw) once they regain decision-making capacity. Both participants and their LAR can choose to withdraw the participant from the study at any time. Explanation will be given regarding what will happen to samples should LAR give consent and then withdraw consent; or the patient declines consent when they regain ability to give self-consent.

When and where the re-consent will take place

Re-consent will most likely occur at the bedside. Obtain consent from the patient as soon as possible after the patient has regained capacity.

3.4.3. Participant Confidentiality

KPMP records will not be shared with those not involved in participants' clinical care or not involved in the KPMP, except as required by law. Records relating to this study will be kept strictly confidential, and all personal health information (PHI) will be protected according to the HIPAA Privacy Rule. PHI will be

stored in a password-protected, encrypted database. Only KPMP personnel will have access to this database. Any paper records will be stored in a locked cabinet in a secure room. Publication of study results will not identify individual study participants.

KPMP data are covered under a Certificate of Confidentiality agreement from the NIH (Section 2012 of 21st Century Cures Act as implemented in 2017 NIH Certificates of Confidentiality Policy). A Certificate of Confidentiality allows researchers to refuse to disclose identifiable research information in response to legal demands. Certificates are issued to researchers to help protect the privacy of human participants enrolled in sensitive, health-related research. A description of the KPMP will be available on http://www.ClinicalTrials.gov. This website will not include information that can identify study participants or PHI but may include a general summary of the data.

The following groups will have access to participant records from the KPMP study:

- Research staff at the Recruitment Sites
- National Institutes of Health/National Institute of Diabetes, Digestive, and Kidney Diseases staff and their representatives
- Washington University IRB
- KPMP Data Coordinating Center at the University of Washington

Kidney tissue from KPMP will be banked and studied by detailed genetic and other omics interrogations. Genetic information, particularly on a scale likely to be generated from genome-wide SNP arrays or whole exome and/or genomic sequencing, is individually identifying and the risks of re-identification of research participants from unauthorized access to their genomic information is a privacy risk [3]. To protect participants from such risks, genetic information will be released only to qualified researchers for selected KPMP-approved ancillary studies. The researchers will sign a data use agreement that includes a stipulation that prohibits attempts to re-identify study participants.

Federal and State laws, including the Genetic Information and Nondiscrimination Act (GINA), make it illegal for health insurance companies, health plans, and employers to discriminate against individuals based on genetic information, which affords some measure of protection for participants in the event of an unintended disclosure of genetic data.

3.5. Protocol Deviations

Two classes of departures from KPMP procedure or protocol are designated for identification, tracking, and reporting. These include Major and Minor protocol Deviations as defined below.

3.5.1. Minor Deviations

Minor Deviations are defined as departures from a study protocol or KPMP methods or procedure that do not have the potential to negatively impact the rights, safety, or welfare of participants or others, and do not adversely affect the integrity or validity of the major scientific goals of the study.

Minor deviations include (but are not limited to):

- failure to obtain appropriate source documentation
- failure to achieve appropriate KPMP certification prior to performing procedures*

- mistimed procedures (performing a lab test or visit outside the window outlined in the protocol when, in the opinion of the investigator, there are no safety implications)
- using an outdated version of a data collection form**
- missed follow-up visits due to Recruitment Site negligence
- use of an expired consent form in which the information contained is not substantively different than the currently approved consent, unless the deviation occurs repeatedly
- a signed copy of the consent form was not given to the participant
- a missing investigator signature on the consent form

*If certification-related deviations persist at a given center and an uncertified individual continues to carry out study procedures without proper KPMP training, serious effects on data quality may result. Such a scenario leads to the possibility of major deviations being assigned.

**Likewise, if an outdated version of a form used by a center in error references incorrect study eligibility criteria, major deviations may be assigned. These situations will be reviewed and classified on a case-by-case basis by the Safety & Adjudication Subcommittee (SAC), in consultation with the DCC and the Clinical Operations Committee.

If a given center experiences a high frequency of minor protocol deviations in a specific area, the DCC will address this issue with the PIs of the center and the NIDDK in an effort to resolve the problem.

Minor deviations (or events that may qualify as minor deviations) should be submitted to the DCC using the REDCap project called KPMP Protocol Deviations within 3 business days of their identification. The SAC will review the event within one week of submission and determine whether any follow-up is advisable (such as re-training, change of supplies, revision to a MOP, notification to stakeholders, etc.). Minor protocol deviations will be summarized and provided to the IRB at the time of the continuing review. Minor deviations from other KPMP methods or procedures (i.e. those that deviate from an MOP or other study material but not from the protocol) will not systematically be reported to the IRB but will be reported via REDCap and reviewed by the SAC to enable trend tracking and nimble intervention where needed.

3.5.2. Major Deviations

A Major Deviation is one that does have the potential to negatively impact the rights, safety, or welfare of participants or others, to adversely affect data quality, to significantly affect the integrity of the major scientific goals of the study, and/or to involve a significant and repeated breach of subjects' privacy. Major deviations include (but are not limited to):

- failure to obtain legally effective informed consent appropriately and prior to initiating research procedures
- informed consent obtained by someone other than individuals authorized by the IRB to obtain informed consent
- enrollment of ineligible subjects (i.e. those who do not meet all inclusion/exclusion criteria)
- performing a study procedure that has not been approved by the IRB

- failing to conduct a study procedure or administer a study assessment that was meant to assess the safety of the individual's continuation in the study mistimed procedures (performing a lab test or visit outside the window outlined in the protocol that, in the opinion of the investigator, may impact the safety of the participant)
- failure to carry out study procedures in the appropriate order, when applicable
- misplacement/loss of biological specimens
- misplacement/loss of study documentation or data/ data collection forms
- Inappropriate release of PHI
- Implementation of recruitment procedures that have not been IRB-approved
- Failure to report an Unanticipated Problem to the IRB

By the nature of their definition, major deviations are considered the most serious class of departure from the study protocol. All major deviations will be reported to the Recruitment Site PI, Safety & Adjudication Subcommittee, DCC, the sIRB, NIDDK, DSMB, and the Clinical Operations Committee.

Major deviations must be reported to the IRB within 10 business days of the occurrence of the event or notification to the PI of the event. The only exception to the timeframe is major deviations resulting in death of a participant, which must be reported within 1 day.

Major deviations (or events that may qualify as major deviations) should also be submitted to the DCC using the REDCap project called "KPMP Protocol Deviations" within 3 business days of their identification. The DCC will notify the DSMB within 3 business days of receipt of the REDCap submission. The SAC will review the event within one week of submission and determine whether any follow-up is advisable (such as re-training, change of supplies, revision to a MOP, notification to stakeholders, etc.). The SAC will also ensure reporting to the IRB, if that step has not yet been completed.

4. Retention

Retention of participants is central to the internal validity of the study and will be an extraordinarily high priority of the investigators and staff. Recruitment Site investigators will consider the expectation of ten years of follow-up when identifying potential participants and throughout the informed consent process, assessing willingness to commit to a long-term follow-up period.

4.1. Strategies to Maximize Retention

A key element to maximize retention is a pleasant, attentive and responsive staff that provides a reasonably flexible visit schedule. Other clinical center features that promote high retention rates include local tracking systems; frequent staff meetings; free and convenient parking; personal contacts through birthday cards, holiday cards, sympathy cards and flowers; small gifts at visits; and modest monetary incentives. We will stay in frequent contact with study participants, through a combination of in-person and remote follow-up visits, newsletters, and personal contacts. We recognize that study participants who feel valued will have a higher likelihood of maintaining study contact and complying with requested biospecimen collections. We anticipate providing research participants with annual incentives from the KPMP to include reusable totes, water bottles, umbrellas, notepads and the like.

A critical component of maintaining a study participant's engagement in the study will be creating an environment in which participants feel truly like a partner in KPMP. We are working with our Community Engagement Committee (CEC) to focus on what participants would like to receive in terms of study information or results, and how best to communicate study findings to participants. The CEC will also explore ways to include the participants actively, such as including them in the CEC itself or providing them with contact information for local patient advocacy groups.

Successful strategies from various prospective cohort studies, including the Assessment, Serial Evaluation, and Subsequent Sequelae in Acute Kidney Injury (ASSESS-AKI), Chronic Renal Insufficiency Cohort Study (CRIC), Nephrotic Syndrome Study Network (NEPTUNE), Multi-Ethnic Study of Atherosclerosis (MESA), Cardiovascular Health Study (CHS), and Clinical Phenotyping Resource and Biobank Core (CPROBE) will be employed, including:

- Reimbursement for time, travel and parking.
- Phone and address listings for participants and their contacts will be updated at each interaction (visits/phone).
- Study newsletters (providing information on the study progress and results, along with general and kidney-specific health messages) will be mailed.
- Personalized birthday, holiday greetings, and sympathy cards will be sent.
- Approximately two to four weeks prior to the time for the follow-up visits, a phone call will be placed to the participant to schedule the date and time of the appointment.
- A reminder letter with the date, time, and location of the visit may be sent to the participant immediately after the visit is scheduled.
- Participating clinical centers will be encouraged to offer evening and weekend appointments to make it possible for participants with work and other obligations that limit their flexibility to attend study visits during regular business hours (8:00 AM – 5:00 PM Monday-Friday).
- Participants who live far from the Recruitment Site or have other issues making travel too burdensome may complete study visits by phone. In such instances, biological specimens and processing will be coordinated with a local laboratory and shipped directly to the KPMP Biorepository.
- Proxy interviews to collect primary outcomes will be conducted if the participant is deceased or has diminished cognitive functioning.
- Social Security Number information that will be used for ascertaining vital status among participants who are lost to follow-up.

The study team is acutely sensitive to the need for high participant retention and will continually evaluate new retention methods that can be tested and implemented in KPMP.

4.2. Follow-up Procedures and Participant Tracking

Research Coordinators should begin contacting participants 2 months prior to their annual visit and follow-up visits. Contact windows are minus and plus 2 months of the target date, therefore, contacting participants early in the visit window allows the Research Coordinator maximum flexibility in scheduling appointments or time to locate missing participants. The REDCap Participant Management Program

provides a calendar application to assist in scheduling participants. A suggested template letter for scheduling clinic visits is available on Basecamp.

To maximize retention, study visits will be scheduled to coincide with clinic visits when possible. This will be done by utilizing electronic health record documents, whereby research coordinators will be asked to surveil the medical appointments of consented participants to schedule their follow-up visits in conjunction with when the participant will already be visiting the clinic. Blood specimens will be coordinated as much as possible to concur with any clinical laboratories being drawn, reducing the number of needle pokes a participant undergoes.

Participants who relocate to an area from which it is no longer feasible (or they refuse) to travel to a Recruitment Site will continue to be contacted annually for a remote visit. Recruitment Sites may offer inducements to participants who relocate in the form of additional travel reimbursement in return for their continued participation.

If a participant cannot be reached by their preferred contact method, all contact methods should be tried, during a variety of days or times (weekdays, weekends, mornings, evenings). A maximum of three contact attempts per visit is allowed. If the first two attempts are unsuccessful, the third should be a personal letter mailed to the participant (see template here). If a third attempt is unsuccessful after more than two weeks, one attempt should be made to reach the secondary contact.

4.3. Missed Annual Visits

If the Research Coordinator is unable to schedule a clinic visit or contact the participant within the two-month window, every effort should be made to complete the contact as soon as possible prior to the next scheduled clinic visit, using all available contact information (phone, address, email, alternative contacts). A visit will be considered late if it occurs after the allowed window of contact. However, the Research Coordinator should continue to attempt to complete this visit information up to 9 months after the anniversary clinic visit date. After the 9-month time window, the next visit window will begin, and the Research Coordinator should apply the clinic visit number of the next appropriate clinic visit. It is preferable to collect as much of the Follow-up CRF data as possible, even if this information is collected in the 'late' window, than to miss the opportunity to complete tests and questionnaires.

A visit is considered "late" when it is conducted outside the original two-month window dates. A clinic visit is considered "missing" if it does not occur before the next clinic visit window has opened.

4.4. Participants Lost to Follow-up

For KPMP, loss to follow-up is defined similarly to ASSESS-AKI: two consecutive years with no visit, no phone call contact, and no outcome data.

Every effort should be made to encourage participants to continue with study visits. Participants may remain in the study and contribute only EHR data if they refuse to participate in follow-up calls and visits. Strategies that KPMP will use to limit loss to follow-up include:

- Collection of contact information is vital and will be updated as needed at each contact point. In addition to collecting address, email and phone numbers for the participant, information for an

emergency contact, and up to three physicians will be collected. Participants will be encouraged to contact their local recruitment site to report changes to contact information that might occur between visits.

- Social media, such as Facebook and LinkedIn, are useful tools for finding participants who have relocated.
- Phone-calls can be used in lieu of an in-person visit if the participant has moved away but is otherwise willing to continue participation.
- Electronic health records can be used to update contact information.

In the current era, a variety of passive surveillance methods can be implemented, allowing for data collection on participants even if they miss clinic visits. These include:

- Collection of data from electronic health records, including vital status, end stage kidney disease status, laboratory data, and hospitalization data.
- Ascertainment of end stage kidney disease from the USRDS
- Ascertainment of vital status from the National Death Index

The only exception to this would be a participant who withdraws consent, in which case they will be lost in terms of ongoing data collection.

4.5. Participant Withdrawal

It is anticipated that over the course of time, a small number of KPMP participants may withdraw consent, asking that their data not be used in the study. This may occur either in-person, or though written notification from the participant to a Recruitment Site PI.

There are many reasons why a participant may choose to withdraw, including:

- Unanticipated events unrelated to the study
- Significant concurrent illness
- Relocation and unwilling to participate in home visits
- Dissatisfaction with study
- Loss of interest in the study

If a participant requests to be withdrawn, Research Coordinators will solicit the participant's reason(s) for withdrawal. Reason(s) for withdrawal will be documented in the End of Study CRF in the Participant Management Program (PMP). If the reason(s) for withdrawal may potentially be remediated, the Research Coordinator in concert with the site PI may explore ways to accommodate the participant to allow their continued participation, taking care not to be coercive or to minimize the participant's concern(s). After a withdrawal, the participant's data folder is clearly marked to indicate withdrawal and is maintained at the Recruitment Site where the participant was recruited and followed.

4.6. Tracking retention of the study population

For each visit, the following metrics will be reported:

- the number of participants who have withdrawn
- the number of participants that attended within the visit window

- the number of participants that attended but out-of-window
- the number who only provided information over the phone
- the number tracked only through passive (non-contact) surveillance
- the number of participants for whom no information was obtained.
- Among those not able to contact, summaries of how many have not had any information obtained within 1 and 2 years respectively.

While the ideal participation level is complete, we recognize that there may be situations where participants miss visits, leave questionnaires incomplete, or do not provide biosamples at the desired timepoints. Any and all data collected will be leveraged to maximize the participant's contribution and missing data will not preclude future participation if a participant has previously been considered lost to follow-up due to missed visits. Rather, attempts will be made to recapture information about the intervening time period to the greatest extent possible.

If a participant death is discovered, update the End of Study CRF to indicate that the participant has died, and attempt to record the date and cause of death, if possible. The Safety and Adjudication Committee reviews death that occur within 28-days of the kidney biopsy. Deaths that occur more than 28-days after biopsy are not reviewed by the SAC. The End of Study form should only be used to update final status change, such as loss of eligibility, death, withdrawal, or lost-to-follow-up. Note that "participant in hospice" is included as a reason for follow-up not completed, but it is not a final status used to indicate an End of Study.

5. KPMP Study Process

5.1. Visit Schedule Information

This section of the manual provides a summary of activities and procedures that occur at each scheduled KPMP Study visit and contact.

Table 2 describes the types of visits and permissible visit intervals (visit windows) used throughout this manual to describe interaction with KPMP Study participants. Visits completed outside the visit window will be recorded as a protocol deviation. The calendar application, which is a tool available in the REDCap Participant Management Program, generates contact windows based on the date of the Biopsy Visit. Contact windows define the period during which a visit is considered on time. Every effort should be made to conduct study visits at regular intervals.

Several tools are available to assist in organizing the required procedures, tests and CRFs associated with each visit and contact. Each KPMP Study visit has an accompanying checklist, which lists procedures for each clinic visit or telephone contact (See Appendix D). Tables 3 and 4a provide lists of KPMP CRFs by visit. Procedures and accompanying CRFs for each participant contact are included in the following sections. Daily clinical and biospecimen collection for AKI participants are summarized in table 4b.

Table 2: AKI and CKD Participant Visit Schedule for first 5 years of study follow-up

	Enrollment	Biopsy	Post-Bx Monitoring				Year 1		Year 2		Year 3		Year 4		Years 5	
Visit	**V0**	**V1**	**M1**	**A1**	**M2**	**M3**	**A2**	**R1***	**V2**	**R2**	**V3**	**R3**	**V4**	**R4**	**V5**	**R5**
Time	0	0	1d	5-7d**	14d	28d	3mo	6m	12m	18m	24m	30m	36m	42m	48m	54m
Window	0	0	12-48h	5-7d	10-20d	28-34d	2-4m	4-9m	9-15m	15-21m	21-27m	27-33m	33-39m	39-45m	45-51m	51-57m
Biospecimen	NO	YES	NO	YES	NO	NO	YES	NO	YES	NO	YES	NO	YES	NO	YES	NO

V = in-person visit with biospecimen sampling

A = AKI only in-person visit

M = Post-Bx monitoring phone calls

R = remote (e.g. telephone) visit; R1* Includes a 6-mo kidney function assessment for AKI participants

** = A1 occurs if participant is discharged prior to 5 days after biopsy. Up to 14 days is allowed with submission of a protocol deviation.

Table 3. CKD CRFs for each clinic and remote visit

	Screening	Enrollment Visit			Biopsy Visit	Post Biopsy			Remote Visits	Follow-up Visits
		In clinic	6w pre biopsy	6w pre to 7d post		24 Hr	2w	28d	6, 18, 30, 42, 54m	12, 24, 36, 48m
Screening Worksheet	X									
New Participant CRF	X									
End of Study		X			X	X	X	X	X	X
Visit Log		X			X				X	X
Eligibility Assessment		X			X					
Informed Consent		X								
Contact Information		X							X	X
Demographics		X								
Laboratory Results		X							X	X
PROMIS Global Health*		X								X
Health Literacy*		X								X (12MO)
Medical History (Participant)		X								
Medical History (Coordinator)		X								
Personal History*		X								X
Medications		X							X	X
Physical Measurements		X								X
Biopsy/ACD Scheduling		X								
Biosample Collection		X								X
Blood, spot urine			X							X
Screening blood labs			X							
Timed urine			X							
Stool*				X						
Pre-Biopsy Clinical Assessment			X							
Pre-Biopsy Safety					X					
Kidney Biopsy Procedure Details					X					
Post biopsy					X					
Tissue tracking					X					
Adverse Events					X	X	X	X		
CKD Adjudication								~1M		
Post Biopsy Phone Call						X	X	X		
Follow-up Clinical Assessment							X	(X)		
Follow-up Visit Completion CRF						X	X	X	X	X
Follow-up Medical Events									X	X
Post Bx Hospitalizations							X	X	X	X

Participant Experience Survey								X	X (6M)	

*can be completed at home and returned at biopsy visit.

Table 4a. AKI CRFs for each clinic and remote visit

	Screening	Enrollment Visit			Biopsy Visit	Post Biopsy			3m AKI Visit	Remote Visits 6, 18, 30, 42, 55m	Follow-up Visits 12, 24, 36, 48m
		In-clinic	48hr pre	24hr pre		daily (up to 7 days)	2w	28d			
Screening Worksheet	X										
New Participant CRF	X										
End of Study		X			X	X	X	X	X	X	X
Visit Log		X			X				X	X	X
Eligibility Assessment		X			X						
Informed Consent		X									
Contact Information		X							X	X	X
Demographics		X									
AKI Hospitalization		X				X					
Laboratory Results		X							X	X	X
Biosample Collection		X							X		X
Blood			X			X**			X		X
Screening blood labs			X								
Spot urine						X**			X		X
Timed urine/Stool				X							
Medical History Participant		X							X*		
Medical History Coordinator		X									
Personal History		X							X*		X
Medications		X							X	X	X
Physical Measurements		X							X		X
Daily AKI Measurements						X					
Pre-Biopsy Clinical Assessment			X								
Daily Progress Note		X			X	X					
Biopsy/ACD Scheduling		X									
Pre-Biopsy Safety CRF					X						
Kidney Biopsy Procedure					X						
Post biopsy					X						
Tissue tracking					X						
Adverse Events					X	X	X	X	X		
AKI Adjudication Report		X				2X					
Post Biopsy Phone Call							X	X			

5-7 Day Specimen Completion CRF						**X**					
Follow-up Visit Completion CRF							**X**	**X**	**X**	**X**	**X**
Follow-up Medical Events										**X**	**X**
Post Bx Hospitalizations							**X**	**X**	**X**	**X**	**X**
Follow-up Clinical Assessment							**X**	**X***			
Participant Experience Survey								**X**		**X (6M)**	
PROMIS Global Health									**X**		**X**
Health Literacy									**X**		**X (12 M)**

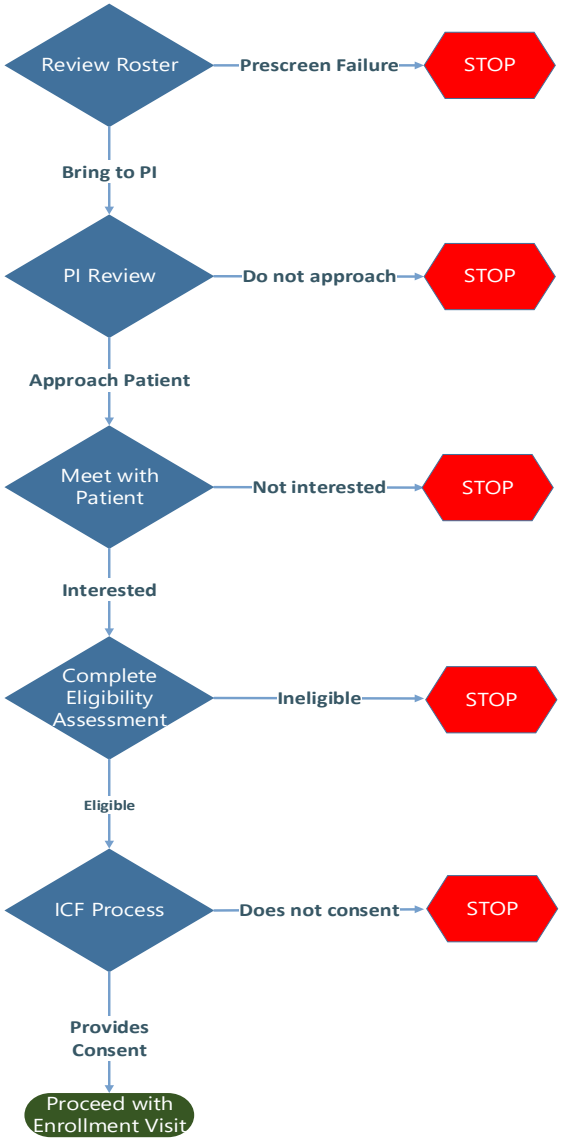
*if not completed in at enrollment visit.

**Blood and spot urine collection should be captured between day 5 and 7 post biopsy. Participants who have samples collected as inpatients on Day 5 and are then discharged satisfy this criterion. Participants who are discharged on Day 4 or earlier will have a clinic or home study visit between Days 5 & 7 to obtain these samples (up to 14 days is allowable with a protocol deviation).

Table 4b: Summary of Daily AKI Clinical and Biospecimen Data Collection

	Time points						
	Pre-bx	**Biopsy**	**0-1 hour post-bx**	**1-2 hours post-bx**	**2-6 hours post-bx**	**6-72 hours post-bx**	**Days 3-7 or until d/c**
Clinical data captured							
Urine output	q12 hours					q12 hours	q12 hours
Blood Pressure	q6 hours		q15 min	q30 min	q60 min	q 6 hours	Daily until discharge
Pulse	q6 hours		q15 min	q30 min	q60 min	q 6 hours	Daily until discharge
Fluid Balance	q12 hours					q12 hours	Daily until discharge
Serum Cr		X				Daily	Daily until discharge
Urine microscopy	X						May add serially when IDEXX available
Daily Progress Note	X (Enrollment)	X				Daily	Daily until discharge
Adjudication Report						X	X (5-7 days post-bx)

Table 5: Flow of CRFs and participant status updates used for the pre-enrollment screening and eligibility process.



Step:	Decision:	New Participant CRF	Consent CRF
Review Roster	Prescreen Failure	Not approached – did not meet pre-screening criteria.	
	Bring to PI	Proceed with screening	
PI Review	Do not approach	Enter Reason not approached	
	Approach patient	Proceed with screening (Final status)	
Meet with Patient	Not interested		
	Interested		
Complete Eligibility Assessment	Ineligible		
	Eligible		
ICF Process	Does not consent		Participant consent not signed
	Provides Consent		Participant signs consent form
After consent, return to New Participant CRF and Eligibility Assessment to enter post-consent PII.			

5.2. Screening Activities

Screening activities include assessment of study eligibility and providing participants with information about the study. Site investigators should be available to answer any questions or provide additional information to those considering KPMP participation. Participant contact may occur on the telephone or in-person.

Determining eligibility is a multiple step process involving the review of medical information, evaluation of screening labs, participant conversation at a screening visit or phone call, and conference with the participant's healthcare team and the KPMP PI. Detailed inclusion and exclusion criteria are presented in section 2.2.

Screening Activities include the following steps:

5.2.1. Tracking Pre-screening Activities:

CRF: New Participant CRF

Pre-screening eligibility Information collected from the medical record or other sources prior to meeting with the participant can be recorded on the Screening Worksheet (see appendix F), or via local spreadsheets or databases. All necessary and relevant screening information will not be available from the medical record. However, even partial review of the information included in the Screening Worksheet should help determine whether a participant is potentially eligible or ineligible for the study.

The Screening Worksheet may contain personal identifying information and is not entered in the PMP. It is strictly a tool for gathering information to assess and contact participants. It is not essential to answer all questions. Store these forms in a locked file cabinet.

All participants who are screened for KPMP are entered in the REDCap KPMP Participant Management Program (PMP) by completing the New Participant CRF. This CRF is used as the KPMP Screening log. Demographics and the results of approaching the potential participant should be entered in the New Participant CRF.

Participant Registration Tools are described in section 11.3.

Record whether a prescreening consent form was used to obtain biospecimens to determine eligibility.

For participants who are quickly eliminated, record the reason in the New Participant CRF by selecting "yes" for "Was the participant excluded through pre-screening criteria?" and choose the outcome "Not approached – did not meet pre-screening criteria". Select one or more reasons for ineligibility and fill out the demographic information.

For participants who pass pre-screening criteria, select "proceed with screening" or select an appropriate "Not approached" reason.

Table 5 describes in detail the flow of CRFs and participant status updates used for the pre-enrollment screening and eligibility process

5.2.2. Eligibility Assessment Activities:

CRF: Eligibility Assessment

If a potential participant passes prescreening, request permission from their Primary kidney care physician to discuss the KPMP Study.

KPMP investigators will contact participants either by phone or in person to determine interest and eligibility for the study.

Once the participant is approached for participation, begin collecting information in the Eligibility Assessment CRF. Items in the Eligibility Assessment CRF that will be assessed later can be marked as "Unknown."

In Eligibility Assessment CRF, if entering data for someone pre-consent, select "no" for "Did participant sign consent?" which allows for data entry without procedure dates. Until the informed consent form is signed and recorded in the Consent CRF, no PHI can be entered in the Eligibility Assessment or New Participant CRFs.

- After consent, change "Did participant sign consent" to "yes", which allows for entry of previously hidden PHI fields. Return to the Eligibility Assessment and New Participant CRFs to enter dates and other PHI after the consent is signed.
- If the participant does not consent, leave the fields blank
- Use the 'Incomplete' form status to leave the form status red until consent decision is reached, providing a visual reminder to back to enter data. After entering PHI data, update the form status to "complete."

If the Research Coordinator is unable to make a determination of ineligible or not ineligible based on the information collected from the medical record and participant interview, the PI should be consulted, and additional sources of information may need to be reviewed.

If lab tests are needed to confirm eligibility prior to enrollment, complete Screening Consent Form. If the participant is found to be ineligible, biosamples will be discarded. Completion of the Screening Consent Form is tracked locally and not in REDCap.

No further information will be collected about participants deemed ineligible.

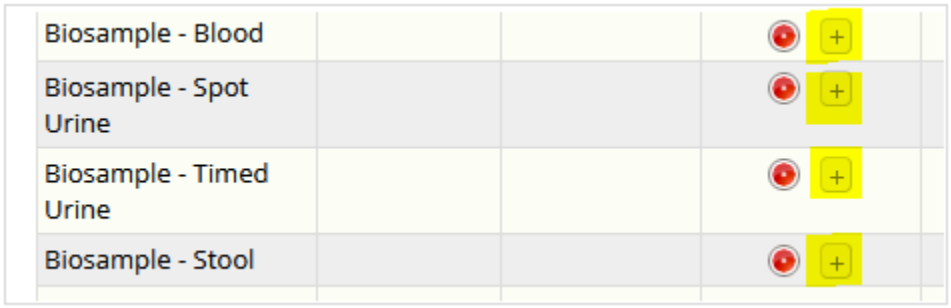
If an eligible potential participant refuses to participate in the study, record the refusal reason on the Consent CRF. Eligible participants that agree to participate are scheduled for an Enrollment Visit.

Schedule participants for the Enrollment Visit as soon as possible, although there are no restrictions or time limits to this interval.

Provide instructions for the Enrollment Visit to the participant. Instruct participants to bring all recent [within the last 30 days] prescription and non-prescription medications with them to the Enrollment Visit so that they can be identified for collection of medication information.

5.2.3. Rescreening Activities:

Biopsies should be scheduled within 6 weeks of baseline biosample collections for CKD and within 48 hours for AKI. If CKD baseline biosamples are collected and the biopsy is not completed within 6 weeks (per the BS MOP), new blood and urine samples can be collected and recorded in a new instance of the Biosample CRFs. Click the '+' icon to create a new instance of the CRF. Do NOT overwrite old data. Tables 1 and 2 in the Biospecimen MOP describe timelines for collection baseline samples. If new biosamples are collected for rescreening activities, both the new and old samples should be shipped to the CBR.



For previously enrolled participants who are re-approached, check over any previously entered CRFs and overwrite any old data with updates. For example, when re-assessing eligibility criteria, if anything has changed from the first evaluation, overwrite (i.e. replace) the old data in the Eligibility Assessment with new. Note the exception to this overwriting rule is the biosample collection forms -- if re-collecting blood and urine, do NOT overwrite the original form (because the old blood and urine are sent to the CBR). Instead, use the + icon to add another copy of the form as noted above).

5.3. Enrollment Visit

The Enrollment Visit requires one or more in-person clinic visit(s) to complete the following study components and procedures:

5.3.1. Provide Visit Date and Participant time burden

CRF: Visit Log

5.3.2. Assessment of inclusion/Exclusion Criteria

CRF: Eligibility Assessment CRF

If lab tests are needed to confirm eligibility prior to enrollment, complete Screening Consent Form.

In Eligibility Assessment CRF, if entering data for someone pre-consent, select "no" for “Did participant sign consent?” which allows for data entry without procedure dates. Until the informed consent form is signed and recorded in the Consent CRF, no PHI can be entered in the Eligibility Assessment CRF.

- After consent, change “Did participant sign consent” to “yes”, which allows for entry of previously hidden PHI fields. Return to the Eligibility Assessment CRF to enter dates and other PHI after the consent is signed.

- If the participant does not consent, leave the fields blank
- Use the 'Incomplete' form status to leave the form status red until consent decision is reached, providing a visual reminder to back to enter data. After entering PHI data, update the form status to “complete.”

Bleeding criteria screening and urine pregnancy tests (if necessary) are completed up to two weeks prior to biopsy for CKD participants, or up to 48 hours prior to biopsy for AKI. These tests may be completed at the Biopsy Visit.

If necessary, place an order to collect bleeding criteria screening labs prior to the Biopsy Visit.

Women who are pre-pubertal, post-menopausal, or with other medical reasons for permanent, irreversible infertility do not require a pregnancy test. If the participant is not of child-bearing potential, record “No” for the pregnancy test completion question on the Eligibility Assessment.

5.3.3. Informed Consent Process

CRF: Informed Consent

After confirming eligibility, participants will sign and date the informed consent form (if not previously completed) in either English or Spanish. Spanish-speaking participants must sign a Spanish-translated IRB-approved version of the informed consent form. A copy of the signed informed consent will be given to the participant. The original signed consent form should be placed in the participant’s study file and/or added to the EHR. A second copy should be placed in a confidential study folder containing copies of consents for all study participants and/or uploaded to the participant EHR as required locally. If a potential participant needs more time to review and complete the ICF, Enrollment Visit study procedures can be completed during an additional study visit after the ICF is signed.

Return to the New Participant and Eligibility CRFs to update PHI data after the ICF is signed.

See instructions in section 3.4.2 for LAR consent procedures for Pittsburgh open biopsies. For Pittsburgh open biopsies, "Was consent signed?" includes response options Participant signed consent form, LAR signed consent form, and Consent not signed. If LAR signed consent, obtain consent from participant when they regain capacity and complete "Did participant sign consent?" question. If yes, collect date. Do not complete the 3 month visit without participant consent.

5.3.4. Collect Contact Information

CRF: Participant Contact

Interview the participant to complete the Participant Contact CRF. Participant Contact CRF information should be reviewed and updated during each subsequent visit

Encourage participants to provide an email address to receive web links to confidential participant experience surveys after the 28-day and 6-month phone visits.

5.3.5. Collect Medications Inventory

CRF: Medications

Complete the Medications CRF by reviewing all prescription and non-prescription medications that participant has taken in the last 30 days. Best practice is to get the information from the participant and then follow up with chart review to ensure that everything is captured.

Record the medications, noting total daily dose, unit, frequency and route, on the Medications CRF. Review the EHR for any missing medications or details.

For AKI participants, record medications from 30-days prior to enrollment, during the biopsy procedure, and until hospital discharge.

5.3.6. Record Medical History

CRF: Participant Medical History, Coordinator Medical History

The Participant Medical History CRF is interview administered by the Research Coordinator. If participants have difficulty answering a question, instruct them to make their best estimate rather than leave a response blank. Questionnaires can be finished by phone interview if necessary (or at the 3-month visit for AKI participants). Information recorded in the Medical History Participant CRF may be updated or verified by the Research Coordinator through reviewing the EHR.

Complete the Coordinator Medical History form by reviewing data and uploading images from the EHR.

5.3.7. Participant Administered Questionnaires

CRFs: Demographics, Personal History, Health Literacy, PROMIS Global Health

Participant-administered CRFs are completed on paper either during the Enrollment Visit, or at home and returned at the biopsy visit. If completed in person, ensure that the participant has quiet space to complete the form where they won't be distracted or rushed. Let the participant know how to contact the research coordinator in case questions come up as they complete the forms.

AKI participants may complete the forms at their 3-month visit if time or circumstances do not allow during their hospitalization.

5.3.8. Physical Exam

CRF: Physical Measurements

Complete physical measurements including height, weight, blood pressure, heart rate, temperature, and edema assessment, recording the measurements on the Physical Measurements CRF. Blood pressures are measured following the procedure outlined in Appendix C of this manual. Record the pulse and 3 sequential BP measurements while the participant is seated, followed by the pulse and one BP measurement while standing (if possible).

5.3.9. Biospecimen Collection

CRF: Biospecimen CRF for Blood, Spot Urine, Timed Urine, Stool, and Biopsy/ACD Scheduling CRF

Samples should be collected as close to the biopsy as possible (up to 6 weeks before the biopsy for CKD participants, or up to 48 hours before the biopsy for AKI participants). See the Biospecimen MOP for additional details. No specimens may be collected until eligibility is confirmed and the ICF is signed.

If ACD tube is drawn, record date of ACD tube collection in Biopsy Scheduling CRF ASAP to notify biorepository. Record scheduled biopsy date, if known.

At the end of the Enrollment Visit, both AKI and CKD participants are given supplies for collecting a timed urine and stool specimen along with instructions for completing the specimen collection and returning it to the clinic at the Biopsy Visit.

5.3.10. Pre-biopsy Clinical Assessment

CRF: Clinician and Investigator Pre-biopsy Clinical Assessment

The KPMP PI and a member of the participant care team will complete the Pre-biopsy Clinician Assessment before knowing the results of the kidney biopsy. The CRF provides an option to track cases where no renal tissue was obtained, and pathology results are not expected. Research Coordinators may need to facilitate completion of the CRFs by providing the paper version and subsequently entering the responses into the REDCap PMP. When entering paper CRFs into REDCap, one research coordinator enters the data and selects the form status "unverified." A second staff member should check that that the data entry is correct and then update the form status to "complete."

Research Coordinators can send clinicians an email containing a URL link to complete the Pre-biopsy Clinician Assessment CRF as a web-survey using the "Send Clinician Pre-Clinical Assessment" CRF.

5.3.11. Laboratory Results

CRF: Laboratory Results

Complete the Laboratory Results CRF using EHR data after the Enrollment Visit.

For AKI participants, enter creatinine and urine protein measures from before the current hospitalization in the Laboratory Results CRF. Record creatine and urine protein measures from the enrollment hospitalization should be recorded in the AKI Daily Measures CRF.

5.3.12. AKI Hospitalization Data

CRF: AKI Hospitalization CRF, AKI Daily Progress CRF, AKI Daily Measures, AKI Adjudication CRF

Site investigators complete the Daily Progress Note for AKI participants on the day of enrollment and then daily until hospital discharge.

Research Coordinators complete the Daily Measures and AKI Hospitalization CRF for AKI participants on the day of enrollment and daily until hospital discharge.

The site investigator, together with a small quorum of KPMP AKI investigators, will complete phase one of the two-step 'AKI Adjudication' process within 72 hours of enrollment. The investigators will convene and complete the Adjudication Report, with the aim of standardizing etiology across sites. Phase two is described in Section 5.4.

5.3.13. Update Participant Status

CRFs: Participant Status or End of Study

Update the Participant Status CRF to indicate any updates (changing from “Screening in progress” to failed screening, passed screening, but participant still deciding, passed screening but did not consent, or participant consented and enrolled.

Once a participant is classified as “consented and enrolled,” further updates to study status such as completed or withdrew from study, deceased, lost to follow-up, or loss of eligibility are recorded in the End of Study CRF. If after enrollment a participant is found to be ineligible (due to laboratory results or other conditions, report them as “Loss of eligibility” in the End of Study CRF.

If a participant is enrolled as eligible and has signed the informed consent form, but later fails safety criteria and can't have the biopsy, all collected biosamples should be kept and sent to CBR.

If a deviation occurs and the biosamples may not be used, be transparent with participants regarding deviations to the biospecimen protocol and inability to use participant samples. Have these conversations in-person if possible instead of sending a letter, to allow participants to ask questions. Details and logistics of these communication are left to sites to allow sites to do what’s best for them.

5.4. Biopsy Visit

The Biopsy Visit requires one or more in-person clinic visit(s) to complete the following study components and procedures:

5.4.1. Provide Visit Date and Participant time burden

CRF: Visit Log

5.4.2. Review Inclusion/Exclusion Criteria

CRF: Eligibility Assessment and Pre-Biopsy Safety

Review bleeding exclusion criteria blood tests and pregnancy test (for women less than 55 years old). Remind participants that they may take their prescribed blood pressure medication with a sip of water on the day of the biopsy.

Women who are pre-pubertal, post-menopausal, or with other medical reasons for permanent, irreversible infertility do not require a pregnancy test. If the participant is not of child-bearing potential, record “N/A” for the pregnancy question on the Pre-Biopsy Safety CRF.

5.4.3. Participant Administered Questionnaires

CRFs: Demographics, Personal History, Health Literacy, PROMIS Global Health

Receive participant administered CRFs if they were completed on paper at home and returned at the biopsy visit.

When entering paper CRFs into REDCap, one research coordinator enters the data and selects the form status “unverified.” A second staff member should check that that the data entry is correct and then update the form status to “complete.”

AKI participants may complete the forms at their 3-month visit if time or circumstances do not allow during their hospitalization.

5.4.4. Biospecimen Collection

CRF: Biospecimen CRF Timed Urine and Stool and Laboratory Results

Record the received timed urine and stool samples and process according to instructions in Biospecimen MOP.

For AKI participants, order urine microscopy from the clinical lab and record the results in the Laboratory Results CRF.

5.4.5. Update Contact Information

CRF: Participant Contact

Review all participant and healthcare provider contact information, making the appropriate updates.

5.4.6. Complete Pre-Biopsy Safety Checklist

CRF: Pre-Biopsy Safety

The Pre-Biopsy Safety CRF must be completed in REDCap before the start of the biopsy. The paper copy is available to give you flexibility to get the data from the operator, but it MUST be transcribed into REDCap BEFORE the biopsy so the system can check the data and flag (red banner) if the participant hasn't passed safety criteria.

An electronic signature field at the end of the CRF must be signed by the operator.

5.4.7. Perform Kidney Biopsy

CRF: Kidney Biopsy Procedure Details

Complete the kidney biopsy according to details in Section 7 and the Pathology MOP.

5.4.8. Tissue and Pathology Tracking and Shipping

CRFs: Tissue Tracking, Pathology Images, Pathology Images QC, Pathology Slides QC, Pathology Findings, Central Path Quality Metrics Assessment

Ship and track kidney tissue, blood, stool, and urine according to Biospecimen and Pathology MOPs.

Report Adverse Events in the REDCap Adverse Events Project.

5.4.9. Post Biopsy Monitoring

CRFs: Post Biopsy Monitoring, Biosample – AKI Blood and Urine, AKI Daily Measurements, AKI Daily Progress, Adverse Event

Follow post-biopsy procedures from the Post Biopsy CRF and from Section 7.1.5 or 7.2.3.

<u>For AKI participants only:</u> Continue with daily collection of urine output, vitals, fluid balance, serum creatinine in the AKI Daily Measures CRF until discharge. PI continues to complete Daily Progress CRF until discharge. If clinical measures are not being ordered, KPMP investigators should follow-up with the clinical team.

Report Adverse Events in the REDCap Adverse Events Project

5.4.10. Other Post-Biopsy Activities

CRF: Follow-up Investigator Assessment, AKI/CKD Adjudication

When AKI participants are released from the hospital, provide the KPMP 3-month Visit Packet with at-home questionnaires, if not already completed, (PROMIS Global Health CRF, Health Literacy CRF, Personal History CRF) and stool collection supplies and instructions (if the stool sample was not collected ruing the hospital stay).

After biopsy results are returned, the primary physician and/or KPMP Investigator complete the Follow-up Clinical Assessment CRF. Research Coordinators can send clinicians an email containing a URL link to complete the Post-biopsy Clinician Assessment CRF as a web-survey using the "Send Clinician Post-Clinical Assessment" CRF.

For AKI participants only: The site investigator, together with a quorum of KPMP AKI investigators, will complete phase two of the two-step 'AKI Adjudication' process five-seven days post-biopsy. The investigators will complete the Adjudication CRF.

For CKD participants only: The site investigator and pathologist, together with a quorum of KPMP CKD investigators, will complete the CKD Adjudication process after pathology slides are received and scanned by the CBR and added to the digital image repository at the DVC. PIs complete the Adjudication CRF.

CRF: Consent

If a legally authorized representative (LAR) provided consent, obtain participant consent when they regain capacity to consent.

5.4.11. Update Participant Status

CRFs: End of Study

Record any study status updates (withdrew from study, deceased, lost to follow-up, loss of eligibility, etc.) in the End of Study CRF. If after enrollment (but before biopsy) a participant is found to be ineligible (due to laboratory results or other conditions), report them as "Loss of eligibility" in the End of Study CRF.

If a participant is enrolled as eligible and has signed the informed consent form, but later fails safety criteria and can't have the biopsy, all collected biosamples should be kept and sent to CBR. A participant who does not have a biopsy does not need to continue with follow-up visits.

5.5. 24-hour Post Biopsy Phone Call

The primary purpose of the 24-hour phone call is to collect details of any adverse events that occurred since the biopsy visit. For this visit, collect details of adverse events since the participant's biopsy. Visit windows are 12-48 hours after biopsy. The Participant Management Program provides for a calendar

application to assist in scheduling participants. If the participant wishes, telephone visits can be completed in-person without being considered a protocol deviation.

The 24-hour Post Biopsy Phone call includes the following steps:

5.5.1. Provide Visit Date and Participant time burden

CRF: Visit Log

5.5.2. Record 24-Hours Post-Biopsy Call Status

CRF: 24 Hour Participant Follow-up

Record the status of the follow-up call. If the call is not done and staff are still working to reach the participant, the CRF status should remain as "attempted" until the visit window closes (see table 2). If the call is not completed before the visit window closes, record the status as not done and record the reason.

If the call did not occur, enter the date when it was determined that the call would not occur, and record the reason. If after leaving messages and calling repeatedly the follow up cannot be obtained, the call status is recorded as "participant unable" and "could not locate."

If a death, withdrawal, or other End of Study status update is discovered within the visit window, update the 24-Hour Participant Follow-up CRF to indicate that the call will not be completed and enter the reason. Also update the End of Study CRF.

If a response on the CRF indicates an Adverse Event, report the AE in the KPMP Adverse Events Reporting REDCap project. If a "yes" response for "Did you experience any other complications from the biopsy procedure that you noticed" indicates to an adverse event, record the ID of the AE in the 24-hour Participant Follow-up CRF after it is entered in the KPMP Adverse Events Reporting REDCap project.

CRF: Adverse Events

Record any adverse events reported during the 24-hour phone call.

5.5.3. Record Post Biopsy Re-hospitalizations

CRF: Post Biopsy Re-hospitalization

If the participant was re-hospitalized after being discharged from their KPMP hospitalization, collect the details in the Post Biopsy Re-hospitalization CRF. Do not fill out this form UNLESS the participant was re-hospitalized after discharge; remember that the details of the precipitating AKI event for AKI participants go in the AKI Hospitalization form.

5.5.4. Update Participant Status

CRFs: End of Study

Record any study status updates (withdrew from study, deceased, lost to follow-up, loss of eligibility, etc.) in the End of Study CRF. If after enrollment a participant is found to be ineligible (due to laboratory results or other conditions, report them as "Loss of eligibility" in the End of Study CRF.

5.5.5. Send Surveys links to local pathologists

CRFs: Send Pathology IF Metadata and Send Dx Core - DCA

Complete these two CRFs within 24 hours after the biopsy. The CRFs will trigger and email to the local pathologist with a link to complete the Pathology IF Metadata and Dx Core Disease Category Assignment CRFs. Pathologists need to have these survey links when they complete the diagnostic workup for the biopsy tissue.

5.6. 5-7 day AKI Specimen Collection

AKI participants require blood and urine specimen collection at least one time within the timeframe 5 to 7 days after biopsy. Participants who have samples collected as inpatients on Day 5 and are then discharged satisfy this criterion. Participants who are discharged on Day 4 or earlier will have a clinic or home study visit between Days 5 & 7 to obtain these samples. During this contact, also collect details of adverse events since the participant's biopsy. Specimen collection window is 5-7 days after biopsy, but it can be completed up to 14 days after the biopsy with submission of a protocol deviation. The Participant Management Program provides for a calendar application to assist in scheduling participants.

The 5-7 day AKI Post Biopsy Specimen Collection includes the following steps:

5.6.1. Provide Date and Participant time burden

CRF: Visit Log

5.6.2. Record 5-7 day AKI Specimen Collection Status

CRF: 5-7 Day AKI Follow-up

Record the status of the specimen collection. If the collection is not done and staff are still working to reach the participant, the CRF status should remain as "attempted" until the visit window closes (see table 2).

If the specimen collection did not occur, enter the date when it was determined that it would not occur in the 5-7 Day AKI Follow-up CRF, and record the reason. If after leaving messages and calling repeatedly the specimen collection cannot be obtained, the status is recorded as "participant unable" and "could not locate."

If a death, withdrawal, or other End of Study status update is discovered within the visit window, update the 5-7 Day AKI Follow-up CRF to indicate that the visit will not be completed and enter the reason. Also update the End of Study CRF.

CRF: Adverse Events

Record any adverse events reported during the 5-7 Day AKI specimen collection.

5.6.3. Record Post Biopsy Re-hospitalizations

CRF: Post Biopsy Re-hospitalization

If the participant was re-hospitalized after being discharged from their KPMP hospitalization, collect the details in the Post Biopsy Re-hospitalization CRF. Do not fill out this form UNLESS the participant was re-hospitalized after discharge; remember that the details of the precipitating AKI event for AKI participants go in the AKI Hospitalization form.

5.6.4. Update Participant Status

CRFs: End of Study

Record any study status updates (withdrew from study, deceased, lost to follow-up, loss of eligibility, etc.) in the End of Study CRF. If after enrollment a participant is found to be ineligible (due to laboratory results or other conditions, report them as "Loss of eligibility" in the End of Study CRF.

5.7. 2-week Post Biopsy Phone Call

The primary purpose of the 2-week phone call is to collect details of any adverse events that occurred since the biopsy hospitalization visit. For this visit, collect details of adverse events since the participant's last contact. Visit windows are 10-20 days after biopsy. Contacting participants early in the visit window allows for maximum flexibility in reaching participants by phone or time to locate missing participants. The Participant Management Program provides for a calendar application to assist in scheduling participants. If the participant wishes, telephone visits can be completed in-person without being considered a protocol deviation.

The 2-week Post Biopsy Phone call includes the following steps:

5.7.1. Provide Visit Date and Participant time burden

CRF: Visit Log

5.7.2. Record 2-Week Post-Biopsy Call Status

CRF: 2-week Participant Follow-up

Record the status of the follow-up call. If the call is not done and staff are still working to reach the participant, the CRF status should remain as "attempted" until the visit window closes (see table 2). If the call is not completed before the visit window closes, record the status as not done and record the reason.

If the call did not occur, enter the date when it was determined that the call would not occur, and record the reason. If after leaving messages and calling repeatedly the follow-up can still not be completed, the call status is recorded as "participant unable" and "could not locate."

If a death, withdrawal, or other End of Study status update is discovered within the visit window, update the 2-week Participant Follow-up CRF to indicate that the call will not be completed and enter the reason. Also update the End of Study CRF.

If a response on the CRF indicates an Adverse Event, report the AE in the KPMP Adverse Events Reporting REDCap project. If a "yes" response for "Did you experience any other complications from the biopsy procedure that you noticed" indicates to an adverse event, record the ID of the AE in the 2-week Participant Follow-up CRF after it is entered in the KPMP Adverse Events Reporting REDCap project.

5.7.3. Record Adverse Events

CRF: Adverse Events

Record any adverse events reported during the 2-week phone call.

5.7.4. Record Post Biopsy Re-hospitalizations

CRF: Post Biopsy Re-hospitalization

If the participant was re-hospitalized after being discharged from their KPMP hospitalization, collect the details in the Post Biopsy Re-hospitalization CRF.

5.7.5. Update Participant Status

CRFs: End of Study

Record any study status updates (withdrew from study, deceased, lost to follow-up, loss of eligibility, etc.) in the End of Study CRF.

5.8. 28-day Post Biopsy Phone Call

The primary purpose of the 28-day phone call is to collect details of any adverse events that occurred since the biopsy hospitalization visit. For this visit, collect details of adverse events since the participant's last contact. Begin contacting participants 28 days after the biopsy visit. Visit windows are 28-34 days after biopsy. The Participant Management Program provides for a calendar application to assist in scheduling participants. If the participant wishes, telephone visits can be completed in-person without being considered a protocol deviation.

The 28-day Post Biopsy Phone call includes the following steps:

5.8.1. Provide Visit Date and Participant time burden

CRF: Visit Log

5.8.2. Record 28-day Post-Biopsy Call Status

CRF: 28-day Participant Follow-up

Record the status of the follow-up call. If the call is not done and staff are still working to reach the participant, the CRF status should remain as "attempted" until the visit window closes (see table 2). If the call is not completed before the visit window closes, record the status as not done and record the reason.

If the call did not occur, enter the date when it was determined that the call would not occur, and record the reason. If after leaving messages and calling repeatedly the follow-up can still not be completed, the call status is recorded as "participant unable" and "could not locate."

If a death, withdrawal, or other End of Study status update is discovered within the visit window, update the 28-Day Participant Follow-up CRF to indicate that the call will not be completed and enter the reason. Also update the End of Study CRF.

If a response on the CRF indicates an Adverse Event, report the AE in the KPMP Adverse Events Reporting REDCap project. If a "yes" response for "Did you experience any other complications from the biopsy procedure that you noticed" indicates to an adverse event, record the ID of the AE in the 28-day Participant Follow-up CRF after it is entered in the KPMP Adverse Events Reporting REDCap project.

CRF: Adverse Events

Record any adverse events reported during the 28-day phone call.

5.8.3. Record Post Biopsy Re-hospitalizations

CRF: Post Biopsy Re-hospitalization

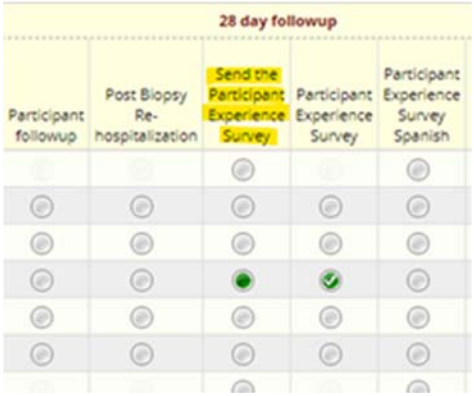
If the participant was re-hospitalized after being discharged from their KPMP hospitalization, collect the details in the Post Biopsy Re-hospitalization CRF.

5.8.4. Collect Participant Experience Survey

CRFs: Participant Experience Survey and Send the Participant Experience Survey CRF

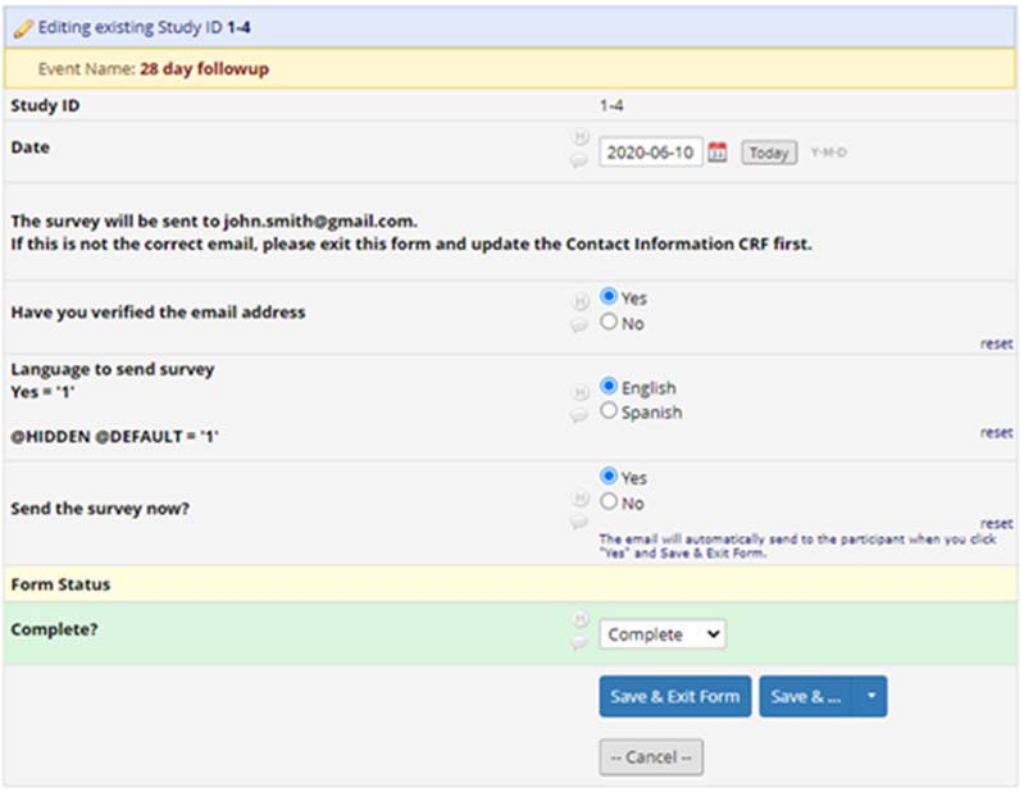
During the 28-day phone call, remind the participant that KPMP would like to send an email link to a confidential Participant Experience survey. If an email address was not provided at a previous visit, ask for an email address where the participant could receive a link to the survey.

After completing the 28-day follow-up CRF, select the "send the participant experience survey" CRF button from the REDCap PMP dashboard:



In the CRF, enter the date and confirm the email address listed for the participant. If it needs updating, enter the new email address on the Contact Information CRF.

Confirm the email address, select the Spanish or English version of the CRF, select "yes" to send the survey, mark CRF as complete, and save and exit the CRF. REDCap will automatically send an email to the participant with a link to the survey once you save and exit the CRF.



Completion status for the emailed Participant Experience Survey can be viewed from within the "Send the Participant Experience Survey" CRF. After receiving the survey email and link, partipcant will be sent weekly reminders for three weeks reminding them to complete the survey. After 4 weeks, DCC queries will prompt Research Coordinators to contact participants about missing surveys.

If the participant does not have an email address, print a paper copy of the CRF in the participant's preferred language (English or Spanish) and mail it to the participant with a stamped envelope addressed to:

KPMP DCC
University of Washington
Bldg29, Suite 310
6200 74th Street NE
Seattle, WA 98115

DCC staff will enter the survey data into the REDCap PMP.

5.8.5. Update Participant Status

CRFs: End of Study

Complete any necessary updates to study status such as completed or withdrew from study, deceased, lost to follow-up, or loss of eligibility; these are recorded in the End of Study CRF.

5.9. 3-month AKI Visit

The 3-month AKI Visit serves as a baseline out-patient visit for AKI participants. Some of the procedures collected for CKD participants at the Biopsy Visit are completed at the 3-month visit for AKI participants: Physical Measurements, PROMIS Global Health, Health Literacy, Personal History.

Begin contacting AKI participants 1 month prior to their target 3-month AKI Visit date. Visit windows are minus and plus 1 month of the target date; therefore, contacting participants early in the visit window allows for maximum flexibility in reaching participants by phone or time to locate missing participants. The Participant Management Program provides for a calendar application to assist in scheduling participants.

If a legally authorized representative (LAR) provided consent, participant consent must be obtained before the 3-month visit.

The 3-month AKI Visit includes the following steps:

5.9.1. Provide Visit Date and Participant time burden

CRF: Visit Log

5.9.2. Record 3-month Visit Status

CRF: 3-Month Participant Follow-up

Prior to the in-clinic visit, remind participants to bring all prescription and non-prescription medications taken in the past 30 days and (preferably) any completed at-home questionnaires.

Record the status of the 3-month visit. If the visit is not done and staff are still working to reach the participant, the CRF status should remain as “attempted” until the visit window closes (see table 2). If the visit is not completed before the visit window closes, record the status as not done and record the reason.

If the visit did not occur, enter the date when it was determined that the visit would not occur, and record the reason. If after leaving messages and calling repeatedly the follow-up can still not be completed, the visit status is recorded as “participant unable” and “could not locate.”

If a death, withdrawal, or other End of Study status update is discovered within the visit window, update the Visit Status CRF to indicate that the visit will not be completed and enter the reason. Also update the End of Study CRF

5.9.3. Update Contact Information

CRF: Participant Contact

Review all participant and healthcare provider contact information, making the appropriate updates.

5.9.4. Collect Medications Inventory

CRF: Medications

Complete the Medications CRF by reviewing all prescription and non-prescription medications that participant has taken in the last 30 days. Best practice is to get the information from the participant and then follow up with chart review to ensure that everything is captured.

Record the medications, noting total daily dose, unit, frequency and route, on the Medications CRF. Review the EHR for any missing medications or details.

If a previous medication is reported with a new dose or frequency, mark the medication as stopped at the previous dose and create a new instance of the CRF for starting the medication at the new dose or frequency.

5.9.5. Record Medical History

CRFs: Participant Medical History, Coordinator Medical History

Review and update information provided during the Enrollment Visit. The Participant Medical History CRF is interview administered by the Research Coordinator. If participants have difficulty answering a question, instruct them to make their best estimate rather than leave a response blank. Questionnaires can be finished by phone interview if necessary (or at the 3-month visit for AKI participants). Information recorded in the Medical History Participant CRF may be updated or verified by the Research Coordinator through reviewing the EHR.

The Coordinator Medical History form is reviewing data and uploading images from the EHR.

5.9.6. Record Post Biopsy Re-hospitalizations

CRF: Post Biopsy Re-hospitalization

If the participant was re-hospitalized after being discharged from their KPMP hospitalization, collect the details in the Post Biopsy Re-hospitalization CRF.

5.9.7. Participant Administered Questionnaires

CRFs: PROMIS Global Health, Personal History, Health Literacy

Complete the PROMIS Global Health CRF, and if not completed at the time of enrollment, the Personal History and Health Literacy CRFs. Participant-administered CRFs are completed on paper either during the visit, or at home and returned at the 3-month visit. If completed in person, ensure that the participant has quiet space to complete the form where they won't be distracted or rushed. Let the participant know how to contact the research coordinator in case questions come up as they complete the forms.

When entering paper CRFs into REDCap, one research coordinator enters the data and selects the form status "unverified." A second staff member should check that that the data entry is correct and then update the form status to "complete."

5.9.8. Physical Exam

CRF: Physical Measurements

Complete physical measurements including height, weight, blood pressure, heart rate, temperature, and edema assessment, recording the measurements on the Physical Measurements CRF. Blood pressures are measured following the procedure outlined in Appendix C of this manual. Record the pulse and 3 sequential BP measurements while the participant is seated, followed by the pulse and one BP measurement while standing (if possible).

5.9.9. Biospecimen Collection

CRF: Biospecimen CRF for Blood, Spot Urine

See the Biospecimen MOP for additional details.

5.9.10. Laboratory Results

CRF: Laboratory Results

Complete the Laboratory Results CRF using EHR data since the Enrollment Visit. If no new laboratory results are available since the last visit, enter "N/A, no new labs since last visit" for the question "Were all available lab values entered" at the end of each section of the CRF.

An Order for 6-month serum creatinine assessment should be placed at the 3-month visit.

5.9.11. Update Participant Status

CRFs: End of Study

Complete any necessary updates to study status such as completed or withdrew from study, deceased, lost to follow-up, or loss of eligibility are recorded in the End of Study CRF.

5.10. Remote Visits R1-5 (6, 18, 30, 42, 54 months)

Remote telephone visits start 6 months after the Biopsy Visit and continue 6 months after each in-person clinic visit to keep participants engaged and to collect data regarding medical events and hospitalizations. If the participant wishes, telephone visits can be completed in-person without being considered a protocol deviation.

Begin contacting participants 2 months prior to their target Remote Visit date. Visit windows are minus and plus 2 months of the target date. Contacting participants early in the visit window allows for maximum flexibility in reaching participants by phone or time to locate missing participants. The Participant Management Program provides a calendar application to assist in scheduling participants.

A visit is considered "late" when it is conducted outside the original two-month window dates. A visit is considered "missing" if it does not occur before the next visit window has opened.

This is an opportunity to discuss the KPMP Study schedule with the participant and to remind them about the next upcoming clinic visit. Consider scheduling the next clinic visit and tests at this time if the participant is willing to do so.

Remote Visit Phone calls include the following steps:

5.10.1. Provide Visit Date and Participant time burden

CRF: Visit Log

5.10.2. Record Remote Visit Call Status

CRF: Remote Follow-up

Record the status of the remote visit call. If the call is not done and staff are still working to reach the participant, the CRF status should remain as "attempted" until the visit window closes (see table 2). If the call is not completed before the visit window closes, record the status as not done and record the reason.

If the call did not occur, enter the date when it was determined that the call would not occur, and record the reason. If after leaving messages and calling repeatedly the follow-up can still not be completed, the call status is recorded as "participant unable" and "could not locate."

If a death, withdrawal, or other End of Study status update is discovered within the visit window, update the Participant Follow-up CRF to indicate that the call will not be completed and enter the reason. Also update the End of Study CRF.

5.10.3. Update Contact Information

CRF: Participant Contact

Review all participant and healthcare provider contact information, making the appropriate updates.

5.10.4. Collect Medications Inventory

CRF: Medications

Complete the Medications CRF by reviewing all prescription and non-prescription medications that the participant has taken in the last 30 days. Best practice is to get the information from the participant and then follow up with chart review to ensure that everything is captured.

Record the medications, noting total daily dose, unit, frequency, and route, on the Medications CRF. Review the EHR for any missing medications or details.

If a previous medication is reported with a new dose or frequency, mark the medication as stopped at the previous dose and create a new instance of the CRF for starting the medication at the new dose or frequency.

5.10.5. Collect Follow-up Medical Events

CRF: Follow-up Medical Events

Review and update Medical History information since the last visit. Information recorded in the Medical History Participant CRF may be updated or verified by the Research Coordinator through reviewing the EHR.

5.10.6. Record Post Biopsy Re-hospitalizations

CRF: Post Biopsy Re-hospitalization

If the participant was re-hospitalized since their last KPMP visit, collect the details in the Post Biopsy Re-hospitalization CRF.

5.10.7. Laboratory Results

CRF: Laboratory Results

Complete the Laboratory Results CRF using EHR data since the last visit. If no new laboratory results are available since the last visit, enter "N/A, no new labs since last visit" for the question "Were all available lab values entered" at the end of each section of the CRF.

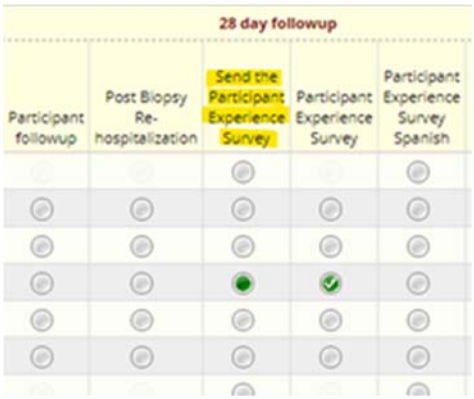
5.10.8. Collect Participant Experience Survey (6-Month Visit Only)

CRF: Participant Experience Survey and Send the Participant Experience Survey CRF

During the 6-month phone call, remind the participant that KPMP would like to send an email link to a confidential Participant Experience survey. If an email address was not provided at a previous visit, ask for an email address where the participant could receive a link to the survey.

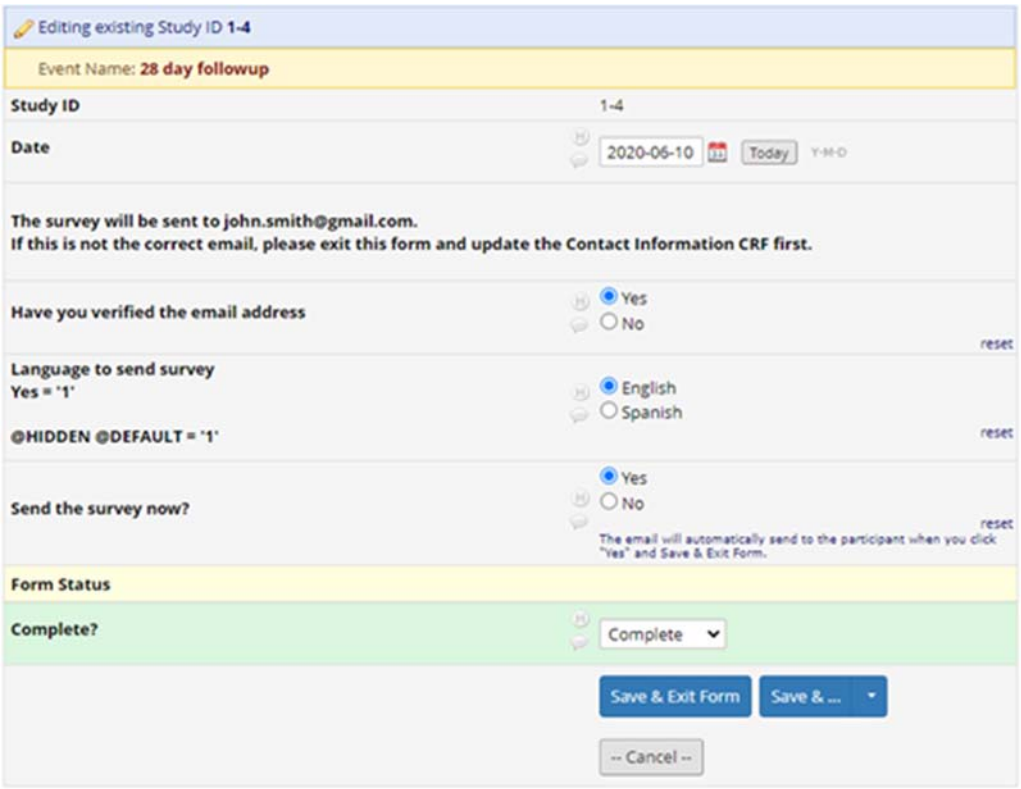
Up to 3 attempts should be made to have the participant complete the 6-month survey. If the participant prefers, the 6-month survey can be completed at the 12-month in-person visit.

After completing the 6-month follow-up CRF, select the "send the participant experience survey" CRF button from the REDCap PMP dashboard:



In the CRF, enter the date and confirm the email address listed for the participant. If it needs updating, enter the new email address on the Contact Information CRF.

Confirm the email address, select the Spanish or English version of the CRF, select "yes" to send the survey, mark CRF as complete, and save and exit the CRF. REDCap will automatically send an email to the participant with a link to the survey once you save and exit the CRF.



Once the participant completes the survey, a green check appears in the radio button on the dashboard.

If the participant does not have an email address, print a paper copy of the CRF in the participant's preferred language (English or Spanish) and mail it to the participant with a stamped envelope addressed to:

KPMP DCC
University of Washington
Bldg29, Suite 310
6200 74th Street NE
Seattle, WA 98115

DCC staff will enter the survey data into the REDCap PMP.

5.10.9. Update Participant Status

CRFs: End of Study

Record any study status updates (withdrew from study, deceased, lost to follow-up, loss of eligibility, etc.) in the End of Study CRF.

5.11. Annual Follow-up Visits (12, 24, 36, 48 months)

Annual in-person visits start 12 months after the Biopsy Visit. Begin contacting participants 3 months prior to their target Annual Visit date. Visit windows are minus and plus 3 months of the target date. Contacting participants early in the visit window allows for maximum flexibility in reaching participants by phone or time to locate missing participants. The Participant Management Program provides for a calendar application to assist in scheduling participants.

A visit is considered “late” when it is conducted outside the original two-month window dates. A visit is considered “missing” if it does not occur before the next visit window has opened.

If the participant has relocated to an area from which it is no longer feasible to travel to the clinical center (or is otherwise unable or unwilling to come to the clinic), the participant will be asked to permit study personnel to contact them annually by telephone or arrange for a home visit. Every effort should be made to encourage continued participation. The Research Coordinator should follow the format described for telephone contact.

If a participant is unwilling to continue participating in the KPMP Study, try to engage the participant in the aspects of the study that can be accomplished during a brief visit or over the course of two visits.

Consider mailing questionnaires (PROMIS Global Health, Personal History) to the participant in advance of the Annual Follow-up Visit so they can be completed at home and returned during the visit.

During the in-person visit, check to see if 6-month participant survey has been completed. If not, provide a paper copy of the survey and a stamped envelope to return it to the DCC. Record the survey attempt in the 6-month Send the Participant Experience Survey CRF.

5.11.1. Provide Visit Date and Participant time burden

CRF: Visit Log

5.11.2. Record Visit Status

CRF: Participant Follow-up

Record the status of the visit. If the visit is not done and staff are still working to reach the participant, the CRF status should remain as “attempted” until the visit window closes (see table 2). If the call is not completed before the visit window closes, record the status as not done and record the reason.

If the visit did not occur, enter the date when it was determined that it would not occur, and record the reason. If after leaving messages and calling repeatedly the follow-up can still not be completed, the call status is recorded as “participant unable” and “could not locate.”

If a death, withdrawal, or other End of Study status update is discovered within the visit window, update the Follow-up CRF to indicate that the call will not be completed and enter the reason. Also update the End of Study CRF.

5.11.3. Update Contact Information

CRF: Contact Information

Review all participant and healthcare provider contact information, making the appropriate updates.

5.11.4. Collect Medications Inventory

CRF: Medications

Complete the Medications CRF by reviewing all prescription and non-prescription medications the participant has taken since the last visit. Best practice is to get the information from the participant and then follow up with chart review to ensure that everything is captured.

Record the medications, noting total daily dose, unit, frequency and route, on the Medications CRF. Review the EHR for any missing medications or details.

If a previous medication is reported with a new dose or frequency, mark the medication as stopped at the previous dose and create a new instance of the CRF for starting the medication at the new dose or frequency.

5.11.5. Collect Follow-up Medical Events

CRF: Follow-up Medical Events

Review and update Medical History information since the last visit. Information recorded in the Medical History Participant CRF may be updated or verified by the Research Coordinator through reviewing the EHR.

5.11.6. Record Post Biopsy Re-hospitalizations

CRF: Post Biopsy Re-hospitalization

If the participant was re-hospitalized since their last KPMP visit, collect the details in the Post Biopsy Re-hospitalization CRF.

5.11.7. Participant Administered Questionnaires

CRFs: Personal History Follow-up, PROMIS Global Health, Health Literacy (12-month only)

Participant-administered CRFs are completed on paper either during the Visit, or at home and returned at the visit. If completed in person, ensure that the participant has quiet space to complete the form where they won't be distracted or rushed. Let the participant know how to contact the research coordinator in case questions come up as they complete the forms.

5.11.8. Physical Exam

CRF: Physical Measurements

Complete physical measurements including height, weight, blood pressure, heart rate, temperature, and edema assessment, recording the measurements on the Physical Measurements CRF. Blood pressures are measured following the procedure outlined in Appendix C of this manual. Record the pulse and 3 sequential BP measurements while the participant is seated, followed by the pulse and one BP measurement while standing (if possible).

If the Annual Follow-up Visit is completed remotely, check the EMR for data from within the visit window to complete the Physical Measurements CRF.

5.11.9. Biospecimen Collection

CRF: Biospecimen CRF for Blood, Spot Urine

See the Biospecimen MOP for additional details.

5.11.10. Laboratory Results

CRF: Laboratory Results

Complete the Laboratory Results CRF using EHR data since the last visit. If no new laboratory results are available since the last visit, enter "N/A, no new labs since last visit" for the question "Were all available lab values entered" at the end of each section of the CRF.

5.11.11. Update Participant Status

CRFs: End of Study

Record any study status updates (withdrew from study, deceased, lost to follow-up, loss of eligibility, etc.) in the End of Study CRF.

6. Case Report Forms

6.1. Acquisition of the Forms

The KPMP PMP provides electronic CRFs that can be completed on a tablet, laptop, or desktop computer. Back-up forms are available as paper Adobe portable document format (PDF) files. The PMP is the primary data collection source and printing paper forms in advance of a visit should not be necessary. If the PMP or data collection tablet is unavailable, a PDF of the CRFs is available to print on the KPMP website. To streamline the printing process, the Research Coordinator-completed forms necessary for each visit are grouped together in one packet and are presented in the order they should be completed. For some visits, instructions on the CRFs or Visit Checklists specify when CRFs should be completed. For example, at the Biopsy Visit, CRFs collecting eligibility criteria should be completed prior to the administration of physical exams or other study procedures.

Each PDF copy of a CRF has a name located in bold at the bottom right of the page. Each form is dated at the bottom left corner to identify the version of the CRF. This is important should a CRF be revised later.

6.2. General Instructions for the Completion of Case Report Forms

Two types of forms are used in this study: Data Forms and Administrative Forms:

- Data Forms contain participant data that are entered in the PMP.
- Administrative Forms are used for processing Data Forms, tracking data flow and in scheduling study procedures and appointments.

All questions must be answered (all fields completed), as specified on the CRF. Be concise, however, avoid using abbreviations and symbols. Indicate "refused" for any questions unanswered. When the participant is not sure of an answer, they should use a "best estimate" rather than not answer the question.

The Research Coordinator is responsible for reviewing all the completed CRFs at the respective visits when recording data. All personal identifying information must be removed from lab or procedure reports prior to forwarding copies to the DCC, if it is applicable/necessary for this to be done. All source documentation sent to the DCC must have all personal identifying information redacted ("blacked out") and replaced with the participant ID number. This is accomplished by photocopying the original document, blacking out the names or other identifying information, and then photocopying the blacked-out copy. These steps assure complete confidentiality.

At the time of data entry, the Research Coordinator ID will be automatically recorded for each CRF in the PMP. Review all CRFs for accuracy and completeness as they are entered in the PMP. The Visit Checklists will assist in documenting the review, entry, and verification process. If errors are found while reviewing the CRFs, the error should be updated directly in the CRF.

6.3. Participant Interview Completed Forms

When completing the participant interview forms, clarify any participant responses that are unclear or incomplete. Ask the participant to elaborate or reconsider an incomplete or inappropriate answer without leading the participant or influencing the content of the answer to avoid creating a biased response.

Some questions addressed in the CRFs are personal and may be considered sensitive by the participant. When a participant shows reluctance in answering a question, reassure the participant regarding the confidentiality of the response and explain the importance of the question.

Electronic medical records can be used to complete information in the Medical History or Medications CRFs if the participant is unsure of an answer or response, or if the participant's response contradicts that which is provided in electronic medical record. In the event of a contradiction, use the information in the EMR.

6.4. Mode of Administration

KPMP CRFs are completed by the Research Coordinator in clinic, or by the participant in either the clinic or at home. Table 6 lists the acceptable method of administration for each CRF. Less preferred but allowed options are noted with an "x" in parentheses.

Table 6: CRF Mode of administration

Form	Physician or operator completed	Research Coordinator Completed without participant	Participant completed at home, self-administered	Participant at home, Research Coordinator administered by phone	Participant in Clinic, Research Coordinator administered	Participant in clinic, self-administered
Screening Worksheet		X				
New Participant CRF		X				
Visit Log		X				
Eligibility Assessment		X				
Informed Consent					X	
Contact Information				X	X	
Participant Status		X				
Pre-Biopsy Clinician Assessment	X					
Follow-up Clinical Assessment	X					
Demographics			X	X	X	X
AKI Hospitalization		X				
Laboratory Results		X				
Biosample Collection					X	
PROMIS Global Health			X	(X)	(X)	X
Health Literacy			X	(X)	(X)	X
Medical History Participant				X	X	
Medical History Coordinator		X				
Personal History			X	(X)	(X)	X
Medications				(X)	X	
Physical Measurements					X	
Biopsy/ACD Scheduling		X				
Pre-Biopsy Safety CRF	X					
Kidney Biopsy Procedure Details		X				
Post biopsy		X				
Daily Progress Note	X					
AKI Daily Monitoring		X				
Adjudication Report	X					
Participant Experience Survey			X			(X)
Adverse Events				X	X	
Follow-up Medical Events				X	X	
Post Bx Hospitalization				X	X	

Post Bx Phone calls (24h, 2w, 28d)				**X**		

7. Biopsy Procedure

7.1. Procedure for Percutaneous Kidney Biopsy

7.1.1. Operator

Only licensed clinicians (nephrologists, radiologists, physician assistants, etc.) that are registered and approved by KPMP will perform the procedure. The operator should have a minimum experience of 35 biopsies over two years with an overall major complication rate (for example: bleeding requiring transfusions/surgery/additional interventions or death or extended hospitalization of more than 48hours) of <10% and >85% of biopsies adequate for diagnosis. The site PI should verify the credentials of the operators at that site on an ongoing basis.

New operators can be certified by the site PI if they performed 35 biopsies under supervision over 2 years, with at least 25 biopsies as the primary operator.

7.1.2. Imaging

Biopsies should be performed under direct image guidance and the passage of the needle should be visualized with real time ultrasound or CT.

The minimal ultrasound requirements will include:

- Ultrasound with Color Doppler flow capabilities
- High frequency body probe (ideally >4MHz)
- Image storage capabilities

The minimal CT scanning requirement will include:

- Image storage

Minimal imaging protocol will include:

- Real time ultrasound or CT-guidance will be used from needle insertion to acquisition of tissue (i.e. biopsy not to be performed blindly)
- Post-biopsy images of the kidney will be obtained and saved
- A perinephric hematoma that demonstrates active extravasation of blood will be compressed until extravasation has ceased.

Ultrasound images obtained will include:

- Images will be obtained pre-biopsy of both kidneys with Doppler flow as described above. This will help define the most avascular plane.
- Images with Doppler flow may be obtained after each pass of the biopsy needle, but it is not required.

- A post-biopsy image with Doppler flow will be obtained to:
    - Identify an extrarenal “jet” (a manifestation of active bleeding). If seen, ultrasound with color Doppler may be performed periodically over the next 15 minutes to document resolution of the jet (the most frequent finding) or a persistent jet and an expanding hematoma
    - Identify post-biopsy arteriovenous fistula (manifested by focal high velocity flow along the needle pass. Potential AVFs would need to be assessed with spectral Doppler, in an ultrasound lab with appropriate expertise and equipment.
- Hematoma images will be measured in the largest dimension upon cessation of blood extravasation. Cessation of blood extravasation will be identified when the hematoma size has been stable on consecutive images as determined by radiology.

CT images obtained will include:

Pre- and post-biopsy kidney images

Hematoma size will be measured

All images will need to be saved on an institutional image server with the ability to transfer to the Central Hub, upon request.

7.1.3. Operative Techniques for Ultrasound-guided Biopsy

Each Recruitment Site has established procedures for doing percutaneous native kidney biopsies that roughly follow the steps outlined below. Established local practices should be followed with KPMP guidelines in order to maximize application of local expertise and safety. The most important recommendation is that the clinician performing the biopsy be comfortable with their protocol and perform all the steps they routinely do during clinically indicated kidney biopsies to ensure a safe kidney biopsy for this research protocol. dDAVP may be administered at the discretion of the biopsy operator when judged to be useful to reduce bleeding risk.

1. Place participant in prone position with wedge under abdomen. Ensure participant can participate in procedure and hold breath when instructed.
2. Blood pressure and pulse should be monitored every 5-10 minutes during the procedure; if your center routinely monitors pulse oxygenation this should be monitored throughout the procedure
3. Ultrasound both kidneys pre-biopsy. Identify which kidney is most appropriate for biopsy. This should be determined by the operator with direct visualization of the kidneys based on their experience. Factors entering in this decision include but are not limited to:
    - Kidney Size and Depth (<13 cm, as measured perpendicular from the skin)
    - Thickness of cortex
    - Complicating features at lower pole (cysts, blood vessel, mass, hydronephrosis, solitary kidney, bowel, large flow vessels-assessed with doppler flow)
    - Proximity of lower pole to bowel
    - Proximity of inferior pole to rib
4. Abort procedure if access to either kidney is not optimal

5. Using real-time ultrasound, evaluate the kidney and identify view that allows best visualization of lower pole. Mark the site for biopsy. The participant needs to hold their breath while undergoing the kidney biopsy.
6. Sterilize the area (chlorhexidine or other).
7. Using sterile precautions (gown, gloves, mask, hairnet), ensure the area surrounding the biopsy site has sterile drapes so the biopsy can be performed using sterile technique. This should include a sterile probe cover for the ultrasound.
8. Apply local anesthetic (lidocaine or other) to the skin and then using real-time ultrasound guidance use a needle to infiltrate the anesthetic down to the capsule. Additionally, conscious sedation may be used at this point to ensure participant comfort during the procedure. (Caution with sedation should be taken to not affect the participant's ability to follow breathing commands).
9. Optional: After local anesthesia has been achieved, use a scalpel to make a small incision in the skin at the marked spot.
10. Using real time ultrasound guidance insert a cylindrical 16-gauge biopsy needle to just above the kidney capsule (1-1.5mm above the capsule). Ensure the needle tip can be visualized.
11. Ask the participant to hold their breath and deploy the biopsy needle.
12. Remove the biopsy needle. The participant can now breathe normally.
13. Follow the tissue processing steps described in the Pathology MOP.
14. Repeat steps 10-13 for each additional biopsy core.
15. Limit number of passes to 5 and 3 cores; distribution between clinical and research is described in the Pathology MOP.
16. After the last core has been obtained, apply pressure to biopsy site until bleeding stops from the surface needle insertion site (~5 minutes).
17. Perform a post-biopsy ultrasound of biopsied kidney to ensure no immediate complications have developed (i.e. hematoma, hydronephrosis, AV fistula).
18. Apply dressing to biopsy site and turn participant over. Optional: gel foam embolization of the site per operator skill and institutional protocol; Return participant to recovery for monitoring post procedure.

7.1.4. Operative Techniques for CT-guided biopsy

1. Place participant on the CT procedure table in the prone position.
    - If the participant is unable to tolerate laying in the prone position the procedure can be performed in either decubitus position. The dependent kidney should be targeted to minimize motion from respiration.
2. The participant should be able to follow simple breathing commands when instructed.
3. Blood pressure and pulse should be monitored during the procedure; if your center routinely monitors pulse oxygenation this should be monitored throughout the procedure.
4. Place a radiopaque grid over each kidney.
    - Review of prior CT scans may help identify the optimal kidney for biopsy.
5. Perform a preliminary CT scan of the kidneys. (Follow department CT parameters for kVp and mAs for CT abdomen).

- Obtain a preliminary scan in a phase of respiration the participant can easily replicate.

6. Choose the most accessible kidney and mark a skin entry site overlying the lower pole focusing on the periphery of the kidney. (The participant needs to hold their breath in the same manner as the preliminary CT scan at the time of marking).
7. Remove the radiopaque grid. Sterilize the area.
8. Using sterile precautions (gown, gloves, mask, hairnet), ensure the area surrounding the biopsy site has sterile drapes so the biopsy can be performed using sterile technique.
9. Apply local anesthetic (lidocaine or other) to the skin followed by a deeper application in the subcutaneous tissue. Additionally, conscious sedation may be used at this point to ensure participant comfort during the procedure. (Caution with sedation should be taken to not affect the participant's ability to follow breathing commands).
10. Optional: After local anesthesia has been achieved, use a scalpel to make a small incision in the skin at the marked spot.
11. Using intermittent helical scans (3 mm slices) or CT-fluoroscopy (3 mm slices), advance the introducer needle from a coaxial biopsy set to the desired target (peripheral tissue of the inferior pole). During each advancement of the needle the participant should be performing the same breath-hold.
12. Once the introducer needle is placed a few millimeters within the renal tissue, proceed to obtain a core sample. (The participant should be performing a breath-hold immediately before deploying the biopsy needle. After the biopsy needle is deployed the participant can breathe normally.)
13. Remove the biopsy needle and carefully submit the sample.
14. Perform a focused helical CT or CT-fluoroscopic scan to assess for hemorrhage.
    - If hemorrhage is present, it is at the operator's discretion to continue or abort the procedure.
15. Repeat steps 12-14 for additional samples.
16. (Optional): Biopsy tract embolization with gel foam, autologous clot or other, injected though the introducer needle, is at the operator's discretion or institutional protocol.
17. Remove the introducer needle and apply manual pressure to the biopsy site until bleeding stops from the surface needle insertion site (~5 minutes). Apply a sterile dressing to the site.
18. Perform a final helical CT scan of the target kidney to assess for hemorrhage or stability of a hematoma.
19. If a hematoma is present, consider a repeat CT scan in 5 or 10 minutes to document stability or growth.
20. Turn the participant over onto their recovery bed and return to recovery for monitoring post-procedure.

7.1.5. Post-Procedure

1. Participants are kept at bed rest for at least 4 hours. They are monitored and vital signs recorded.
2. Vital signs are monitored every 15 minutes for an hour, every 30 minutes for an hour, and then hourly. Only the vitals (pulse and blood pressure) at the four-hour mark post-biopsy need to be

recorded in REDCap. Pain level is assessed immediately and 4 hours after the procedure. This schedule may be modified to match local hospital standards.

3. Participants void their bladder at least once post-procedure to verify no obstruction from clot. A bedside commode is permitted, as appropriate after 2 hours of bed rest if initial urine is clear of gross blood.
4. If there is gross blood in the urine, participants remain at bed rest until urine is clear.
5. Participants are observed for 4 hours in the post-procedure recovery area at the participating site. At the end of 4 hours, hemoglobin is measured. If participants are stable, they continue to maintain bedrest with bathroom privileges to complete the period of observation.
6. If participant is deemed unstable by the biopsy operator, they are admitted to the observation unit or inpatient service consistent with their condition and as assessed by the operating clinician, and care is provided as clinically appropriate.
7. Stability is defined by appropriate clinical and laboratory metrics including vital signs, symptoms such as flank pain, gross hematuria or other evidence of post-biopsy bleeding such as abdominal tenderness on the side of the biopsy. A fall in hemoglobin of more than 2 grams/dL or more than 1 gram/dL to less than 9 grams/dL requires extended observation, with follow-up measurement of hemoglobin after an interval of at least 2 hours. Additional observation, including overnight observation or hospital admission, will be done if clinically indicated.
    a. Note that an Adverse Event should be reported for a hemoglobin drop of more than 1 gram/dL.
8. If hematuria, falling hematocrit, or local pain suggests a hematoma, the period of bed rest is extended, and the hematoma size is monitored by serial ultrasonography of the kidney.
9. If bleeding fails to stop or the circulation is compromised by the size of the hemorrhage, a surgeon and an interventional radiologist (if necessary) are consulted regarding possible embolization of the bleeding vessel or surgical intervention.
10. If admitted, participants must have a stable hemoglobin status and hemodynamics (less than 1g/dL drop) prior to discharge.
11. When participants are stable to go home, either after 6 hours of observation or after an inpatient stay, they are instructed to avoid heavy physical activities for a week. Warfarin can be resumed the evening of the biopsy if no active bleeding. Aspirin and other anti-coagulation medications can be resumed 24-48 hours after the procedure if no active bleeding.

7.2. Procedure for Open Biopsy

7.2.1. Operator

Only licensed clinicians (nephrologists, radiologists, physician assistants, etc.) that are registered and approved by KPMP will perform the procedure. The operator should have a minimum experience of 35 biopsies over two years with an overall major complication rate (for example: bleeding requiring transfusions/surgery/additional interventions or death or extended hospitalization of more than 48hours) of less than10% and more than85% of biopsies adequate for diagnosis. The site PI should verify the credentials of the operators at that site. If the KPMP biopsy will be performed by a KPMP-certified physician's assistant, they must be accompanied by a KPMP-certified physician.

All KPMP-certified biopsy operators (MDs and non-MDs) should

- Ensure their medical staff bylaws allow their participation in research as a key provider
- Be covered by hospital/institution insurance and
- Be covered by KPMP no-fault harm insurance.

New operators can be certified by the site PI if they performed 35 biopsies under supervision over 2 years, with at least 25 biopsies as the primary operator.

7.2.2. Operative Techniques

In general, deference is given to the operative attending surgeon regarding the conduct of the procedure, based on their clinical judgment to safely acquire the intended specimens. As such, the following technique is deliberately flexible to permit the surgeon appropriate latitude within specified limits.

1. The determination of whether or not to proceed with the research biopsy will be at the sole discretion of the operative attending surgeon who will quantify and qualify the risks and benefits of the procedure based on their clinical experience and the study's informed consent document.
2. At a time and interval appropriate to conduct the research biopsy, expose the right or left kidney, whichever is easiest. The determination of which kidney to biopsy with be at the discretion of the operative attending surgeon.
3. Incise Gerota's fascia transversely over the inferior pole to the level of the renal capsule.
4. Using a 16-gauge[4] core needle, obtain 3 cores with a maximum of 5 passes.
    - Orient the tract of the biopsy to avoid the renal calyx and any observable cysts.
    - Orient the tract to obtain both cortex and medulla.
    - Insert the needle to a depth sufficient to obtain a minimum length biopsy $\geq$ 1.4 cm.
5. Place and wrap each core in a normal (0.9%) saline-soaked TELFA™ gauze and in a biopsy container.
6. Obtain hemostasis at the renal capsule (in step-wise fashion):
    - Electrocautery, Aquamantis, or another suitable coagulator.
    - Fibrin glue injection into the biopsy site, using an 18- or 20-gauge angiocatheter.
    - Gel-foam pledgeted tamponade buttress placed, using 3-0 monofilament, absorbable suture with tapered needle.
7. Close Gerota's fascia with 2-0 polygalactone suture in running layer.

7.2.3. Post-Operative Monitoring

1. Hemoglobin concentration is serially measured for all participants every 4 hours for 24 hours and then every 12 hours for hours 24-48.
2. In the event that significant bleeding (>2g/L drop in Hgb from baseline concentration) is identified, a non-contrast CT is obtained emergently.
3. If CT imaging shows perinephric fluid consistent with a hematoma, the biopsied kidney is further investigated with a repeat CT in 12 hours. Hemoglobin concentrations are serially measured every six hours.

4. The following circumstances prompt interventional radiology consultation for angioembolization.
    - Volumetric enlargement of hematoma >25% from baseline measurement.
    - A drop in Hgb more than 2g/dL in a 24-hour interval.
    - Any hemodynamic instability (SPB less than 90, or at the discretion of the operator) considered to be due to bleeding from biopsy site.
5. After IR angioembolization, all safety measures are repeated.

7.3. QC Assessment of biopsy complication rates to suspend biopsies and trigger DSMB review

To assess these occurrences, more than 10 participants are needed for bleeding, nephrectomy and death, or 20 for angiography. If less than 10 participants are enrolled, occurrence of any of the following in more than one participant will result in suspension of biopsies.

Individual Recruitment Site biopsy complication rates:

For CKD

- Occurrence of bleeding requiring transfusion in ≥ 10% of participants.
- Occurrence of bleeding requiring angiographic intervention in ≥ 5% of participants.
- Occurrence of bleeding requiring nephrectomy in > 1 participant until enrollment of 30 participants, afterwards ≥ 3 % of participants.
- Occurrence of death directly related to biopsy in > 1 participant until enrollment of 40 participants, afterwards ≥ 2 % of participants.

AKI

- Occurrence of bleeding requiring transfusion in ≥ 20% of participants.
- Occurrence of bleeding requiring angiographic intervention in ≥ 10% of participants.
- Occurrence of bleeding requiring nephrectomy in > 1 participant until enrollment of 40 participants, afterwards ≥ 5% of participants.
- Occurrence of death directly related to biopsy in > 1 participant until enrollment of 50 participants, afterwards ≥ 2% of participants.

Study-wide Recruitment Site biopsy complication rates:

CKD

- Occurrence of bleeding requiring transfusion in ≥ 7 % of participants.
- Occurrence of bleeding requiring angiographic intervention in ≥ 3% of participants.
- Occurrence of bleeding requiring nephrectomy in ≥ 2% of participants
- Occurrence of death directly related to biopsy in ≥1 % of participants.

AKI

- Occurrence of bleeding requiring transfusion in ≥ 10 % of participants.
- Occurrence of bleeding requiring angiographic intervention in ≥ 5 % of participants.

- Occurrence of bleeding requiring nephrectomy in ≥ 3% of participants.
- Occurrence of death directly related to biopsy in ≥1 % of participants.

8. Recording and Reporting Adverse Events

Kidney biopsies have known risks (See table 7). The KPMP protocol is designed to minimize these risks. Nonetheless, the KPMP will closely monitor adverse events (AEs) related to kidney biopsies and other procedures in order to detect AEs and identify whether known potential AEs are occurring at unexpected rates. The KPMP will organize regular, systematic review of these AEs and alter protocols as needed to maximize safety for current and future participants.

AEs will be collected through three methods:

1. The presence or absence of known potential AEs of kidney biopsies will be prospectively surveyed by Research Coordinators or other study staff at the time of kidney biopsy and 24 hours, 2 weeks, and 28 days after kidney biopsy using standard case report forms.
2. Participants will be asked to report pain and related AEs using a standardized questionnaire 28 days after kidney biopsy.
3. Site investigators will report any AEs potentially related to KPMP procedures using standard case report forms in the PMP.

All AEs will be classified in terms of severity and relation to KPMP activities as well as whether they constitute a serious AE (SAE). AEs identified from any source will be reviewed by the KPMP Safety and Adjudication Committee (SAC). All AEs will be collated and reported regularly to the Steering Committee, IRB, DSMB, and NIDDK. SAEs will be reported individually within specified time intervals.

8.1. Adverse Events related to KPMP Biopsy Procedure

Recruitment sites will report all deaths occurring within 28 days of a KPMP biopsy, all serious adverse events occurring within 28 days of a KPMP biopsy, and adverse events occurring within 28 days of a KPMP biopsy that are determined by site personnel to be possibly or definitely related to the biopsy procedure. The timeline for reporting is detailed in Table 8. All deaths and unanticipated non-fatal adverse events involving risks to participants or others that occur within 28 days of a KPMP biopsy will be reported to the Data Coordinating Center, DSMB, NIDDK, and IRB on an expedited basis. This will include both serious and non-serious adverse events that are assessed by the local site investigator and/or the Data Coordinating Center to be (a) an untoward event that is unexpected in terms of nature, severity, or frequency with respect to the KPMP kidney biopsy and related procedures and the characteristics of the CKD/AKI population being studied; and (b) definitely or possibly related to the KPMP kidney biopsy and related procedures. Anticipated non-fatal adverse events will be promptly reported to the Data Coordinating Center, DSMB, and NIDDK. These events will only be reported in aggregate to the IRB and SAC, in accordance with the timeline shown in Table 8. The study will systematically collect all serious adverse events, regardless of whether they are possibly or definitely related to the biopsy procedure, and will report these promptly to the DSMB, NIDDK, and IRB. The study will not systematically collect unrelated, non-serious adverse events.

The rationale for this approach is that adverse events that are unanticipated may change assessment of the risks and safety of the KPMP biopsy procedure and may therefore require prompt revision of study procedures and documents, including the informed consent form. In contradistinction, individual adverse events that are considered anticipated complications associated with the KPMP biopsy procedure or with the population of participants being studied cannot be meaningfully interpreted as individual events but need to be evaluated in aggregate to assess overall rates and trends within the study and at individual study sites.

Each site's Principal Investigator and their research team (co-Investigators, research nurses, clinical coordinators, and data managers) are responsible for identifying adverse events and determining if the event is anticipated or unanticipated as a complication of the KPMP biopsy or the nature of the CKD/AKI populations being recruited. A list of anticipated biopsy-related adverse events is provided in Table 7. Pain in the area of biopsy needle insertion and a feeling of internal discomfort on the side of the biopsy are common but generally mild complications that require only modest analgesia. These symptoms may occur only after the local anesthetic has worn off and will be assessed on a follow-up call or prior to discharge from observation the day after the procedure. Pain and discomfort should resolve within a few days of the biopsy. A small number of participants may have macroscopic hematuria, which usually occurs shortly following the biopsy. Subcapsular and perinephric hematomas are common, may be asymptomatic, but should be readily identified by the post-procedure kidney ultrasound, and usually do not require intervention. Some complications like soft tissue infection, arteriovenous fistula, and perhaps adjacent organ puncture may not be apparent at the time of biopsy or shortly thereafter but may develop over time. For any participant who develops late complications, assessment must be performed to determine relatedness to the KPMP biopsy; and if related, whether it constitutes an unanticipated event.

8.2. Prospective surveillance of adverse events by the study team

At the time of kidney biopsy, 24 hours, 2 weeks, and 28 days after kidney biopsy, Research Coordinators or other study staff will prospectively survey known potential AEs of kidney biopsies. The adverse events that will be assessed are shown in Table 7. Information will be recorded in the Adverse Events CRF.

Table 7. Anticipated Kidney Biopsy-related Adverse Events

Complication	Data collected	Type of Event
Death	Timing relative to biopsy, cause, autopsy	SAE
Soft tissue infection	Antibiotics required and duration. Hospitalization, LOS, nosocomial complications, white blood cell count, blood cultures, urine culture.	SAE
Puncturing of adjacent organs	Related complications – Rare but possible	SAE
Hemorrhage (retroperitoneal or other)	Nature of bleed, baseline Hgb, pre-transfusion Hgb, number of units of blood	SAE, if requires transfusion, radiologic or surgical intervention

	transfused, other interventions to control bleeding (e.g., surgery, interventional radiology)	
Arteriovenous fistulae	Hematuria, hypotension, high-output heart failure. Most clinically silent. Need U/S to diagnose.	SAE, if symptomatic. If incidentally found on an ultrasound and not associated with clinical manifestations, hospitalization or prolongation of hospitalization, it is a non-serious AE
Perinephric Hematoma	Transfusion support required (amount), imaging, hospitalization, LOS, intervention required, AKI, hypotension, Intensive Care Unit, nephrectomy, death, nosocomial complications, time to pain resolution, size of hematoma	Usually an AE, but if it requires intervention (pressor support or transfusion) or participant kept overnight instead of going home after 6 hours, or if resulting in prolongation of existing hospitalization, it becomes an SAE.
Subcapsular Hematoma	PRBCs, blood pressure, kidney function, imaging, hospitalization, LOS, nosocomial complications, time to pain resolution, size of hematoma	Usually an AE, but if it requires intervention (pressor support or transfusion) or participant kept overnight instead of going home after 6 hours, or if resulting in prolongation of existing hospitalization, it becomes an SAE.
Hematuria	Clots, obstruction, bladder irrigation, transfusions, hospitalization, length of stay (LOS), time to resolution	Usually an AE, but if it requires intervention (pressor support or transfusion) or participant kept overnight instead of going home after 6 hours, or if resulting in prolongation of existing hospitalization, it becomes an SAE.
Pain (beyond what is handled through the normal standard of care)	Intensity and follow up, medication required to control pain	Usually a non-serious AE, unless resulting in change in plan of management with unplanned hospitalization or prolongation of hospitalization, in which case an SAE

Other Anticipated Kidney Adverse Events:

IV complications
- infiltration
- bruising
- phlebitis
- infection

Biopsy site complications
- cutaneous bleeding
- bruising

GI symptoms
- nausea
- vomiting
- abdominal pain
- constipation
- diarrhea

GU Symptoms
- dysuria
- urinary retention

Light-headedness
Dizziness
Hypertension
Hypotension
Fever
Falls
Headache

Cardiac Symptoms
- Chest pain
- Arrythmia
- Tachycardia
- Bradycardia
- Shortness of breath

Pulmonary Symptoms
- Cough
- Shortness of breath
- Wheezing
- Pneumonia

8.3. Prospective surveillance for participant-reported adverse events

Each participant will be called to inquire about potential AEs 24 hours, 2 weeks, and 28 days after the kidney biopsy. In addition, a Participant Experience Survey will be collected at 28 days and 6 months after the biopsy. The questionnaire assesses pain and anxiety during and after the kidney biopsy as well as any impact on function and attitudes.

8.4. Non-serious adverse events

Adverse events (AEs) that do not meet the definition for an SAE will be considered to be non-serious AEs. Only non-serious AEs that occur within 28 days of a participant undergoing a KPMP biopsy and which are determined by site personnel to be possibly or definitely related to the biopsy procedure will be systematically reported. If a non-serious AE occurs in a hospitalized participant and it cannot be determined if it is due to a KPMP kidney biopsy or the participant's underlying condition, it should be reported.

8.5. Serious adverse events (SAE)

A serious adverse event (SAE) will be defined as any undesirable experience meeting one or more of the following criteria:

1. Death: all deaths within 28 days from the time of kidney biopsy regardless of relatedness to study participation will be reported to the DSMB.
2. New hospitalization: all new hospitalizations that occur that occur within 28 days from the time of kidney biopsy will be reported as SAEs.
3. Prolonged hospitalization: if a KPMP kidney biopsy is done in a hospitalized participant and the hospitalization is prolonged due to an adverse event occurring within, this will be reported as an SAE.
4. Any life-threatening event that that occurs within 28 days of the kidney biopsy will be reported as an SAE.
5. Any other event occurring within 28 days of the kidney biopsy that results in persistent, significant, or permanent harm or disability will be reported as an SAE

All SAEs of any etiology that occur within 28 days of a participant undergoing a KPMP biopsy should be reported to the DSMB. Reporting timelines and responsibilities are listed in Table 8. Reporting to the Washington University single IRB will be consistent with current single IRB policies.

8.6. Timeline for reporting adverse events

AEs will be reported to the DCC, KPMP Safety and Adjudication Committee, IRB, DSMB, and NIDDK according to the following guidelines:

Table 8. Reporting Timelines and Responsibilities

Event	Reporting to DCC	Reporting to SAC	Reporting to IRB	Reporting to DSMB and NIDDK
Death	1 business day	1 business day	2 business days	1 business day

Unanticipated non-fatal AE[a,b]	3 business days	1 week	10 business days	3 business days
Anticipated non-fatal AE[a,c]	3 business days	Weekly summary	Continuing Review	3 business days
Unrelated non-fatal AE[a,d]	3 business days	weekly summary	Continuing Review	3 business days

[a]All non-fatal SAEs regardless of relatedness and all non-serious AEs that are determined by site personnel to be possibly or definitely related and that occur within 28 days of the KPMP kidney biopsy will be systematically reported. Non-serious AEs in hospitalized participants whose relatedness to the KPMP kidney biopsy cannot be determined will be reported as possibly related.

[b]An unanticipated AE is defined by the KPMP IRB as an untoward event that is 1) unexpected in terms of nature, severity, or frequency with respect to the KPMP kidney biopsy and related procedures (see Table 7) and the characteristics of the CKD/AKI population being studied; and 2) is definitely or possibly related to the KPMP kidney biopsy and related procedures.

[c]An anticipated AE is an untoward event that is 1) definitely or possibly related to the KPMP kidney biopsy and related procedures; and 2) is expected in terms of nature, severity, or frequency with respect to the KPMP kidney biopsy and related procedures (see table 7) or the characteristics of the CKD/AKI population being studied.

[d]Non-serious AEs that are determined by site personnel to be unrelated to the biopsy procedure will not be systematically reported, but if reported to the DCC will be included in aggregate reports to the SAC, IRB, DSMB and NIDDK.

8.7. KPMP Safety and Adjudication Committee

The KPMP Safety and Adjudication Committee will review all AEs reported by KPMP sites. Fatal events will be reviewed by the Committee or a portion of the Committee within 24 hours of reporting, and non-fatal SAEs will be reviewed within 3 business days of reporting. The committee will be charged with making a determination (adjudicating) whether each SAE is an anticipated or unanticipated adverse event. Unrelated AEs will be reviewed regularly, i.e. monthly. The Committee will regularly review the cumulative frequency of observed AEs (collated by the DCC) to identify any AEs that are unanticipated or occurring at higher than expected frequencies. The Committee will report their findings regularly to the KPMP Steering Committee and make recommendations to the Steering Committee regarding any changes that should be made to the KPMP protocol to mitigate AEs. Determinations of the Safety and Adjudication Committee will also be made available as requested to the IRB, DSMB, and NIDDK in order to help assess the safety of KPMP activities. All deaths and serious adverse events (regardless of relation to biopsy) occurring within 28 days of a KPMP biopsy will be immediately reported to the DSMB upon entry into the PMP.

8.8. Adverse Event Reporting Procedures

Adverse events are reported in REDCap in the “KPMP Adverse Event Reporting” project. Noting an AE as “resolved” in the REDCap CRF does not require that all symptoms be 100% resolved. In the CRF, an AE disposition of “resolved” means that no further follow-up is needed for the safety of the participant, and that the study investigator feels that the case is settled. If the Safety & Adjudication Committee agrees, the AE is resolved. If the SAC disagrees, the AE is left open with continued monitoring.

Adverse event reporting procedures and timelines are displayed visually in figure 2.

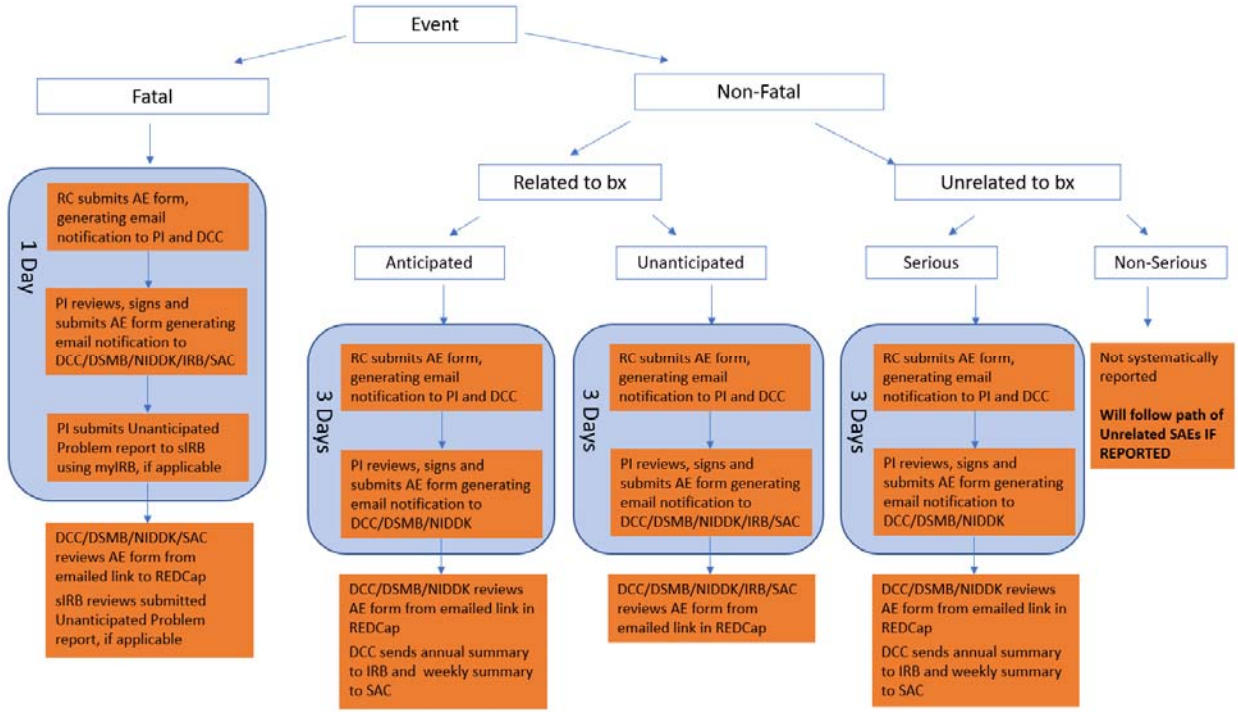


Figure 2. Adverse event reporting procedures and timelines

8.8.1. Fatal Event (occurring within 28 days of the biopsy)

All deaths in this time frame need to be reported in REDCap and confirmed by RS PI within 1 day of knowledge of the event. Deaths that occur more than 28-days after biopsy are not reviewed by the SAC.

- If the death appears related or possibly related to KPMP participation, ALSO report it in *my*IRB, using the Reportable Event Form. This form also needs to be submitted within 1 day of knowledge of the event.

Did a KPMP participant pass away within 28 days of the biopsy?

- **Yes?** Report right away in REDCap (within 1 day)

Was the death possibly or definitely related to KPMP participation?

- **Yes?** Also report right away in myIRB (within 1 day)

8.8.2. Non-Fatal Event (occurring within 28 days of the biopsy)

Any adverse event in this time frame that appears related or possibly related to KPMP participation needs to be reported in REDCap and approved by the RS PI within 3 days of knowledge of the event.

- Any adverse event in this time frame that appears related or possibly related to KPMP participation and is unanticipated ALSO needs to be reported in *my*IRB, using the Reportable Event Form. Submit this form within 10 days of knowledge of the event.

Any adverse event in this time frame that appears unrelated to KPMP participation but is nonetheless Serious needs to be reported in REDCap and approved by the RS PI within 3 days of knowledge of the event.

Does the AE seem related to the biopsy?

- **Yes?** Report in REDCap (within 3 days)
- No? Is it a Serious AE? **If Yes**, Report in REDCap (within 3 days)

Does the AE qualify as an Unanticipated Problem?

- **Yes?** Also report in myIRB (within 10 days)

8.8.3. Unanticipated Problems (IRB definition):

IRB defined Unanticipated Problems as unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied; Are related or possibly related to participation in the research; and suggest that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

9. Laboratory

9.1. Collection, Processing and Shipping of Samples

Recruitment Sites will collect blood, DNA, stool and urine samples from study participants at baseline and follow-up visits. Sample type, volume, processing, and priority at visits are described in the Biospecimen MOP.

10. Biopsy Adjudication Process

10.1. AKI Adjudication Subcommittee

When an AKI patient is enrolled, the Central Hub will contact the Recruitment Site PI to schedule two adjudication calls within 72 hours and 3-5 days after biopsy. Multiple cases may be presented on the same call, and reviewers for first and second adjudication calls are not required to be the same. A minimum of 5 committee members are needed for the call, not including representatives of the presenting Recruitment Site. If AKI Adjudication Subcommittee Chairs cannot be on the call, the Central Hub will appoint a chair to lead the call.

The Recruitment Site PI or designee (e.g. a co-I who enrolled the patient) develops a brief summary to discuss on the call and should also have access to the patient's chart during the call to answer any questions that come up. Summary should include medical history, lab work, date of AKI onset, physical exam, duration of elevated creatinine and likely etiology. Summary information will not be distributed prior to the adjudication phone call. Adjudicators will ask questions and then a collective decision will be

made regarding the clinical diagnosis and disease course. If there is not a unanimous decision a vote may be taken.

The Site PI or Research Coordinator enter the final adjudication information into the 24-72 hour and 3-5 day AKI Adjudication CRFs in the REDCap data collection program after each call.

10.2. CKD Adjudication Subcommittee

After CKD pathology slides are uploaded into the DVC Whole Slide Image Viewer, DCC contacts CKD PI and Pathologist to schedule case presentation. Recruitment Site PI or designee (e.g. a co-I who enrolled the participant) presents a clinical vignette (omitting the pathology results) and answers reviewer questions (consulting the EHR if necessary). Committee members ask questions and adjudicate an agreed upon diagnosis based on the provided information. If there is not a unanimous decision a vote may be taken.

The RS Pathologist reviews biopsy slides (using the DVC Whole Slide Image Viewer when possible) and reads the diagnosis recorded in the pathology report. The Committee then re-adjudicates the final diagnosis based on clinical information and pathology review.

After the call, the presenting PI completes the CKD Adjudication CRF in the KPMP REDCap program, describing the clinical case and summarizing the collective thoughts of the group.

11. Data Management System User Guide

11.1. Accessing KPMP Data Management System (DMS) Tools

Initial access to KPMP DMS Tools will be granted after completion of the KPMP user intake form. A link to the intake form will be on the main KPMP application login page.

- The intake survey collects institution, role, email and other contact information. Users are required to enter an email address; they are encouraged to enter the email from their KPMP member institution.
- KPMP central hub personnel will review the survey response. Access to applications will be controlled by which study role (Researcher, Provider or Participant) is entered in the survey.
- Each site will have a primary KPMP contact who will be contacted to confirm access for those researchers belonging to their site. For those researchers not belonging to a KPMP study site, a reference will be asked for in the survey. Participants and providers do not need to go through this process.
- Most institutional logins from KPMP study sites will serve as a person's login to KPMP applications. A login account will be provided for those who do not have a compatible institutional login account.
- REDCap will be set up to send out an email with a survey link yearly for people (and their site contact or reference) to fill out to keep their access to KPMP applications. Once a renewal survey is filled out, study personnel will review the survey and update the renewal and expiration dates for that person. People who do not respond to the survey would not retain access to the applications.

After completion of the intake process a user will access applications by logging in through the KPMP application menu found at kpmp.org.

11.2. Data Collection Tablet Best Practices

All data collection applications used within the KPMP will be web-based with password protection. Access to these applications will not be restricted to KPMP-provided tablets.

Instructions for KPMP-provided tablet handling can be found in Appendix E “iPad Tablet User Guide". The central hub may provide study iPad tablets for use by the Recruitment Sites if needed. However, all data collection applications used by KPMP will be web based and data entry will not be limited to iPad devices. If a site has iPads or other computers/tablets they will be able to use those.

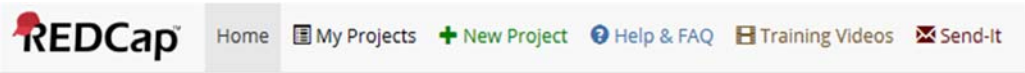
Security best practices for all devices used for KPMP data access including tablets:

- Password protection should be enabled, and devices should be locked when not in use.
- All KPMP applications and other programs containing participant information should be closed and logged out of when not in use.
- Never share personal passwords between employees.
- Ensure all computers have updated anti-virus software installed.
- Software updates to the operating system and applications should be completed promptly when available

11.3. Research Coordinator - Participant Registration Tools

11.3.1. KPMP Research Coordinator Electronic Data Capture System (REDCap)

After logging into the KPMP REDCap instance (redcap.kpmp.org) you are taken to the REDCap Home Page. On the top navigation menu choose **My Projects.**

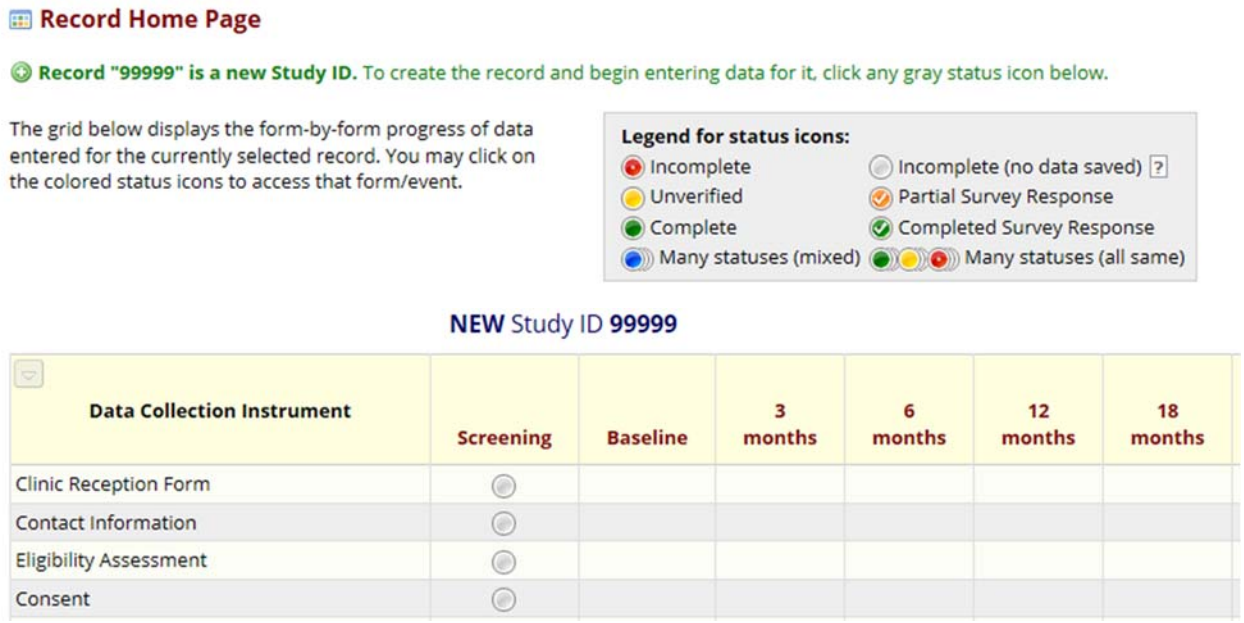


From the My Projects screen choose **KPMP Participant Management Program**

When the homepage for the **KPMP Participant Management** comes up, you can add a new participant record or edit an existing record find the ‘**Add / Edit Records**’ link in the left navigation panel.

11.3.2. Potential Participant Registration Module

To register a potential new participant in the KPMP REDCap instance, select the ‘**Add /Edit Records**’ button and on the following page select the ‘**Add new record**’ button. This will take you to a new study record page:



Click the radio button for one of the initial 'Screening' participant CRFs, complete the required information and save to register the potential participant to the study.

11.3.3. Assigning Participant ID

On completion of the initial CRF, a unique sequential 5-digit (NNNNN) Study ID will be assigned by the KPMP REDCap system. KPMP participant IDs will be unique across all study sites and will contain no identifying information.

11.3.4. Registering Participants to KPMP

To register a participant as enrolled in KPMP within the DMS complete all CRFs listed in the Screening section to indicate that the participant has met all requirements for enrollment to the study.

On successful completion of these CRFs according to study protocol the participant record status will change to enrolled and additional CRFs for post enrollment data will be available in the participant study record.

11.4. Biopsy Kit Requests

Biopsy/Specimen kit requests should be entered in the REDCap KPMP Inventory Request form. Kit requests should be completed with appropriate lead time so new kits arrive before stock is depleted. A link to the KPMP Inventory Request form can be found in the left nav of the KPMP redcap project:

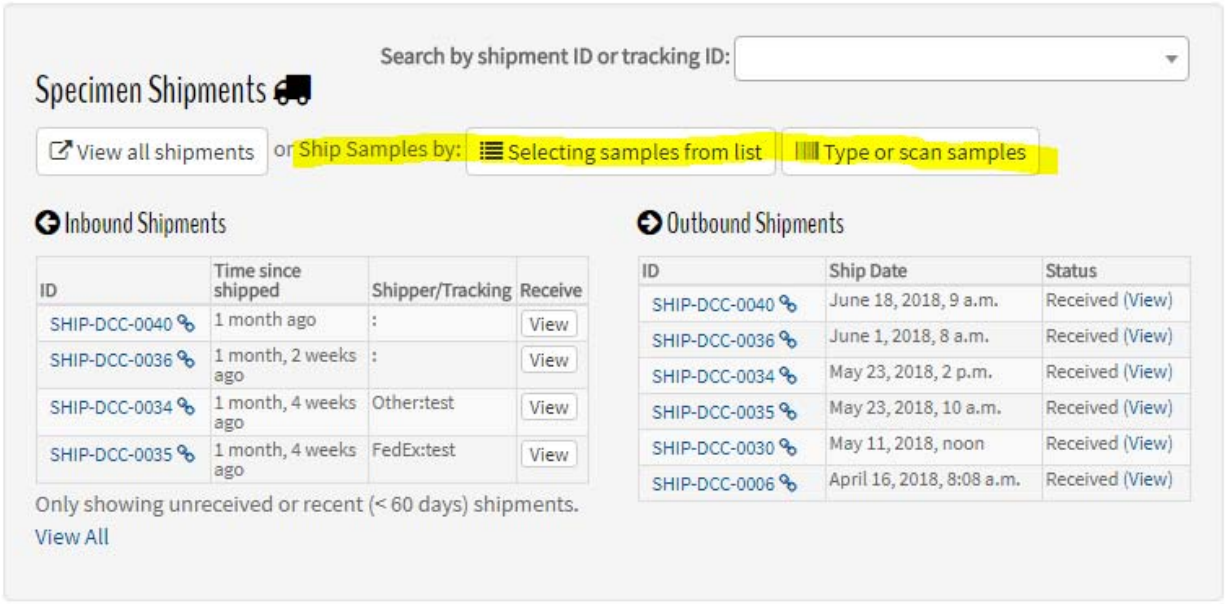
11.5. Specimen Tracking

The KPMP Specimen Tracking system (SpecTrack) (specimen.kpmp.org) will be used to track the movement, derivative creation, processing and status of all participant specimens collected within the KPMP study. Specimen types which will be tracked include: Biopsy, Blood, Urine and Stool.

The initial record indicating a participant specimen was collected will be recorded in the appropriate participant CRF. The samples will be labeled with unique study barcodes from the provided participant specimen kit. These samples will then be available for tracking in the specimen tracking system.

11.5.1. Outbound Specimen Shipment

All outbound specimen shipments should be recorded promptly in the specimen tracking system so that the destination site is notified of the inbound shipment and prepared for receipt. To record a specimen shipment, access the specimen tracking system at (specimen.kpmp.org). The shipments pane provides information about current inbound and outbound shipments for your site and provides two options for generating a new shipment, either by selecting samples from a list or typing/scanning sample identifiers.

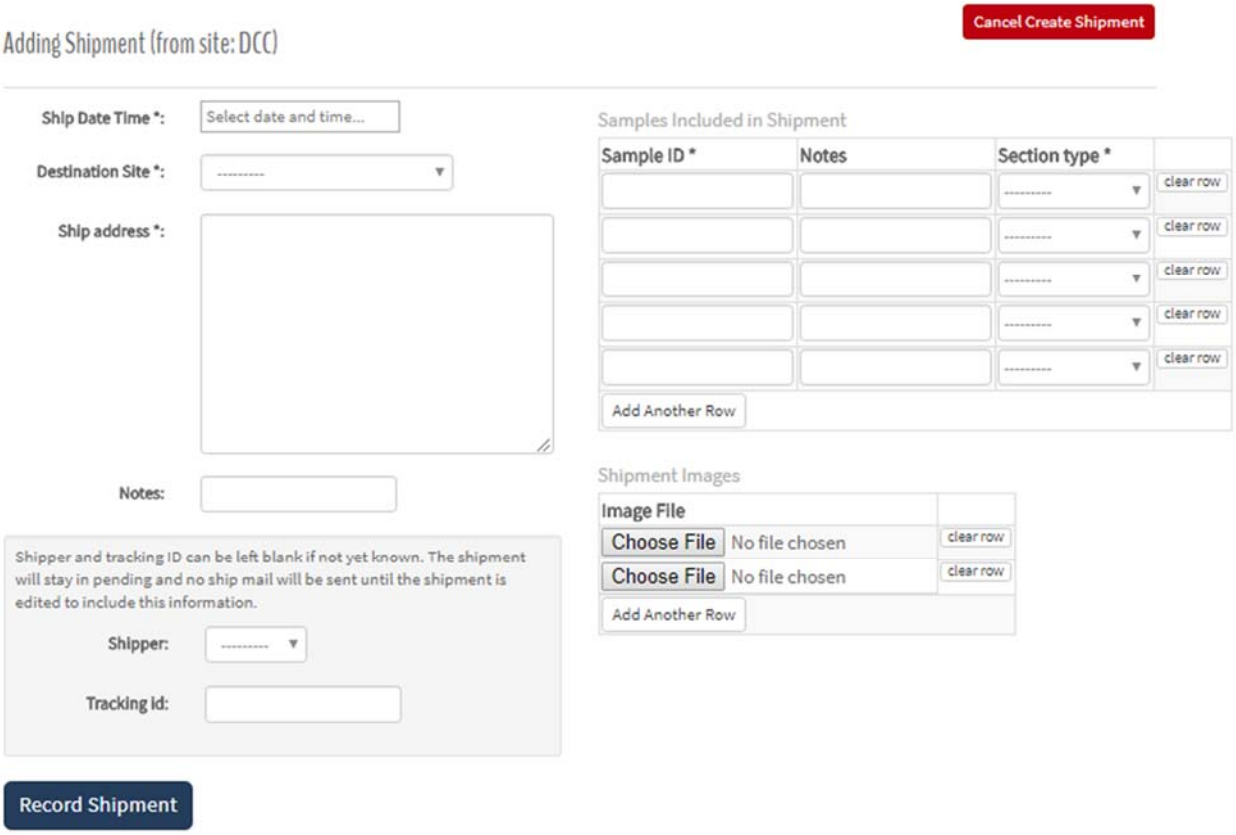


Outbound shipments are typically entered in two steps:

1. Define shipment contents, destination site and upload images
    a. Choose one of the methods listed on the shipping tab to select items for shipment, these include selecting samples from a list of available samples at your site or typing/barcode scanning sample identifiers.

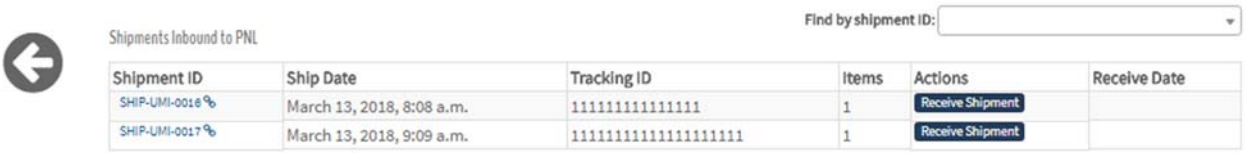
b. Select the destination site. The shipping address will be populated by the specimen tracking system but should be verified.
c. Record any shipment images collected for QA purposes

2. Record shipper and tracking ID
   a. Shipper and tracking ID can be provided when initially recording the shipment information or can be left blank until known.
   b. To add the shipper and tracking ID at a later time, find the shipment record on the 'Shipments' tab using the shipment search box or in the outbound shipment list and select the 'Update' link.
   c. Once the shipper and tracking ID have been provided email message will be dispatched to contacts at the destination site. This email message includes shipment contents, notes and tracking information.

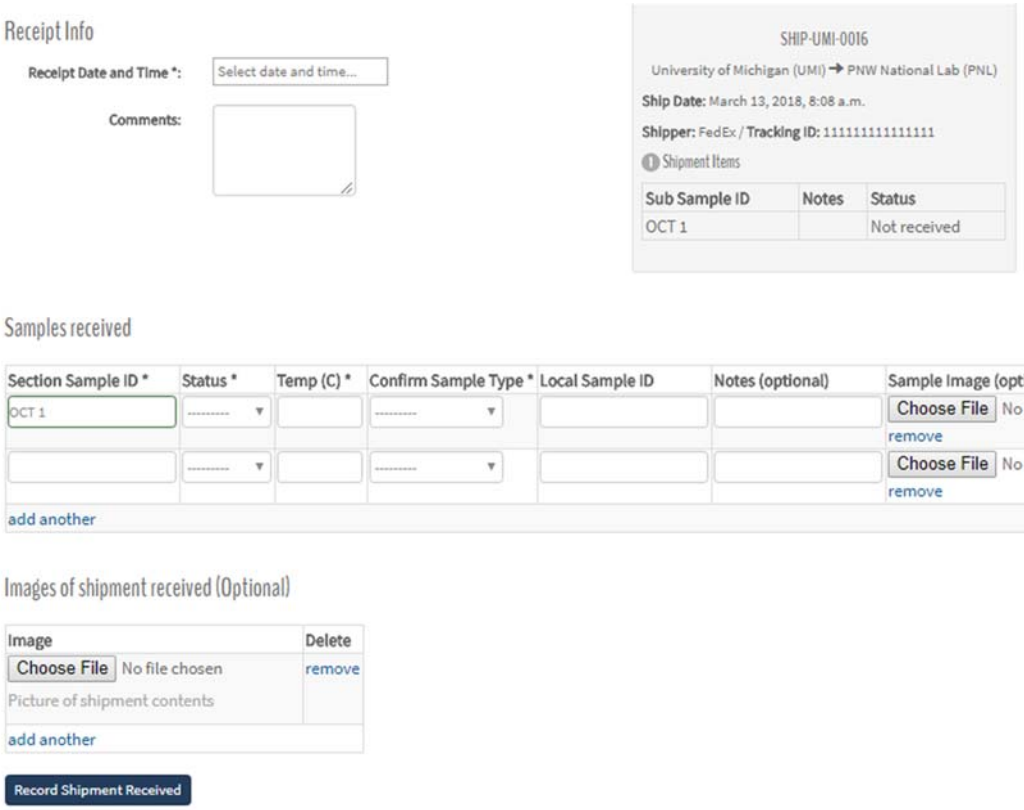


11.5.2. Specimen Shipment Receipt

Inbound specimen shipment receipt should be recorded promptly in the specimen tracking system so that any data quality or content issues can be quickly resolved. To record a specimen shipment receipt, access the specimen tracking system at (specimen.kpmp.org). Locate the shipment by searching by shipment or tracking ID or by finding the shipment record in the inbound shipment list.



Review the shipment contents carefully and record the status, temperature and any local non-KPMP identifier applied to the shipment samples on receipt.

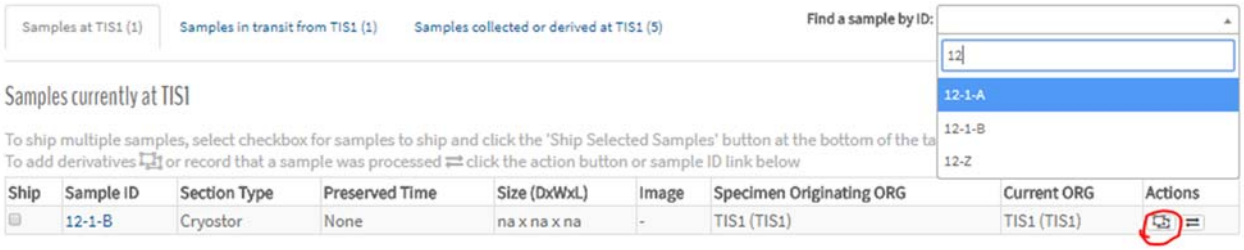


If shipment contents discrepancies are found or if samples are damaged in shipment, the shipping site should be notified promptly.

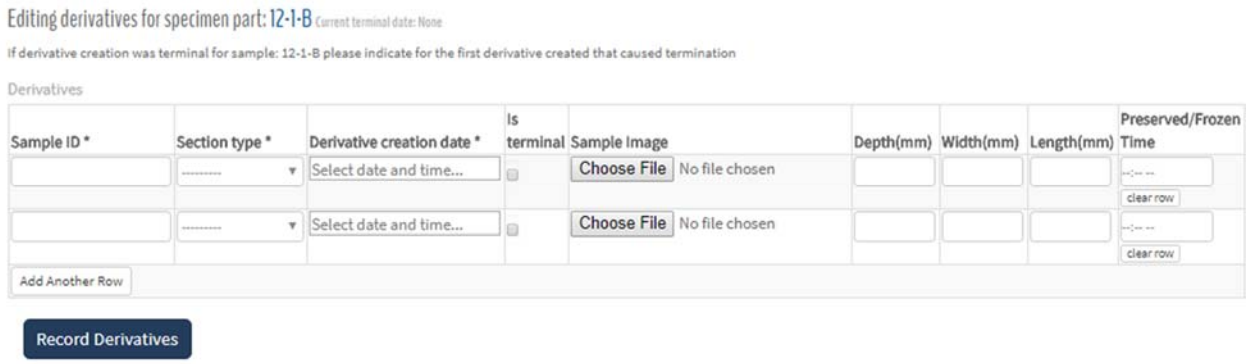
11.5.3. Specimen Derivatives and Processing

All derivative creation and sample processing that occurs after initial specimen collection should be recorded in the specimen tracking system.

To record derivative creation for a sample at your site access the specimen tracking system at (specimen.kpmp.org) and select the 'Samples' tab. Find the sample in the list of samples on site or search by sample ID and select the 'add derivatives' action.



Record when the derivatives were created and the sample type of the new derivatives. If creation of the derivatives was terminal for the parent sample, indicate that as well so we can track that the parent sample is no longer valid.



Sample processing, such as slide staining can be recorded in a similar fashion. Find the sample as above then select the sample processed action:

Record the time the processing occurred and any changes to the human readable identifier.

11.5.4. Sample Labeling and Barcoding

All KPMP samples will be labeled with a KPMP specific label. This label will include both a barcode and a human readable identifier. Both the REDCap application and the Specimen Tracking system will support the scanning of sample identifiers for entry of data related to those samples. Labels for the initial collection of participant samples will be provided in kits to the Recruitment Site. The barcode on these labels will include an immutable identifier that will not change, this will allow the human readable identifier to change when needed while maintaining a robust link between the participant record and all samples related to the participant.

11.5.5. Data Quality Management Procedures

Several standardization procedures will be employed to ensure high quality data in this study. Standard protocols and training manuals are provided. Site personnel are trained in the data collection system. Data collection software will be programmed with range, logic, and missing data checks.

Additional logic and cross-form data checks will be implemented as data quality rules. When a data quality discrepancy is encountered a data query can be issued to the data collection site. The data can then be corrected or resolved as verified

11.6. Resolving Data Quality Discrepancies

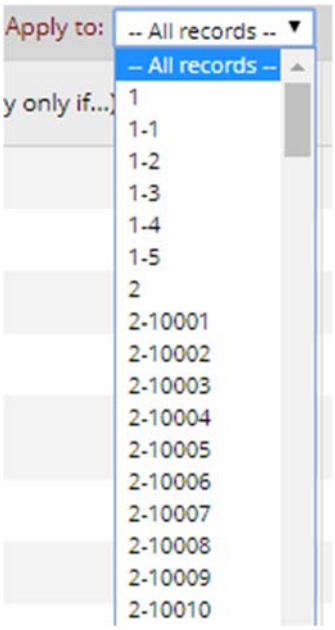
REDCap has a feature to run data quality rules to check for discrepancies in the collected data. These data quality rules should be run and resolved at the conclusion of each study visit. Research Coordinators should check the “Resolve Issues” link 1-2 times per week to address any queries send from the DCC. To get started, within the REDCap PMP, click on Data Quality from the left menu under "Applications".

It will open the Data Quality Module:

Data Quality Rules — **Execute rules:** All | All except A&B | All custom | Clear — Apply to: -- All records --

	Rule #	Rule Name	Rule Logic (Show discrepancy only if...)	Real-time execution [?]	Total Discrepancies
	A	Missing values*	-		Execute
	B	Missing values* (required fields only)	-		Execute
	C	Field validation errors (incorrect data type)	-		Execute
	D	Field validation errors (out of range)	-		Execute
	E	Outliers for numerical fields (numbers, integers, sliders, calc fields)**	-		Execute
	F	Hidden fields that contain values***	-		Execute
	G	Multiple choice fields with invalid values	-		Execute
	H	Incorrect values for calculated fields	-		Execute
	1	New Patient - outcome should be 'proceed with screening' before filling out Eligibility Assessment	if([np_outcome(1)] != 1 and [sc_disease_type] != '', True, False)	✓	Execute
	2	New Patient - Participants age below 18 or above 90	datediff([np_visit_date], [np_dob], "y", "ymd") < 18 or datediff([np_visit_date], [np_dob], "y", "ymd") > 90	✓	Execute
	3	Eligibility Assessment BP1: Systolic < 140 and Diastolic < 90	[sc_bp_1st_systolic] < 140 and [sc_bp_1st_diastolic] < 90 and [sc_bp_1st_systolic] != '' and [sc_bp_1st_diastolic] != ''	✓	Execute
	4	Eligibility Assessment BP2: Systolic < 140 and Diastolic < 90	[sc_bp_2nd_systolic] < 140 and [sc_bp_2nd_diastolic] < 90 and [sc_bp_2nd_systolic] != '' and [sc_bp_2nd_diastolic] != ''	✓	Execute

1. Under the "Apply to:" dropdown, choose a participant.



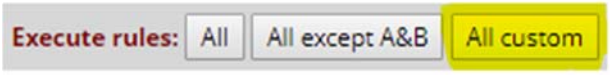
2. Click on "Execute" Execute for the following rules:
   B: Missing values* (required fields only)
   D: Field validation errors (out of range)

Rule #	Rule Name	Rule Logic (Show discrepancy only if...)	Real-time execution [?]	Total Discrepancies
A	Missing values*	-		Execute
B	Missing values* (required fields only)	-		Execute
C	Field validation errors (incorrect data type)	-		Execute
D	Field validation errors (out of range)	-		Execute

Data Quality Rules — Processing Complete! Execute rules: All | All except A&B | All custom | Clear
Apply to: 14-1

Rule #	Rule Name	Rule Logic (Show discrepancy only if...)	Real-time execution [?]	Total Discrepancies
A	Missing values*	-		Execute
B	Missing values* (required fields only)	-		29 view
C	Field validation errors (incorrect data type)	-		Execute
D	Field validation errors (out of range)	-		0 view

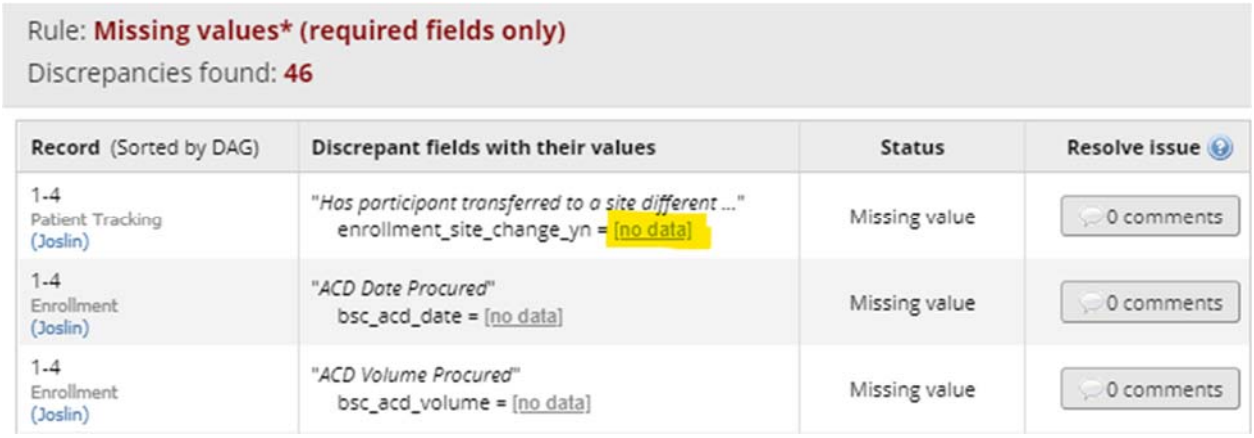
3. Click on "All Custom", which will run the rules 1, 2, 3, ...



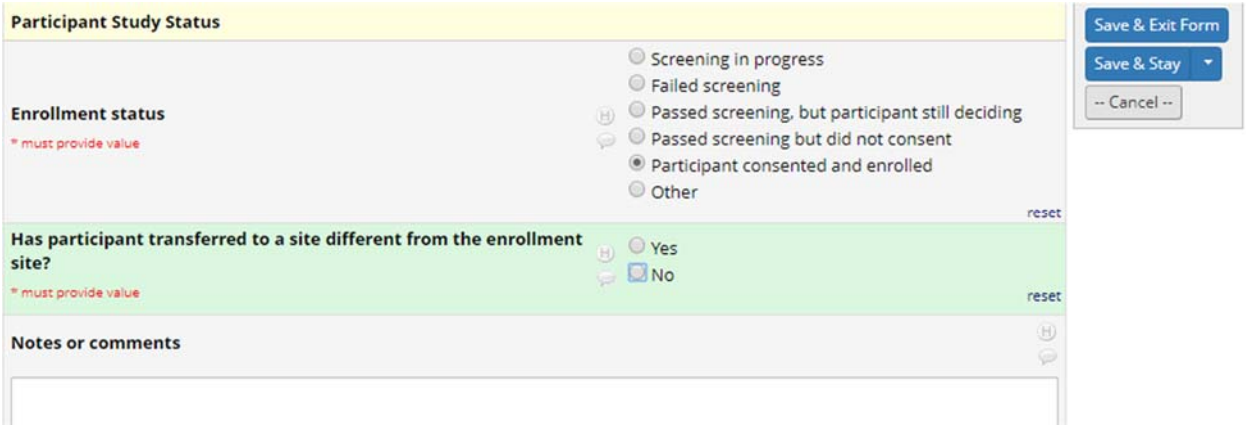
4. For all discrepancies (highlighted in pink/red) click on the "view" link.

This will show the list of discrepancies. The values involved in the data quality rule will be shown.

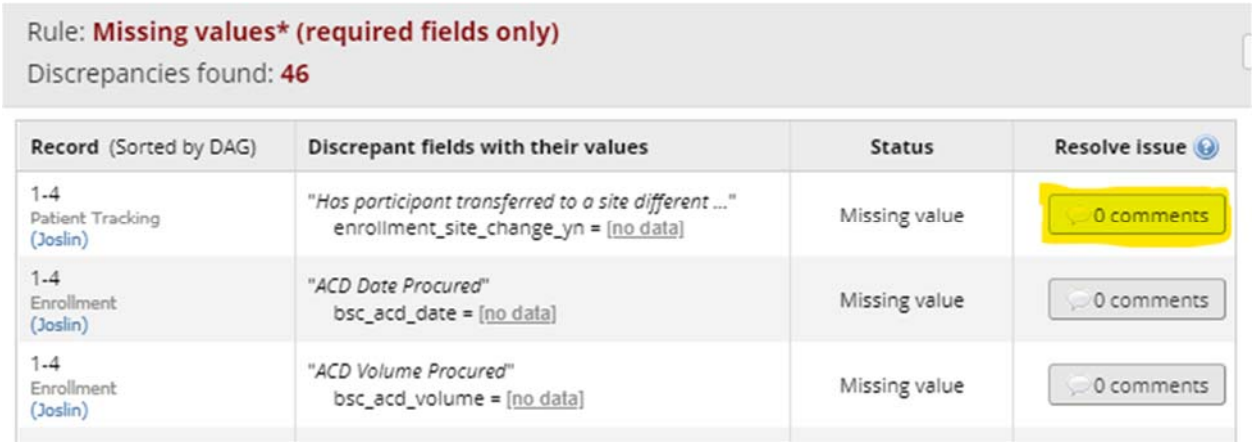
5. Click on the link to the value



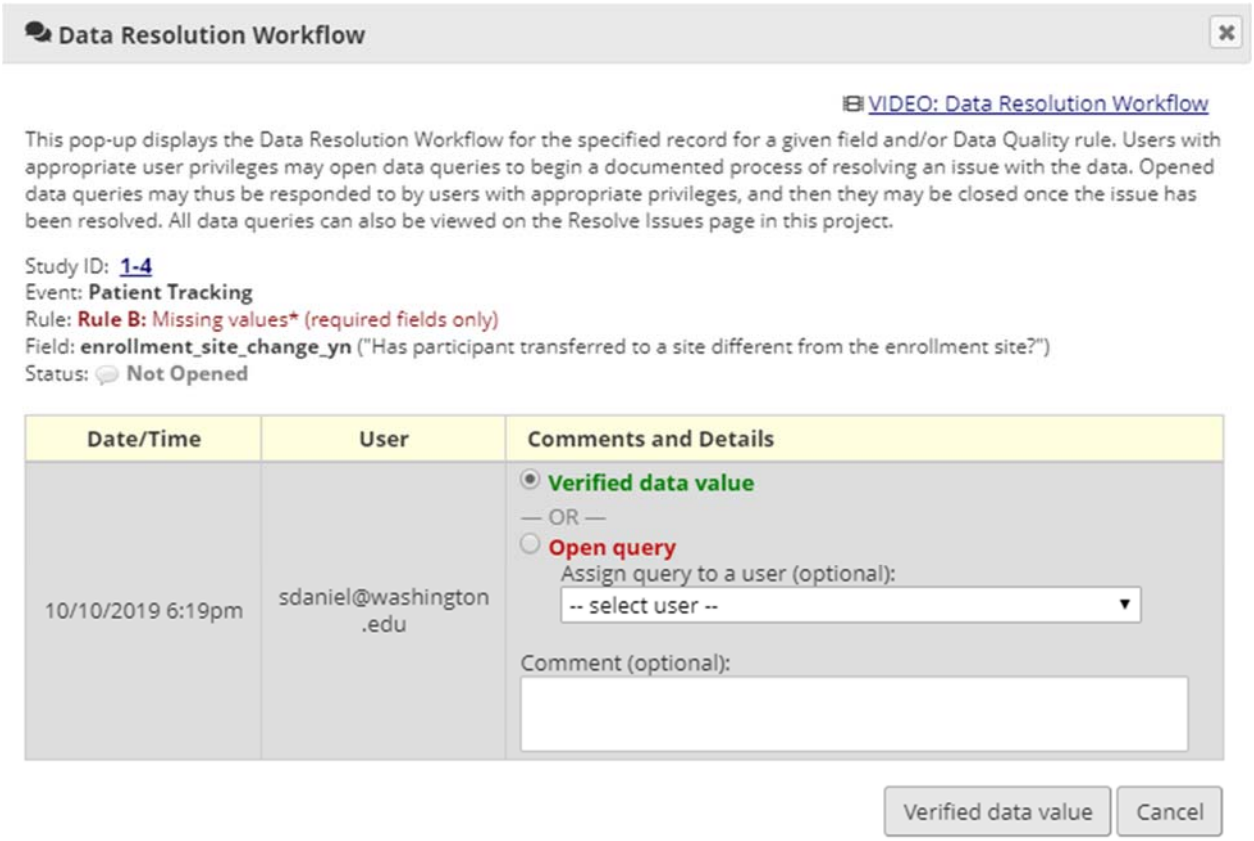
6. The CRF will open. Enter the data or change the data as appropriate.



7. If it is not appropriate to change the data, then enter a comment



8. This will open the Data Resolution Workflow



8.1. Verified data value means that the data is correct and should not be changed, despite triggering a discrepancy.

8.2. Open query allows you to comment on the value, and optionally assign the query to a user. This could possibly lead to a back-and-forth discussion about the value.

9. Creating data queries (data resolution workflow) directly from the data entry form

9.1. From the data entry form, you can click on this button  next to any field to open a data query about that field.

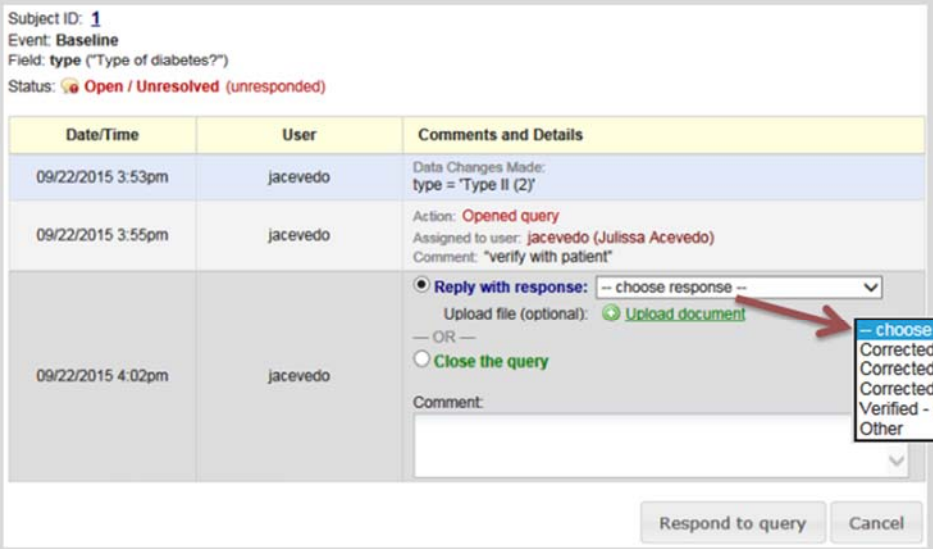
10. Responding to Data Queries

Click on "Resolve Issues" to view the Data Resolution Dashboard

This page displays all data queries that are currently unresolved or have already been resolved using the Data Resolution Workflow. Some issues may have been initiated by users on data collection instruments, and others may have been initiated after executing Data Quality rules on the Find Issues tab. The table lists the name of the record and the specific field or Data Quality rule to which the data query belongs, as well as the user assigned to the query (if applicable), the number of days the data query has been open, and a brief snippet of the query's first and last comment. The results in the table can be filtered by the query status type (e.g., open,

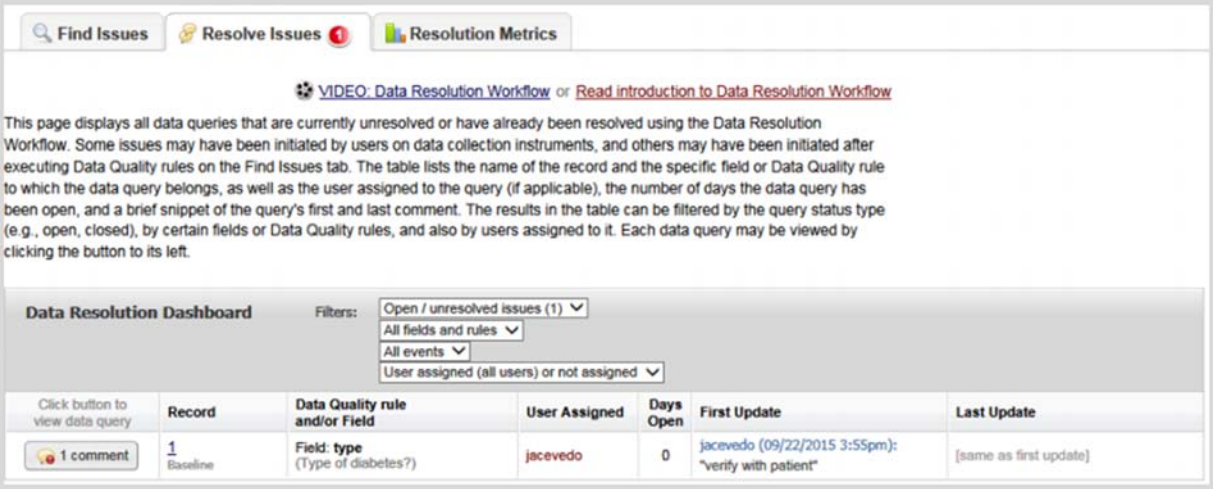
closed), by certain fields or Data Quality rules, and also by users assigned to it. Each data query may be viewed by clicking the button to its left.

Any user with 'respond' privileges will be able to respond to an open query (even if it is assigned to a specific user). The responder may select a response type (e.g. typographical error) and provide a descriptive comment with the ability to also attach a file (optional). Once a query has been responded to, a user with 'close' privileges may close the query, after which it will be considered resolved.



11. Using the Resolve Issues Page

While data queries will be opened either on a data entry form or via the results of a Data Quality rule, users will most likely respond to and close queries on the 'Resolve Issues' page (seen on left-hand menu). This page will serve as a dashboard that will neatly organize all queries (both open and closed) so that they may be reviewed and so that any open queries may be easily responded to and closed. That page can serve as a nice to-do list for addressing all open queries.



12. Reporting of Results

12.1. Reporting Biopsy Results to Participants and Health Care Providers

KPMP investigators and coordinators recognize the importance of sharing information with participants and their health care providers. Return of results with the appropriate clinical interpretation in language the participant will comprehend is an important goal of the study and essential to build and maintain trust among KPMP participants and investigators. Return of results will first be discussed during the informed consent process, when participants will be given clear details about what results will be provided, and how and when results will be made available. Participants need to understand the utility of the results and what information the results can or cannot provide. Participant expectations for returning results should be addressed during the informed consent process to aid in their decision about whether to participate in the study. Participants should update their contact information if there are any changes on who should receive results (i.e. change of primary care provider).

Baseline study results will include CLIA-certified clinical biopsy results generated by the site pathologist and eGFR measures. These results will be included in the participant's electronic medical record.

The primary report will be available within a few weeks after the KPMP Biopsy Visit and will include CLIA-certified results of the clinical biopsy and eGFR (based on serum creatinine). A KPMP investigator or the participant's primary kidney doctor will interpret the local pathology report and explain its contents using plain language (through a language interpreter, if necessary) appropriate to the participant's level of

understanding. This report will be shared at the convenience of the participant. Participants can specify how they would like to receive their study results in the Contact CRF, where research coordinators record whether the participant would like to receive results by phone, mail, or at an in-person visit. With their initial printed results, participants will receive a template cover letter thanking them for their participation and describing the content of the biopsy report. Because participants can choose for their primary (non-KPMP) kidney doctor to explain the biopsy report contents, the template letter will be an important communication tool from the KPMP investigator to the KPMP participant.

KPMP cases where biopsy tissue was obtained will undergo diagnostic review by the clinical adjudication committee. In case any novel diagnostic findings are revealed during this process, such findings will be related back to the primary clinical pathologist, providing opportunities for the primary pathology report to be amended. The new finding or diagnosis will then be discussed with the participant by their PCP, nephrologist and/or KPMP investigator.

During the course of the KPMP study visits and assessments, the study physician may learn something about the participant that has significant health implications but may not be related to KPMP study participation or the kidney biopsy. In these circumstances, the study physician will alert the physician primarily responsible for the participant's care so that appropriate evaluation can be done. The KPMP investigators will facilitate referral to an independent nephrologist, or relevant sub-specialist, but will not themselves provide care to participants to avoid conflict-of-interest or the appearance of conflict-of-interest. RS physicians are welcome write up a brief summary of the specific findings to add to the Cover letter and Full report when providing biopsy results to patients. This summary does not need IRB approval prior to providing it to the participant.

12.2. Reporting Genetics and "omics" Results to Participants and Health Care Providers

Participants in KPMP are likely to undergo whole exome and/or whole genome sequencing, although the timing of this is currently uncertain. For those participants who agree to the receipt of individual results from genetic analyses, any medically actionable findings (as defined by the American College of Medical Genetics and Genomics or ACMG) may be communicated to the participant, as well as the physician chosen by the participant (as state laws allow). Additionally, participants may have the option of having information about risk alleles related to kidney function (for example risk variants of the *APO-L1* gene, if assay is performed in a CLIA-certified lab) returned even if not known to be medically actionable. A process within the KPMP will guide decisions of how and when to return genomic results to participants including common language explanations. This process will include a designated panel of KPMP stakeholders, experts, and patient partners for KPMP guidance and oversight. When such results may become available in the course of KPMP research is indeterminate. The KPMP return of results process will include periodic re-evaluation of risks and benefits associated with return of results from KPMP and from knowledge gained in other similar studies and as updated by the ACMG.

In KPMP there will be additional results obtained from non-diagnostic, research-only "omics" tests run on the kidney biopsy tissue. However, since these research methods often do not have the accuracy of diagnostic tests, we do not currently plan to return these results to participants on an individual level.

However, aggregated, de-identified “omics” datasets will be available for participants to access online. Given the deep molecular phenotyping of the biospecimens and biopsies, there may be identification of potentially actionable, but currently “silent” incidental findings. Any clinically actionable findings may need to be confirmed by a clinical test performed in a certified diagnostic laboratory. Therefore, if a potentially actionable finding is detected, study staff may recommend an appropriate diagnostic test to confirm the findings if the participant has agreed to receive such information. If necessary, the study staff will facilitate referral to a nephrologist, clinical geneticist, or other relevant sub-specialist, but will not themselves provide care to participants. They and their treating physicians will together decide whether they want to perform such confirmatory test(s). Participants may be given the option to receive these data or indicate that they wish not to be informed of such findings. For those participants who agree to the receipt of individual results, any medically actionable findings will be communicated to the participant, as well as the physician chosen by the participant.

13. Electronic Health Record Data

13.1. Collection of electronic health record data

- Individual sites will collect electronic health record data for enrolled participants at regular intervals throughout the project, following the timing described in the clinical protocol.
- Health record data will be collected at each Recruitment Site by the Recruitment Site team and prepared for submission to the Central Hub.
- Recruitment Sites will replace patient identifiers with the participant’s research identifier. None of the HIPAA safe harbor variables or data elements will be included in a submission.
- EHR data will be submitted to the Central Hub in a common data model/format. Currently that format is the OHDSI OMOP standard, and data will be submitted from the sites as a compressed archive containing .csv files.
- The submission will be made through a REDCap form at http://redcap.kpmp.org/ and the Recruitment Site will fill in submission metadata on the form (see Section 11: Data Management System User Guide).
- The Central Hub will incorporate the EHR data into a relational database (EHRdb).
- All extractions of data from the EHRdb will utilize an honest broker, that is, a member of the DCC team that is authorized to prepare data for the purpose it is to be used for, including de-identification.
- Extracted data for use in the Kidney Tissue Atlas and within the DVC will be uploaded into the KPMP Data Lake.

13.2. EHR Data Use Best Practices

- KPMP EHR data, whether at the site or the Central Hub, will always be stored in an encrypted location with basic HIPAA auditing functions in place. All user access will be tracked.
- Honest brokers will be used whenever possible for the movement of EHR data across systems (such as Recruitment Site to DCC or DCC to KPMP Data Lake)
- EHR data will be mapped to the Observational Medical Outcomes Partnership (OMOP) data model by the Recruitment Sites.

13.3. Preparing EHR data

Sites will work with their informatics, Analytics or Research IT teams for data preparation. EHR data will be extracted across the timeframe requested using the institutions' home policies. It is the responsibility of the site to follow their home institution's policies and governance regarding data access of protected health information for research.

Data will be mapped to OHDSI OMOP format described here (https://www.ohdsi.org/data-standardization/the-common-data-model/). The OMOP version to be mapped will be officially stated on the REDCap submission form. OMOP data will likely be managed at each site in a secure, HIPAA-aligned relational database system and then extracted to plain text .CSV files for submission to the Central Hub.

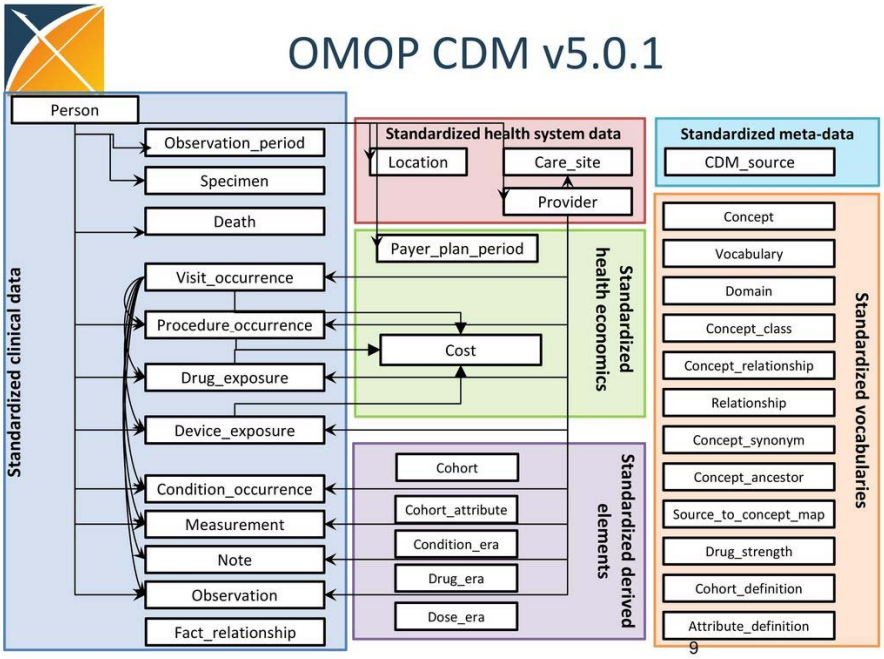


Figure 3. Schema for the OMOP Data Model as described in documentation at http://www.ohdsi.org/web/wiki/doku.php?id=documentation:cdm

13.4. Submitting EHR data through REDCap

Bundles of CSV files for submission to the Central Hub will be zipped archives containing all .CSV files for each submission. Each submission can contain multiple participants. Files will be attached to the REDCap form to be linked on the KPMP intranet website.

The form will be filled out to specify the submitting site, time frame being submitted, a time stamp and the submitting user at the site.

13.5. Submitted file processing

The REDCap submitted zip files will be extracted, csv files processed and merged with a DCC local relational EHR database using a script. This database will serve as the system of record for all health record data to be used by the hub and will employ full access auditing and encryption.

Quality control scripts will be applied to ensure data integrity and accuracy. Any data conflicts will be ameliorated between the DCC informatics personnel and the site informatics team.

13.6. Health record data access

Raw KPMP health record data will be made through a request to the by emailing the honest broker (to be named by the KPMP DCC PI). De-identified or datasets prepared for dissemination or integration into the Kidney Tissue Atlas will be accessed through a self-service web portal maintained by the KPMP DVC.

14. Personnel Training and Certification

14.1. Standardization of Clinical Procedures

Ongoing studies at the Recruitment Sites will result in data accumulated by study personnel and derived from adhering to multiple procedures in the course of their responsibilities. By standardizing study procedures and requiring such data-gathering individuals need to demonstrate the required level of procedural knowledge and competency, the opportunity for inconsistent data will be greatly reduced.

14.2. Responsibilities and Qualifications of Coordinators and Data Entry Personnel

Personnel are required to successfully demonstrate competency to the satisfaction of an authorized qualified individual following the completion of online and/or in-person training sessions. In the case of personnel turnover during the study, replacement personnel shall complete standard training and certification prior to their participation in KPMP activities. Research Coordinator

The Research Coordinator is responsible for all study operations of their respective Recruitment Sites. The Research Coordinator will share all information related to specific tests and procedures including manuals of operation (MOP), forms, and training materials related to the protocol with study personnel (clinic coordinator, technicians, data entry personnel) as appropriate.

14.3. KPMP Recruitment Site Data Entry and Clinical Operations Training and Certification

Consistency in performing protocol-defined procedures and recording study data strengthens the ability to achieve scientifically accurate outcomes. Therefore, it is crucial that research staff are trained and certified in all KPMP procedures. The DCC designs sessions to train the Recruitment Site staff in skills necessary to collect, record, and process protocol data, such as using the secure KPMP web site, recording data in the PMP, using the Specimen Tracking System, and performing all KPMP procedures. The DCC will develop protocol training sessions as well as web-based or videoconference training presentations. When there is turnover in the Lead Research Coordinator position at a Recruitment Site, the DCC will provide protocol and application training for the new Lead Research Coordinator. Replacement personnel will complete standard training and certification prior to their participation in KPMP clinic activities. Research Coordinator training will be web-based to maximize participation, be cost-effective, and be available to the other sites.

14.4. KPMP Recruitment Sites Data Entry and Clinical Operations Training and Re-Certification

If a Research Coordinator leaves KPMP, they are inactivated in the KPMP certification module. If they return within two years, they will need to review KPMP procedures and have oversight/supervision by the lead Research. If a Research Coordinator returns more than two years after leaving the study, they will follow training and certification procedures as defined for new Research Coordinators.

14.5. Human Subjects Protection Training

NIH requires that KPMP personnel complete Human Subjects Protection training. The original tutorial, exam, and certification documentation are available at https://ohsr.od.nih.gov/. Clinical staff follow training and certification guidelines their institutions' Human Subject Protection Office (HSPO) to ensure they meet their institutional requirements. Site Visits

Each Recruitment Site will have a pre-study initiation site visit to facilitate training and certification and assure compliance with the KPMP protocol.

After study initiation, on-site reviews of Recruitment Sites may be scheduled on an as-needed basis to:

- Assess the overall performance of the Recruitment Sites, and the conduct of the ongoing protocol training
- Assess the quality of data collection
- Provide consultation in identifying and solving problems
- Transfer effective approaches from one Recruitment Sites to another

Components of the site visit will include:

- Meeting with personnel.
- Examining facilities
- Reviewing administrative organization within the center
- Evaluating conduct of a pilot biopsy and tissue triage procedure
- Other activities proposed by the DCC, the NIDDK, and the EEP.

The site visit team will include representatives from the Central Hub and possibly NIDDK or a member of the EEP or another Recruitment Site. The DCC will prepare site visit reports which will include specific recommendations for the center. The report will be sent to the PI and Research Coordinator at the Recruitment Sites where the site visit was performed, NIDDK, and the Chair of the SC. If serious problems are detected, the report will also be sent to the Steering Committee for review. Each Recruitment Sites will be site-visited, as necessary, during the project period.

14.6. Certification

14.6.1. Summary of Certification Requirements

Certification Requirements for KPMP Study Procedures are outlined in table 9. Training and certification for tissue handling is described in the Pathology MOP.

In addition to the detailed requirements listed in the table by personnel type, the following certification requirements apply to all components:

- Trainees must thoroughly read the relevant section in the MOP.
- Appropriate supporting documents (e.g. checklists and tests) must be completed when required.
- Retain a copy of the supporting certification documents at the Recruitment Site for local records in a designated binder.

Table 9: Certification Requirements

Required minimal training activities for the role of KPMP Research Coordinator include:

Informed Consent
Listened to Consent Training Webinar
Completed Informed Consent Quiz
Non-Renal Biosamples
Listened to Biospecimen Training Webinar
Completed Biospecimen Quiz
Watched 'reverse pipetting' and 'DNA and urine pellets' videos
Biopsy and Tissue Triage
Listened to Biopsy Training Webinar
Completed Biopsy Tissue Quiz
Watched 'Tissue processing' video
Clinical Operations
Listened to Clinical Operations Training Webinar
Completed Clinical Operations Quiz
General Operations
Watched REDCap and SpecTrack videos
Set up institutional log-in in REDCap/SpecTrack
Added to Basecamp, RC meetings, directory, etc.
Set up access to KPMP iPad

Suggested minimal criteria and training for the role of KPMP Biopsy Operator include:

Experience
Minimum of 35 renal biopsies performed in last two years
Overall major complication rate of <10%
>85% of biopsies adequate for diagnosis
Training Recommendations
Reviewed the KPMP Protocol
Reviewed "Biopsy Procedure" Section in the Recruitment Site MOP
Reviewed "Study Eligibility Criteria" Section in the Recruitment Site MOP

Suggested minimal criteria and training for the role of KPMP Pathology Personnel include:

Training Recommendations
Reviewed the Pathology MOP
Watched 'Tissue processing' video
Completed Biopsy Tissue Triage Quiz

14.6.2. Summary of Certification Maintenance Requirements

To maintain readiness, sites must complete a biopsy at least every 8 weeks – either a patient biopsy (after study activation) or an apple biopsy. Apple biopsies should be video-recorded, and data should be entered in the Biopsy Procedure Details CRF.

15. Appendix A: Recruitment Site Initiation Check list

Kidney Precision Medicine Project

Recruitment Site Initiation Checklist

Date:

Recruitment Site: _____

_____

_____

Investigator: _____ Phone: _____

Sub-Investigator: _____ Phone: _____

Sub-Investigator: _____ Phone: _____

Key Study Contact: _____ Phone: _____

Research Coordinator: _____ Phone: _____

(If other than Key Study Contact)

A. Confirm information provided to/from the site	Yes	No	Comments
1. Confidentiality Disclosure Agreement signed by Investigator	☐	☐	
2. Material/Data Transfer Agreement signed by Investigator	☐	☐	
3. Duality of Interest Disclosure statement signed by Investigator	☐	☐	
4. Protocol received and reviewed by Investigator. *Version:* _____	☐	☐	
5. Recruitment Site MOP received and reviewed by Investigator. *Version:* _____	☐	☐	
6. Biospecimen MOP received and reviewed by Investigator. *Version:* _____	☐	☐	
7. Pathology MOP received and reviewed by Investigator. *Version:* _____	☐	☐	
8. Monitoring plan and schedule in place (if applicable)	☐	☐	
9. KPMP supplies inventory management strategy	☐	☐	
10. Reporting and record-keeping requirements	☐	☐	
11. Potential for Investigator's clinical study audit (if applicable)	☐	☐	

Kidney Precision Medicine Project

Recruitment Site Initiation Checklist

B. Clinical study regulatory requirements	Discussed?		Comments
1. *Obligations of Investigator and key study personnel*	Yes	No	
• Conduct study according to written protocol, federal regulations, IRB and other applicable regulatory requirements	☐	☐	
• Document all unanticipated events and immediately contact study Monitor for follow-up instructions	☐	☐	
• Accurately report all data and observations of anticipated and unanticipated adverse events	☐	☐	
• Observe Good Clinical Practice (GCP) and Good Laboratory Practice (GLP)	☐	☐	
2. *Human subject safety and confidentiality*	Yes	No	
• Conduct informed consent process according to regulatory and IRB requirements	☐	☐	
• Participant identifiers will be properly masked, and samples will be coded per protocol requirements	☐	☐	
• Storage of participant records secure, protects their confidentiality	☐	☐	
3. *Reporting of study results*	Yes	No	
• Return of Results policies; appropriate use in participant diagnosis or management	☐	☐	
• Policies for scientific publications and presentations at professional meetings	☐	☐	

C. Study management and record-keeping requirements	Discussed?		Comments
1. *Data collection, verification and transmission procedures*	Yes	No	
• Timely completion of case report forms (CRFs)	☐	☐	
• CRF review and verification for accuracy	☐	☐	
2. *Contents of Investigator's study file*	Yes	No	
• Signed delegation of responsibilities log for all study personnel (to include operator, pathologist, pathology tech, research coordinators)	☐	☐	
• Protocol, MOPs, CRFs, and amendments	☐	☐	
• Copies of relevant correspondence (Investigator, IRB)	☐	☐	
• Participant approach log	☐	☐	
3. *Record retention and accessibility*	Yes	No	N/A
• Administrative and subject records maintained for at least two years(?) after the study is closed out	☐	☐	☐
• Requirement for review of records by DSMB (if applicable)	☐	☐	☐
• Requirement for review of records by government officials (NIH, state) (if applicable)	☐	☐	☐

Recruitment Site Initiation Checklist

D. Adverse event reporting requirements	Discussed? Yes	No	Comments
1. File written reports as stipulated by DSMB and IRB			
• Serious, life-threatening or fatal adverse event to REDCap within 24 hours	☐	☐	
• Non-serious adverse events to REDCap within 20 days	☐	☐	

E. Reviewed protocol with Investigator and key study personnel	Discussed? Yes	No	Comments
1. Purpose of the study	☐	☐	
2. Inclusion/exclusion criteria	☐	☐	
3. KPMP operator reviewed and agreed to biopsy protocol and signed delegation of responsibilities log	☐	☐	
4. Specimen collection, storage and processing procedures	☐	☐	
5. Data collection and completion of case report forms	☐	☐	
6. Criteria for study completion or termination	☐	☐	
7. Documenting minor and major protocol deviations	☐	☐	

F. Conducted site visit (personnel and facilities)	Yes	No	Comments
1. Investigator has sufficient time and adequate training and experience to conduct the study.	☐	☐	
2. Investigator has adequate staff and other resources for timely conduct of study.	☐	☐	
3. Facilities Checklist complete and appear adequate for the study (space, equipment, etc.)	☐	☐	
4. Storage for participant and study files, specimens, and source documents is adequate and secure	☐	☐	
5. Adequate written standard operating procedures are available	☐	☐	
6. Sufficient eligible participants (patients, samples) are available	☐	☐	
7. Personnel succesfully demonstrated Pilot 3 exercise	☐	☐	

Recruitment Site Initiation Checklist

G. Completed training	Yes	No	Comments
1. Completed CRF training	☐	☐	
2. Completed SpecTrack training	☐	☐	
3. Completed REDCap training	☐	☐	
4. Completed Pilot 3 successfully	☐	☐	
5. Completed biospecimen collection and processing training	☐	☐	
6. Completed specimen storage and shipping training	☐	☐	
7. Completed Delegation of Responsibilities log	☐	☐	
8. Completed recruitment and informed consent training	☐	☐	
9. Completed clinical operations training	☐	☐	

H. Discuss Significant Concerns

I. Summary and Conclusion

Recruitment Site Initiation Checklist

Reviewer's Name (print)	Signature	Date

Investigator's Name (print)	Signature	Date

16. Appendix B: Personnel Log

Recruitment Site Personnel Responsibilities and Training Log

Date:

Recruitment Site:

PI Name:

RESEARCH COORDINATOR

The person(s) listed below have been trained in the tasks assigned to KPMP Research Coordinators and are authorized to conduct those activities (including identification of eligible patients, recruitment, consent, enrollment, case report form completion, biosample collection and processing, biopsy cart preparation and biopsy data entry, de-identification of pathology materials, packaging and shipping of samples, query resolution, etc.).

Required minimal training activities for the role of KPMP Research Coordinator (initial to attest to completion of each):

	Coordinator Initials					
Informed Consent						
Listened to Consent Training Webinar						
Completed Informed Consent Quiz						
Non-Renal Biosamples						
Listened to Biospecimen Training Webinar						
Completed Biospecimen Quiz						
Watched ‘reverse pipetting’ and ‘DNA and urine pellets’ videos						
Biopsy and Tissue Triage						
Listened to Biopsy Training Webinar						
Completed Biopsy Tissue Quiz						
Watched ‘Tissue processing’ video						

Recruitment Site Personnel Responsibilities and Training Log

Clinical Operations						
Listened to Clinical Operations Training Webinar						
Completed Clinical Operations Quiz						
General Operations						
Watched REDCap and SpecTrack videos						
Set up institutional log-in in REDCap/SpecTrack						
Added to Basecamp, RC meetings, directory, etc.						
Set up access to KPMP iPad						

RESEARCH COORDINATOR

Contact information and PI attestation:

Name of Coordinator *(Please Print)*	Phone number	Email	Signature	Dates Active on Study From	To	PI Initials *

Recruitment Site Personnel Responsibilities and Training Log

BIOPSY OPERATOR

The person(s) listed below have reviewed the KPMP biopsy protocol and agree to execute the procedures as written, including the use of a 16-gauge biopsy needle. The person(s) listed below has performed at least 35 renal biopsies over the last 2 years with an overall major complication rate (e.g. bleeding requiring transfusions/surgery/additional interventions or death or extended hospitalization of >48 hours) of <10% and >85% of biopsies deemed adequate for diagnosis.

Suggested minimal criteria and training for the role of KPMP Biopsy Operator (initial to attest to completion of each):

	Operator Initials					
Experience						
Minimum of 35 renal biopsies performed in last two years						
Overall major complication rate of <10%						
>85% of biopsies adequate for diagnosis						
Training Recommendations						
Reviewed the KPMP Protocol						
Reviewed “Biopsy Procedure” Section in the Recruitment Site MOP						
Reviewed “Study Eligibility Criteria” Section in the Recruitment Site MOP						

Contact information and PI attestation:

Name of Operator *(Please Print)*	Phone number	Email	Signature	Dates Active on Study From	To	PI Initials *

PATHOLOGY PERSONNEL

Recruitment Site Personnel Responsibilities and Training Log

The person(s) listed below have reviewed the KPMP Pathology MOP and agree to execute the procedures as written.

Suggested minimal criteria and training for the role of KPMP Pathology Personnel (initial to attest to completion of each):

	Pathology Personnel Initials					
Training Recommendations						
Reviewed the Pathology MOP						
Watched 'Tissue processing' video						
Completed Biopsy Tissue Triage Quiz						

Contact information and PI attestation:

Name of Operator *(Please Print)*	Phone number	Email	Signature	Dates Active on Study From	To	PI Initials *

Recruitment Site Personnel Responsibilities and Training Log

* My initials on each row confirm that I authorize the site personnel to perform the study-conduct responsibilities as noted.

_____ _____

PI Signature Date

_____ _____

Co-PI Signature (if applicable) Date

Specify which local investigator(s) should receive immediate email notification when an Adverse Event is reported:

_____ _____

Name Email

_____ _____

Name Email

_____ _____

Name Email

_____ _____

Name Email

17. Appendix C Physical Measurements

17.1. Anthropomorphic Measures

17.1.1. Height

- Height is measured in conjunction with the weight measurement. It may precede or follow this procedure.
- A wall mounted stadiometer should be used that can be calibrated with a rod.
- Remove any hat, hair bows, or other head gear that would interfere with the top of the stadiometer touching the crown of the head.
- The participant should be in stocking feet or non-slip slippers and stand on a flat surface that is at a right angle to stadiometer. The weight is evenly distributed between both feet, and the arms are hanging by the sides with palms facing the thighs. The heels are together, touching the stadiometer. The feet are spread at a 60-degree angle to each other. Whenever possible, the head, scapula and buttocks should also be touching the stadiometer. The head is erect with eyes focused straight ahead.
- Lower the horizontal board of the stadiometer to the most superior point on the head, compressing the hair. Standing height is measured to the nearest 0.1 cm.
- Repeat measurement. The 2nd measurement should be within 0.5 cm of the first.
- Record the first of the 2 measurements. If the 2nd measurement is not within 0.5 cm of the first measurement, repeat measurement until you obtain two that are within 0.5 cm of each other. Record the first of these 2 measurements.
- If the participant cannot stand for the height measurement, it may be recorded from a recent clinic visit in the EMR.

17.1.2. Weight

A traditional balanced beam scale has been considered a reliable instrument for population measurement. In the past years, they have often been replaced by electronic digital scales, which are easier to operate. Either type of scale should be calibrated regularly by a reliable vendor, or according to clinic protocol. The floor surface on which the scale rests must be hard and should not be carpeted or covered with other soft material.

- Balance the scale so that the indicator is at zero.
- Participant should empty bladder.
- Have the participant remove any heavy external clothing, shoes, belts, or heavy jewelry.
- Measure weight twice, having the participant step off the scale to repeat zero balance between measurements. The second measurement should be within 0.1 kg of the first measurement. Record the first measurement on the Physical Measurements CRF.
- If the difference between the 2 measurements is greater than 0.1 kg, repeat the measurement until 2 results are within 0.1 kg and record the first of the 2 measurements on the CRF.

- The scale should be calibrated per unit policy. If the scale is moved on a frequent basis, it should be calibrated more often. If it is stationary, the scale should be calibrated yearly by a certified scale calibration vendor.
- If the participant cannot stand for the weight measurement, it may be recorded from a recent clinic visit in the EMR.

17.2. Temperature Measurement

Body temperature can be measured according to clinic standard operating procedures. Record the temperature in degrees Celsius in the Physical Measurements CRF and indicate the location of measurement (oral, aural, forehead, arterial line).

- Oral Measurement: taken as a buccal measurement (in the cheek) or sublingual measurement (under the tongue). Ensure participant has not had anything to eat or drink that was very hot or cold prior to the measurement or engaged in strenuous activity, both of which can affect the core body temperature. It is important that the participant keep their mouth closed during the measurement.
- Ear (Aural) Measurement: the tip of the thermometer is simply inserted properly into the ear canal.
- Forehead Measurement: The forehead thermometer is placed at the center of the forehead of the participant and then slowly slide across the forehead towards the top of the ear, maintaining contact with the skin. An infrared sensor detects the highest measured value, while a second sensor measures the ambient temperature. The difference between these two provides the body temperature.
- Arterial Line Measurement: If an arterial line is placed, review the monitor for a current temperature reading

17.3. Pulse Measurement

The pulse is observed by palpation of the radial artery at the wrist. Alternatively, the pulse may be recorded from an automated blood pressure machine.

- The same arm should be used for both pulse and blood pressure measurements. Indicate which arm is used to measure pulse and blood pressure on the Physical Measurements CRF.
- A good stopwatch should be used for the 5-minute waiting period prior to blood pressure measurement, 30 second pulse measurement, and 60 second intervals between blood pressure readings.
- The measurement of pulse is performed only after the participant has been seated quietly, with feet flat on the floor, in an erect but comfortable posture, for at least five minutes.
- The participant should refrain from caffeine, smoking, and exercise at least one-half hour prior to and until completion of blood pressure measurement.
- The elbow and forearm should rest comfortably on the table. With the palm of the hand turned upward, the radial pulse is palpated and counted for 30 seconds exactly.

- The number of beats in 30 seconds is recorded, multiplied by 2, and the product recorded as the heart rate.
- Pulse may also be recorded from an arterial line.

17.4. Blood Pressure Measurements

17.4.1. Overview of Blood Pressure Measurement

In the KPMP Study, sitting and standing blood pressure is measured at a resting state, using three sitting measurements and one standing measurement. Blood pressure measurements will be recorded on the Physical Measurements CRF.

Blood pressure measurement steps outlined here can be followed satisfactorily for most participants in the outpatient setting. Exceptional situations occasionally arise with serious obstacles to successful blood pressure measurement.

17.4.2. Preparation for Blood Pressure Measurement

Some of the many extraneous factors influencing blood pressure are controlled by standardizing the measurement technique and the environment in which the measurement is made. Uncontrolled factors (time of day, identity of the observer) are recorded, so that they can be considered during analysis.

Try to keep the blood pressure measurement as pleasant as possible. Participants should be given full explanation and instructions about the preparation for the blood pressure examination and an opportunity for brief questions. The setting in which blood pressure measurements are made will be standardized, and should take place in a separate, quiet room where no other activity is taking place, and where temperature fluctuations are minimal. Equipment should be checked when waiting for the participant. Arm measurement, cuff selection and placement should be completed prior to a five-minute rest period in this quiet room. The participant should be relaxed, seated with back supported with legs uncrossed and feet comfortably flat on the floor, not dangling.

17.4.3. Materials and Equipment

- Automated or manual blood pressure device
- Blood pressure cuffs in a variety of sizes
- Measuring tape (for arm circumference).
- Watch or stopwatch (to time five-minute rest and resting heart rate).
- Copy of chart for choosing correct BP cuff size (see Table 10).

17.4.4. Preparation

Before the BP measurement procedure, explain to the participant what to expect and how long the procedure will take. The following script is suggested:

> ***This part of the exam involves taking your seated and standing blood pressure. It will take about 10 minutes. We would like you to sit with both feet on the floor and your arm supported on the table. We will have you sit quietly for five minutes. Then we will take your seated blood pressure three times, one minute apart, using an automated device, followed by one standing blood***

pressure. We will give you your blood pressure readings and some material to help you interpret them at the end.

17.4.5. Arm Measurement and Cuff Size

Use the proper cuff size to avoid under- or over-estimation of the correct blood pressure. Selection of the proper sized cuff is based on the guideline that the length of the inflatable bladder in the cuff should be at least 40% greater than the arm circumference. Measurement of the bladder length in the cuffs confirms that the chart in Table 10 conforms to this guideline. A copy of this chart should be available during the BP measurement procedure for easy reference. Selection of cuff size should be based on the chart in Table 10. If the participant's arm size falls in a range in which there is overlap of two cuff sizes, use the larger cuff.

Measure the arm circumference as follows:

- Ask the participant to bare the upper arm that will be used to measure blood pressure.
- Ask the participant to sit or stand holding forearm horizontal, i.e., parallel to the floor.
- Measure arm length from the acromion (bony extremity of the shoulder girdle) to the olecranon (tip of the elbow) using a metric tape.
- Note the midpoint on the dorsal (back) surface of the arm.
- Ask participant to relax arm along the side of the body.
- Draw the measuring tape snugly around the arm at the midpoint mark, keeping the tape horizontal. Tape should not indent the skin. Record the arm circumference measured to the closest (0.1) cm in the Physical Measurements CRF.
- Use the criteria in Table 10, below, to determine cuff size, if necessary.

Table 10: Cuff Size Indicated by Measured Arm Circumference

Arm Circumference* (cm)	Cuff Name	Bladder Length (cm)
12-19	Child	8
19.1-25	Small Adult	10
25.1-33	Adult	13
33.1-40	Large Adult	17
40.1-50	Thigh	

17.4.6. Positioning the Participant

- The workstation should be free of excessive noise or distractions.
- The participant should be seated and relaxed in a comfortable chair, to ensure that:
    - He or she is sitting up (not slouched).
    - Both feet are on the floor (legs/ankles not crossed).
    - Right forearm is supported resting on the table.
- The participant should not talk, eat, or drink during the procedure.
- Ideally, the machine output will not be visible to the participant during the measurement, as this may cause anxiety.

17.4.7. Application of the Blood Pressure Cuff

Place the appropriate cuff around the arm so that the mid-height of the cuff is at heart level. Palpate the participant's brachial artery and place cuff so that the artery is aligned with the cuff arrow marked "artery."

Place the lower edge of the cuff, with its tubing connections, two centimeters above the natural crease across the inner aspect of the elbow.

Wrap the cuff snugly around the arm, with the palm of the participant's hand turned upward.

Secure the wrapped cuff firmly by applying pressure to the locking fabric fastener over the area where it is applied to the cuff.

Do not wrap the cuff too tightly around the arm. You should be able to insert the first joint of two fingers under the cuff. The cuff should be snug but not tight.

Be sure all air is squeezed out of the cuff before each inflation.

17.4.7.1. Sitting Pulse and Blood Pressure Measurement

Separate each of three measurements by one minute.

Record the SBP, DBP and pulse in the Physical Measurements CRF

Report the average of the last two blood pressures to the participant both verbally and in writing. The average of the two measurements will be calculated in the Physical Measurements CRF. This average is also used for reporting SBP and DBP alert values.

17.4.7.2. Standing Pulse and Blood Pressure Measurement

After completing 3 seated blood pressure readings, raise the bedside table at the participant's side so that unnecessary movement or walking will not occur when the participant is asked to stand. The participant is then asked to stand slowly with their arms relaxed at their sides for 2 minutes.

- After 2 minutes, place the participant's arm on a pillow on the bedside table with the palm of the hand turned upward.
- The bedside table needs to be elevated so the arm can rest at heart level for the standing pulse and blood pressure.
- Take one standing blood pressure and pulse measurement as described above and record the values in the Physical Measurements CRF.

17.4.8. Reporting the Blood Pressure Results to the Participant

The participant may wish to know his or her results before the results are entered into the database. If so, report the average the second and third readings that is calculated in the Physical Measurements CRF. State clearly the systolic and diastolic pressures and offer to write down these values for the participant.

17.5. Edema Assessment

Edema is the swelling of tissues as a result of excess fluid accumulation. This swelling can occur in a single area, or across the whole body. For KPMP, we are looking for swelling in the legs (lower extremity edema), at the base of the spine (sacrum), or throughout the body (anasarca). This assessment is performed with a “pit” test. The edema assessment is not intended to record the presence of non-pitting edema.

Steps for performing a pit test:

- Press firmly on the areas listed in the Physical Measurements CRF with your fingers or thumb for 5 seconds.
    - lower extremity (around the ankle)
    - Sacrum (base of the spine)
    - Anasarca (whole body swelling of the skin)
- After 5 seconds stop pressing, remove your finger, and check for a persistent depression in the skin.
- If there is a depression, or “pit” present, the participant is positive for edema for the assessed area.
- Mark “present” or “absence” for edema for each area listed in the Physical Measurements CRF.

18. Appendix D: Visit Checklists

CKD Screening before Enrollment Visit Checklist

Screening Activities:

Check as completed	Procedure	CRF
	Review potential subject's medical record for eligibility and track using Screening Worksheet.	Screening Worksheet
	Approach potential participant's physician about study participation	n/a
	Register screened patients in Participant Management Program (PMP) Update enrollment/screening status Record initial demographics data	New Participant CRF
	Schedule screening or informational visits with study team members and the participant to assess eligibility	Eligibility Assessment CRF

If participant appears eligible and is interested in enrolling:

Check as completed	Procedure	CRF
	Schedule enrollment visit with study team members and the participant	n/a
	Prepare a new Subject Source Document Binder with copies of your site's current approved consent/HIPAA forms.	n/a
	Provide instructions for the Enrollment Visit to the participant. Instruct participants to bring all recent [within the last 30 days] prescription and non-prescription medications with them to the Enrollment visit.	n/a

After Screening:

Check as completed	Procedure	CRF
	Call participant to confirm enrollment visit date. Reminder to bring medications.	n/a

CKD Enrollment Visit Checklist

Prior to Enrollment Visit:

Check as completed	Procedure	CRF
	Review potential participant's medical record for additional eligibility data prior to visit.	n/a
	Ensure supplies are available for biosample collection (blood and spot urine kits)	n/a

Enrollment Visit:

Check as completed	Procedure	CRF
	Record Visit Date and participant time burden	Visit Log CRF
	Assessment of inclusion/exclusion criteria	Eligibility Assessment CRF
	Informed consent process and obtain written informed consent	Informed Consent CRF
	Complete any labs necessary for inclusion/exclusion screening tests. Bleeding criteria screening tests and urine pregnancy tests (if necessary) may be completed at the Biopsy Visit.	Eligibility Assessment CRF
	Collect participant and physician contact information	Contact Information CRF
	Collect vitals, anthropometry, blood pressures, edema assessment	Physical Measurements CRF
	Blood draw and spot urine collection and processing, up to 6 weeks prior to the biopsy procedure	Biosample: Blood, Spot urine
	If ACD tube drawn, record date of ACD tube collection in Biopsy Scheduling CRF ASAP to notify biorepository. Record scheduled biopsy date, if known.	Biopsy/ACD Scheduling
	Record Demographics information	Demographics CRF
	Record prescription and non-prescription medications taken in the past 30 days	Medications CRF
	Record Medical History information (interviewer-administered participant CRF and coordinator CRF)	Medical History CRF for participant and coordinator

	Provide instructions and supplies for stool and timed urine collection and for the biopsy procedure	n/a
	Provide Participant CRFs packet (for CKD participants)	PROMIS Global Health CRF Health Literacy CRF Personal History CRF
	Update participant status (if necessary)	End of Study CRF
	Order bleeding criteria labs and pregnancy test (if necessary)	n/a

After Enrollment Visit:

Check as completed	Procedure	CRF
	Primary kidney care physician and KPMP investigator complete Pre-Clinical Assessment CRF	Pre-Clinical Assessment CRF
	Enter Laboratory Results Data from EHR	Laboratory Results CRF
	Ensure supplies are available for Biopsy Visit (Biopsy Kit)	n/a
	Record date of scheduled biopsy and ACD tube collection in Biopsy Scheduling CRF (if not previously done)	Biopsy/ACD Scheduling

CKD Biopsy Visit Checklist

Prior to Biopsy Visit:

Check as completed	Procedure	CRF
	Confirm the Biopsy Visit with study team members and the participant.	n/a
	Prepare Biopsy kit and biopsy cart	n/a

At Biopsy Visit:

Check as completed	Procedure	CRF
	Record Visit Date and participant time burden	Visit Log CRF
	Receive, process, and store stool and timed urine sample	Biosample: Stool, Timed urine
	Receive and record at-home CRFs packet	PROMIS Global Health CRF Health Literacy CRF Personal History CRF
	Complete bleeding exclusion criteria blood tests	Eligibility Assessment CRF
	Urine Pregnancy test (for all women under 55 years old of child-bearing potential)	Eligibility Assessment CRF
	Review and update Contact Information CRF	Contact Information CRF
	Perform kidney imaging to confirm anatomical or imaging eligibility	Pre-Biopsy Safety CRF
	Complete Pre-Biopsy Safety CRF	Pre-Biopsy Safety CRF

Biopsy-Related Activities:

Check as completed	Procedure	CRF
	Perform Kidney Biopsy	Kidney Biopsy Procedure Details CRF
	Tissue tracking and shipping	Tissue Tracking From, SpecTrack
	Post biopsy monitoring	Post Biopsy CRF Post Biopsy Hospitalization CRF
	Post biopsy adverse events reporting	Adverse Events CRF(as needed)

After Biopsy Visit:

Check as completed	Procedure	CRF
	Update participant status (if necessary)	End of Study CRF
	Ship biopsy samples and derivatives, blood, urine, and stool aliquots.	SpecTrack
	Run REDCap data quality rules to check for missing or questionable data	
	Store paper blood/urine/stool sample collection and processing forms as source documentation in the participant folder	
	Schedule case for CKD Adjudication Committee review	CKD Adjudication CRF

CKD 24-hour Post - Biopsy Follow-up Checklist

At 24-Hour Post-Biopsy Follow-up:

Check as completed	Procedure	CRF
	Continue post-biopsy procedure CRF (if necessary)	Post Biopsy CRF
	Call participant to complete 24-hour post biopsy phone call questions and AE assessment (if discharged) Record outcome of contact attempt (visit occurred, not occurred, or attempted)	24-hour Post Biopsy Phone Call CRF
	Collect adverse event information (if necessary)	Adverse Event CRF
	Collect hospitalization information (if necessary)	Post Biopsy Hospitalization CRF
	Update participant status (if necessary)	End of Study CRF
	Send REDCap surveys to pathologists	Send Pathology IF Metadata CRF Send Dx Core – DCA CRF
	Run REDCap data quality rules to check for missing or questionable data	

CKD 14-day Post-Biopsy Follow-up Checklist

At 14-day Post-Biopsy Follow-up Call:

Check as completed	Procedure	CRF
	Call participant to complete 14-day post biopsy phone call questions and AE assessment (if discharged). Record outcome of contact attempt (visit occurred, not occurred, or attempted)	14-day Post Biopsy Phone Call CRF
	Record details of any post-biopsy hospitalizations	Post Biopsy Hospitalization CRF
	Report any biopsy-related adverse events	Adverse Event CRF

After 14-day Post-Biopsy Follow-up:

Check as completed	Procedure	CRF
	Primary kidney care physician and KPMP investigator to complete Follow-up Clinical Assessment (after biopsy results are available)	Follow-up Clinical Assessment CRF
	Send biopsy results to participant (or when available)	n/a
	Update participant status (if necessary)	End of Study CRF
	Run REDCap data quality rules to check for missing or questionable data	

CKD 28 day-Post-Biopsy Follow-up Checklist

At 28-day Post-Biopsy Follow-up Call:

Check as completed	Procedure	CRF
	Call participant to complete 28-day post biopsy phone call questions and AE assessment (if discharged). Record outcome of contact attempt (visit occurred, not occurred, or attempted)	28-day Post Biopsy Phone Call CRF
	Record details of any post-biopsy hospitalizations	Post Biopsy Hospitalization CRF
	Report any biopsy-related adverse events	Adverse Event CRF
	Provide instructions for completing the Participant Experience Survey	Participant Experience Survey
	Remind participant of the upcoming 6-month remote visit	n/a

After 28-week Post-Biopsy Follow-up:

Check as completed	Procedure	CRF
	Send biopsy results to participant (or when available)	n/a
	Run REDCap data quality rules to check for missing or questionable data	

CKD Remote Visit Checklist (Month 6, 18, 30, 42, 54 ± 3 Months)

At Remote Visit:

Check as completed	Procedure	CRF
	Record outcome of contact attempt (visit occurred, not occurred, or attempted)	Participant Follow up CRF
	Record Visit Date and participant time burden	Visit Log CRF
	Review and update Contact Information CRF	Contact Information CRF
	Record prescription and non-prescription medications taken in the past 30 days	Medications CRF
	Assess study outcomes/medical events since last contact	Follow-up Medical Events CRF
	Assess study outcomes/hospitalizations since last contact	Post Biopsy Hospitalization CRF
	Provide instructions for completing the Participant Experience Survey (6 months only)	Participant Experience Survey
	Schedule annual follow-up visit	n/a

After Remote Visit:

Check as completed	Procedure	CRF
	Enter Laboratory Results Data	Laboratory Results CRF
	Update participant status (if necessary)	End of Study CRF
	Run REDCap data quality rules to check for missing or questionable data	

CKD Annual Follow-up Visit Checklist (Month 12, 24, 36, 48 ± 3 Months)

Prior to Annual Visit:

Check as completed	Procedure	CRF
	Send at-home questionnaire packet to participant	PROMIS Global Health CRF Health Literacy CRF (12 months only)
	Confirm appointment with participant, remind them to bring current medications to the appointment and at-home questionnaire packet to the visit.	n/a
	Ensure supplies are available for biosample collection (blood and spot urine kits)	n/a

At Annual Visit:

Check as completed	Procedure	CRF
	Record outcome of contact attempt (visit occurred, not occurred, or attempted)	Participant Followup CRF
	Record Visit Date and participant time burden	Visit Log CRF
	Review and update Contact Information CRF	Contact Information CRF
	Receive and record at-home CRFs packet. Health literacy data is collected only at 12-month visit.	Personal History Follow-up PROMIS Global Health CRF Health Literacy CRF (12m only)
	Update Personal History information	Personal History CRF
	Record prescription and non-prescription medications taken in the past 30 days	Medications CRF
	Collect, process, and store biospecimens	Biosample: Blood, Spot urine

	Collect vitals, anthropometry, blood pressures, edema assessment	Physical Measurements CRF
	Assess study outcomes/medical events since last contact	Follow-up Medical Events CRF
	Assess study outcomes/hospitalizations since last contact	Post Biopsy Hospitalization CRF
	12-month only: Check to see if 6-month participant survey has been completed. If not, provide a paper copy of the survey and a stamped envelope to return it to the DCC.	Send the Participant Experience Survey CRF
	Remind participant of upcoming remote visit	n/a

After Annual Visit:

Check as completed	Procedure	CRF
	Enter Laboratory Results Data	Laboratory Results CRF
	Update participant status (if necessary)	End of Study CRF
	Ship blood and urine aliquots	SpecTrack
	Store paper blood/urine/stool sample collection and processing forms as source documentation in the participant folder	
	Run REDCap data quality rules to check for missing or questionable data	

AKI Screening before Enrollment Visit Checklist

Screening Activities:

Check as completed	Procedure	CRF
	Review potential subject's medical record for eligibility and track using Screening Worksheet.	Screening Worksheet
	Approach potential participant's physician about study participation	n/a
	Register potential participant in Potential participant Management Program (PMP). Update enrollment/screening status Record initial demographics data	New Participant CRF
	Schedule screening or informational visits with study team members and the participant to assess eligibility	Eligibility Assessment CRF

If potential participant appears eligible and is interested in enrolling:

Check as completed	Procedure	CRF
	Schedule enrollment visit with study team members and the participant	n/a
	Prepare a new Subject Source Document Binder with copies of your site's current approved consent/HIPAA forms.	n/a
	Provide instructions for the Enrollment Visit to the participant. Instruct participants to bring all recent [within the last 30 days] prescription and non-prescription medications with them to the Enrollment visit.	n/a

After Screening:

Check as completed	Procedure	CRF
	Call or visit participant to confirm enrollment visit date. Reminder to bring medications.	n/a

AKI Enrollment Visit Checklist

Prior to Enrollment Visit:

Check as completed	Procedure	CRF
	Review potential participant's medical record for additional eligibility data prior to visit.	n/a
	Ensure supplies are available for biosample collection (biopsy, blood and spot urine kits)	

Enrollment Visit:

Check as completed	Procedure	CRF
	Record Visit Date and participant time burden	Visit Log CRF
	Assessment of inclusion/exclusion criteria	Eligibility Assessment CRF
	Informed consent process and obtain written informed consent	Consent Form
	Complete any labs necessary for inclusion/exclusion screening tests. Bleeding criteria screening tests and urine pregnancy tests (if necessary) may be completed at the Biopsy Visit.	Eligibility Assessment CRF
	Collect participant and physician contact information	Contact Information CRF
	Collect vitals, anthropometry, blood pressures, edema assessment	Physical Measurements CRF
	Capture urine output and fluid balance every twelve hours and blood pressure and pulse every six hours from enrollment until biopsy	Physical Measurements and Laboratory Results CRFs
	Capture clinical urine microscopy results	Laboratory Results CRF
	Blood draw and spot urine collection up to 48 hours prior to the biopsy procedure	Biosample: Blood, Spot urine
	If ACD tube drawn, record date of ACD tube collection in Biopsy Scheduling CRF ASAP to notify biorepository. Record scheduled biopsy date, if known.	Biopsy/ACD Scheduling
	Record Demographics information	Demographics CRF

	Record prescription and non-prescription medications taken in the past 30 days	Medications CRF
	Record Medical History information (interviewer-administered potential participant CRF and coordinator CRF)	Medical History CRF for participant and coordinator
	Provide instructions and supplies for stool and timed urine collection and for the biopsy procedure	n/a
	Enter AKI Hospitalization information	AKI Hospitalization Form
	Update participant status (if necessary)	End of Study CRF
	Order bleeding criteria labs and pregnancy test (if necessary)	n/a
	Site investigator to complete Daily Progress Note on day of Enrollment and every day until discharge or day 7 post-biopsy.	Daily Progress Note

After Enrollment Visit:

Check as completed	Procedure	CRF
	Primary kidney care physician and KPMP investigator complete Pre-Clinical Assessment CRF	Pre-Clinical Assessment CRF
	Site investigator to complete Daily Progress Note each day following enrollment (until discharge or day 7 post-biopsy)	Daily Progress Note
	Enter Laboratory Results Data from EHR	Laboratory Results CRF
	Ensure supplies are available for Biopsy Visit (Biopsy Kit)	n/a
	AKI Adjudication committee to complete first Adjudication Report with the site investigator within 72 hours of enrollment	Adjudication Report
	Record date of scheduled biopsy and ACD tube collection in the Biopsy Scheduling CRF, if not previously done.	Biopsy/ACD Scheduling

AKI Biopsy Visit Checklist

Prior to Biopsy Visit:

Check as completed	Procedure	CRF
	Confirm the Biopsy Visit with study team members and the participant.	n/a
	Prepare Biopsy kit and biopsy cart	n/a

At Biopsy Visit:

Check as completed	Procedure	CRF
	Record Visit Date and participant time burden	Visit Log CRF
	Receive stool and timed urine sample (if available)	Biosample: Stool, Timed urine
	Complete bleeding exclusion criteria blood tests	Eligibility Assessment CRF
	Urine Pregnancy test (for all women under 55 years old of child-bearing potential))	Eligibility Assessment CRF
	Order urine microscopy from the clinical lab (AKI only)	Laboratory Results CRF
	Review and update Contact Information CRF	Contact Information CRF
	Perform kidney imaging to confirm anatomical or imaging eligibility	Pre-Biopsy Safety CRF
	Complete Pre-Biopsy Safety CRF	Pre-Biopsy Safety CRF
	Provide 3-month Visit at-home questionnaire packet	PROMIS Global Health Health Literacy Personal History
	Site investigator to complete Daily Progress Note (daily after Enrollment, until discharge)	Daily Progress Note

Biopsy-Related Activities:

Check as completed	Procedure	CRF
	Perform Kidney Biopsy	Kidney Biopsy Procedure Details CRF
	Tissue tracking and shipping	Tissue Tracking From, SpecTrack
	Post biopsy monitoring	Post Biopsy CRF Post Biopsy Hospitalization CRF
	Post biopsy adverse events reporting	Adverse Events CRF (as needed)

After Biopsy Visit:

Check as completed	Procedure	CRF
	Update participant status (if necessary)	End of Study CRF
	Ship biopsy samples and derivatives, blood, urine, and stool aliquots.	SpecTrack
	Store paper blood/urine/stool sample collection and processing forms as source documentation in the participant folder	
	Run REDCap data quality rules to check for missing or questionable data	

AKI Post - Biopsy Follow-up Checklist

Post-Biopsy Follow-up:

Check as completed	Procedure	CRF
	Continue post-biopsy procedure CRF	Post Biopsy CRF
	Urine samples every 24 hours, until discharge or Day 7	Biosample – Urine AKI
	Blood sample every 24 hours, until discharge or Day 7	Biosample: Blood AKI
	Continue with daily collection of urine output, vitals, fluid balance, serum creatinine (daily after Enrollment, until discharge	AKI Daily Measures
	Site investigator to complete Daily Progress Note (daily after Enrollment, until discharge)	Daily Progress Note
	Record any adverse events	Adverse Events CRF
	If consent was obtained through LAR, the participant must consent prior to the 3-month visit.	Consent CRF
	Update participant status (if necessary)	End of Study CRF

Blood and spot urine collection should be captured between day 5 and 7 post biopsy. Participants who have samples collected as inpatients on Day 5 and are then discharged satisfy this criterion. Participants who are discharged on Day 4 or earlier will have a clinic or home study visit between Days 5 & 7 to obtain these samples.

AKI 24-hour Post - Biopsy Follow-up Checklist

At 24-Hour Post-Biopsy Follow-up:

Check as completed	Procedure	CRF
	Continue post-biopsy procedure CRF	Post Biopsy CRF
	Call participant to complete 24-hour post biopsy phone call questions and AE assessment (if discharged). Record outcome of contact attempt (visit occurred, not occurred, or attempted)	24-hour Post Biopsy Phone Call CRF
	Collect adverse event information (if necessary)	Adverse Event CRF
	Collect hospitalization information (if necessary)	Post Biopsy Hospitalization CRF
	If consent was obtained through LAR, the participant must consent prior to the 3-month visit.	Consent CRF
	Update participant status (if necessary)	End of Study CRF
	Send REDCap surveys to pathologists	Send Pathology IF Metadata CRF Send Dx Core – DCA CRF
	AKI Adjudication committee to complete first Adjudication Report with the site investigator within 72 hours of enrollment	

After 24-Hour Post-Biopsy Follow-up (5-7 Days):

Check as completed	Procedure	CRF
	AKI Adjudication committee to complete second Adjudication Report with the site investigator within 5-7 days post-biopsy	Adjudication Report
	Run REDCap data quality rules to check for missing or questionable data	

Blood and spot urine collection should be captured between day 5 and 7 post biopsy. Participants who have samples collected as inpatients on Day 5 and are then discharged satisfy this criterion. Participants who are discharged on Day 4 or earlier will have a clinic or home study visit between Days 5 & 7 to obtain these samples.

AKI 14-day Post-Biopsy Follow-up Checklist

At 14-day Post-Biopsy Follow-up Call:

Check as completed	Procedure	CRF
	Call participant to complete 14-day post biopsy phone call questions and AE assessment (if discharged). Record outcome of contact attempt (visit occurred, not occurred, or attempted)	14-day Post Biopsy Phone Call CRF
	Record details of any post-biopsy hospitalizations	Post Biopsy Hospitalization CRF
	Report any biopsy-related adverse events	Adverse Event CRF

After 14-day Post-Biopsy Follow-up:

Check as completed	Procedure	CRF
	Primary kidney care physician and KPMP investigator to complete Follow-up Clinical Assessment (after biopsy results are available)	Follow-up Clinical Assessment CRF
	Send biopsy results to participant (or when available)	n/a
	Update participant status (if necessary)	End of Study CRF
	Run REDCap data quality rules to check for missing or questionable data	

AKI 28 day-Post-Biopsy Follow-up Checklist

At 28-day Post-Biopsy Follow-up Call:

Check as completed	Procedure	CRF
	Call participant to complete 28-day post biopsy phone call questions and AE assessment (if discharged) Record outcome of contact attempt (visit occurred, not occurred, or attempted)	28-day Post Biopsy Phone Call CRF
	Record details of any post-biopsy hospitalizations	Post Biopsy Hospitalization CRF
	Report any biopsy-related adverse events	Adverse Event CRF
	Provide instructions for completing the Participant Experience Survey	Participant Experience Survey
	Schedule 3-month AKI visit	n/a

After 28-week Post-Biopsy Follow-up:

Check as completed	Procedure	CRF
	Send biopsy results to participant (or when available)	n/a
	Update participant status (if necessary)	End of Study CRF
	Run REDCap data quality rules to check for missing or questionable data	

AKI 3-Month Visit Checklist (± 1 month)

Prior to 3-month Visit:

Check as completed	Procedure	CRF
	Confirm appointment with participant, remind them to bring current medications to the appointment and at-home questionnaire packet to the visit.	n/a
	If consent was obtained through LAR, the participant must consent prior to the 3-month visit.	Consent CRF

At 3-month Visit:

Check as completed	Procedure	CRF
	Record outcome of contact attempt (visit occurred, not occurred, or attempted)	Participant Followup CRF
	Record Visit Date and participant time burden	Visit Log CRF
	Review and update Contact Information CRF	Contact Information CRF
	Receive and record at-home CRFs packet	PROMIS Global Health CRF Health Literacy CRF Personal History CRF
	Record Medical History information (interviewer-administered potential participant CRF and coordinator CRF), if not completed at enrollment visit	Medical History CRF for participant and coordinator
	Record prescription and non-prescription medications taken in the past 30 days	Medications CRF
	Collect biospecimens	Biosample: Blood, Spot urine, Timed urine, Stool
	Collect vitals, anthropometry, blood pressures, edema assessment	Physical Measurements CRF
	Report any biopsy-related adverse events	Adverse Event CRF

	Assess study outcomes/hospitalizations since last contact	Post Biopsy Hospitalization CRF
	Remind participant of upcoming 6-month remote visit	n/a

After 3-month Visit:

Check as completed	Procedure	CRF
	Place order for 6-month AKI kidney function assessment	n/a
	Enter Laboratory Results Data	Laboratory Results CRF
	Update participant status (if necessary)	End of Study CRF
	Ship blood and urine aliquots	SpecTrack
	Store paper blood/urine/stool sample collection and processing forms as source documentation in the participant folder	
	Run REDCap data quality rules to check for missing or questionable data	

AKI Remote Visit Checklist (Month 6, 18, 30, 42, 54 ± 3 Months)

Prior to Remote Visit:

Check as completed	Procedure	CRF
	Order test for Kidney function assessment (for AKI participants at 6-month only)	n/a

At Remote Visit:

Check as completed	Procedure	CRF
	Record outcome of contact attempt (visit occurred, not occurred, or attempted)	Participant Followup CRF
	Record Visit Date and participant time burden	Visit Log CRF
	Review and update Contact Information CRF	Contact Information CRF
	Record prescription and non-prescription medications taken in the past 30 days	Medications CRF
	Assess study outcomes/medical events since last contact	Follow-up Medical Events CRF
	Assess study outcomes/hospitalizations since last contact	Post Biopsy Hospitalization CRF
	Provide instructions for completing the Participant Experience Survey (6 months only)	Participant Experience Survey
	Schedule annual follow-up visit	n/a

After Remote Visit:

Check as completed	Procedure	CRF
	Enter Laboratory Results Data	Laboratory Results CRF
	Update participant status (if necessary)	End of Study CRF
	Run REDCap data quality rules to check for missing or questionable data	

AKI Annual Follow-up Visit Checklist (Month 12, 24, 36, 48 ± 3 Months)

Prior to Annual Visit:

Check as completed	Procedure	CRF
	Send at-home questionnaire packet to participant	PROMIS Global Health CRF Health Literacy CRF (12 months only)
	Confirm appointment with participant, remind them to bring current medications to the appointment and at-home questionnaire packet to the visit.	n/a
	Ensure supplies are available for biosample collection (blood and spot urine kits)	n/a

At Annual Visit:

Check as completed	Procedure	CRF
	Record outcome of contact attempt (visit occurred, not occurred, or attempted)	Participant Followup CRF
	Record Visit Date and participant time burden	Visit Log CRF
	Review and update Contact Information CRF	Contact Information CRF
	Receive and record at-home CRFs packet	Personal History Follow-up PROMIS Global Health CRF Health Literacy CRF (12 months only)
	Record Medical History information (interviewer-administered potential participant CRF and coordinator CRF), if not completed at enrollment visit	Medical History CRF for participant and coordinator
	Record prescription and non-prescription medications taken in the past 30 days	Medications CRF

	Collect, process, and store biospecimens	Biosample: Blood, Spot urine
	Collect vitals, anthropometry, blood pressures, edema assessment	Physical Measurements CRF
	Assess study outcomes/medical events since last contact	Follow-up Medical Events CRF
	Assess study outcomes/hospitalizations since last contact	Post Biopsy Hospitalization CRF
	12-month only: Check to see if 6-month participant survey has been completed. If not, provide a paper copy of the survey and a stamped envelope to return it to the DCC.	Send the Participant Experience Survey CRF
	Remind participant of upcoming remote visit	n/a

After Annual Visit:

Check as completed	Procedure	CRF
	Enter Laboratory Results Data	Laboratory Results CRF
	Update participant status (if necessary)	End of Study CRF
	Ship blood and urine aliquots	SpecTrack
	Store paper blood/urine/stool sample collection and processing forms as source documentation in the participant folder	
	Run REDCap data quality rules to check for missing or questionable data	

19. Appendix E: iPad Tablet User Guide

KPMP | iPad Instructions

For general guidance, refer to https://support.apple.com/guide/ipad/.
For hardware assistance from the Coordinating Center, contact kpmpdcc@uw.edu.
To report issues with the online data collection forms, contact Fred Dowd at dowdf@uw.edu.

Unlocking the iPad

You will receive an 8-digit password on receipt of your iPad. To log in, do one of the following:

> **Keyboard controls:** Press any key on the attached keyboard to turn on the screen, then press any key again to display the password prompt. Enter the password and press Enter.
>
> **Touch controls:** Press the Home button on the front of the iPad to turn on the screen, then press Home again to display the password prompt. Use the on-screen keypad to enter the password, then touch OK.

If a window is open, return to the home screen by pressing the Home button on the iPad or the square button near the top left corner of the keyboard, above '2'.

Accessing the EDC

Select the REDCap app  from the home screen. Log in with your username and password.

Managing the iPad

The Coordinating Center manages the following:

- iPad configuration
- Software updates
- App installation
- Maintaining data collection forms
- Resetting passwords
- Replacing defective hardware

The KPMP site manages the following:

- Keeping the iPad charged
- Cleaning the iPad and protecting it from damage

Software and form updates are applied automatically. Please do not attempt to alter or remove the iPad from remote management. You may receive a prompt to install updates – please do this at your earliest convenience and note that the iPad may take a few minutes to complete installation.

Data collection form updates occur online and are independent of the iPad.

See the following page for charging and care instructions.

Charging and Power

Charging

Insert the charging cable into the bottom of the iPad. The following will occur when the iPad is successfully plugged in:

- When screen is off: The battery percentage indicator will appear in the center of the screen. After the screen turns back off, press the Home button, or any button on the keyboard, to see the current charge level.
- When screen is on: The battery percentage indicator will have a lightning bolt in its center

Note: *The iPad can be charged either in a wall outlet (with the AC adapter) or in a computer or other charging station (with a USB plug).*

Ensure the iPad is charged before any KPMP activities. A full charge will last approximately 10 hours. The battery symbol in the top right corner of the screen will turn red when only a 10% charge remains. If the battery fully drains, it will need to be plugged in, and until it reaches a minimum level of charge you will not be able to turn it on.

Note: *The battery will slowly drain while in sleep mode. Ensure that the device remains charged when not in use for an extended period.*

Power

The iPad is designed to be left in sleep mode rather than powered off. However, if the device is responding slowly, you may wish to restart it.

To turn off the iPad, hold the Sleep/Wake button on the top of the device until the **Slide to power off** prompt appears. To turn on the iPad, press the same button for about 1 second, after which the Apple logo will appear.

Note: *The Coordinating Center will not be able to supply updates if the iPad is powered off.*

Care and cleaning

To minimize wear and tear, keep the iPad in its protective case.

To clean the screen, wipe it with a soft cloth (dampened slightly with water or eyeglass cleaner if desired). Sani-Cloth CHG 2% and Clorox wipes are also effective for disinfecting the iPad.

If the iPad is damaged, contact kpmpdcc@uw.edu.

20. Appendix F: Screening Worksheets

Screening Worksheet: Diabetic CKD

Name:_____ MRN:_____

General Exclusion Criteria	Yes	No	Notes
Under 18 years of age			
Does not speak English or Spanish			
Severe allergy to iodinated contrast			
Pregnancy			
Transplant recipient (includes solid transplant and bone marrow)			
Additional vulnerable individuals (incarcerated, institutionalized, or otherwise unable to participate in the study)			
Inability to provide informed consent			
Clinical diagnosis of kidney disease from an autoimmune disease, dysproteinemia, viral disease or glomerular disease other than DKD or H-CKD			
Unwilling to receive blood transfusion (if needed)			
Any other imaging abnormality, which in the judgement of the operator, prevents biopsy being performed safely.			
Blood pressure above 160/100 mmHg			

Anatomical Imaging Exclusion Criteria If unknown, determine on day of biopsy	Yes	No	Notes
Kidney depth more than 13 cm (percutaneous biopsies only)			
Kidney size less than 8 cm (percutaneous biopsies only)			
Solitary or single functioning kidney			

Evidence of urinary tract obstruction or hydronephrosis			
Multiple bilateral kidney cysts			
Kidney infection, peri-renal infection, or cutaneous infection that overlies the kidney (percutaneous biopsies only)			

Bleeding Risk Exclusion Criteria	**Yes**	**No**	**Notes**
International Normalized Ratio (INR) greater than 1.4			
Platelet count less than 100,000/uL			
Hemoglobin less than 9 g/dL			
Chronic anticoagulation			
Inability to withdraw aspirin, clopidogrel, cilostazol, or similar anti-platelet agents for at least 7 days prior to biopsy (unless bleeding time is normal before open surgical biopsy); clinical judgement will be used in the case of nonsteroidal anti-inflammatory drugs (NSAID) exposure occurring less than 7 days before percutaneous biopsy.			

Diabetic Kidney Disease Inclusion Criteria	**Yes**	**No**
Diagnosis of diabetes mellitus (type 1 or 2) established by at least one of the following criteria: • Hemoglobin A1C greater than or equal to 6.5%, confirmed with a repeat test *within the past year* • Fasting blood sugar greater than or equal to 126 mg/dL, confirmed with a repeat test *within the past year* • Use of glucose-lowering therapy (insulin or oral or other subcutaneous agents)		

Must be present on at least two assessments (including the most recent) at least 3 months apart. Most recent measure must be within the past year, first (older) assessment must be within the past 3 year.	**AND**	**Must be present at least once (most recent available measurement):**		
Estimated glomerular filtration rate 30-59 mL/min/1.73m2	**AND**	--		
Urine albumin excretion greater than or equal to 30 mg/g (or mg/day creatinine) **-or-** Urine protein excretion greater than or equal to 150 mg/g creatinine (or 150 mg/day)	**AND**	**Estimated glomerular filtration rate greater than or equal to 60 mL/min/1.73m2**		

Screening Worksheet: Hypertension-Associated CKD

Name:_____ MRN:_____

General Exclusion Criteria	Yes	No	Notes
Under 18 years of age			
Does not speak English or Spanish			
Severe allergy to iodinated contrast			
Pregnancy			
Transplant recipient (includes solid transplant and bone marrow)			
Additional vulnerable individuals (incarcerated, institutionalized, or otherwise unable to participate in the study)			
Inability to provide informed consent			
Clinical diagnosis of kidney disease from an autoimmune disease, dysproteinemia, viral disease or glomerular disease other than DKD or H-CKD			
Unwilling to receive blood transfusion (if needed)			
Any other imaging abnormality, which in the judgement of the operator, prevents biopsy being performed safely.			
Blood pressure above 160/100 mmHg			

Anatomical Imaging Exclusion Criteria	Yes	No	Notes
Kidney depth more than 13 cm (percutaneous biopsies only)			
Kidney size less than 8 cm (percutaneous biopsies only)			
Solitary or single functioning kidney			
Evidence of urinary tract obstruction or hydronephrosis			

Multiple bilateral kidney cysts			
Kidney infection, peri-renal infection, or cutaneous infection that overlies the kidney (percutaneous biopsies only)			

Bleeding Risk Exclusion Criteria	**Yes**	**No**	**Notes**
International Normalized Ratios (INR) greater than 1.4			
Platelet count less than 100,000/uL			
Hemoglobin less than 9 g/dL			
Chronic anticoagulation			
Inability to withdraw aspirin, clopidogrel, cilostazol, or similar anti-platelet agents for at least 7 days prior to biopsy (unless bleeding time is normal before open surgical biopsy); clinical judgement will be used in the case of nonsteroidal anti-inflammatory drugs (NSAID) exposure occurring less than 7 days before percutaneous biopsy.			

Hypertension-Associated Kidney Disease Inclusion Criteria			**Yes**	**No**
Diagnosis of hypertension (HTN) established by **at least one** of the following criteria: • BP greater than 140/90 mmHg measured on three occasions over at least 1 month • Taking antihypertensive medication for blood pressure (BP) control • International Classification of Diseases (ICD) 9/10 diagnostic code for hypertension				
Must be present on at least two assessments (including the most recent) at least 3 months apart. Most recent measure must be within the past year, first (older)	**AND**	**Must be present at least once (most recent available measurement):**		

assessment must be within the past 3 year.				
Estimated glomerular filtration rate 30-59 mL/min/1.73m2	AND	albuminuria or proteinuria less than 2000 mg/d or 2000 mg/g creatinine.		
Urine albumin excretion 30-2000 mg/g creatinine (or mg/day for 24-hour urine) -or- Urine protein excretion 150-2000 mg/g creatinine (or mg/day for 24-hour urine) within the past year	**AND**	Estimated glomerular filtration rate greater than or equal to 60 mL/min/1.73m2		

Screening Worksheet: AKI Open Biopsy

Name:_____ MRN:_____

General Exclusion Criteria	Yes	No	Notes
Under 18 years of age			
Does not speak English or Spanish			
Severe allergy to iodinated contrast			
Pregnancy			
Transplant recipient (includes solid transplant and bone marrow)			
Additional vulnerable individuals (incarcerated, institutionalized, or otherwise unable to participate in the study)			
Inability to provide informed consent or provide LAR consent			
Clinical diagnosis of kidney disease from an autoimmune disease, dysproteinemia, viral disease or glomerular disease other than DKD or H-CKD			
Unwilling to receive blood transfusion (if needed)			
Blood pressure above 160/100 mmHg			
Any other condition where in the judgement of the operator, biopsy cannot be performed safely.			

Anatomical Imaging Exclusion Criteria	Yes	No	Notes
Solitary or single functioning kidney			
Evidence of urinary tract obstruction or hydronephrosis			
Multiple bilateral kidney cysts			

Bleeding Risk Exclusion Criteria	Yes	No	Notes
International Normalized Ratios (INR) greater than 1.4			
Platelet count less than 100,000/uL			
Hemoglobin less than 9 g/dL			
Chronic anticoagulation			
Inability to withdraw aspirin, clopidogrel, cilostazol, or similar anti-platelet agents for at least 7 days prior to biopsy (unless bleeding time is normal before open surgical biopsy); clinical judgement will be used in the case of nonsteroidal anti-inflammatory drugs (NSAID) exposure occurring less than 7 days before percutaneous biopsy.			

Open AKI Inclusion Criteria	Yes	No	Notes
Baseline estimated glomerular filtration rate greater than 45 mL/min/1.73m2 defined as the median of the last three outpatient serum creatinine measurements from day 7 to 365 prior to enrollment. OR If there are no sCr values available for 7 to 365 days prior to enrollment, the patient can be enrolled with an estimated baseline (as defined in the Recruitment Site MOP, but only if there is no past medical history of chronic kidney disease			
AND one of the following: 1. Elevated serum creatinine (greater than 1.5 times baseline) or an increase in serum creatinine greater than or equal to 0.3 mg/dL within 48 hours, above admission serum creatinine. OR			

2. High risk for acute kidney injury defined by **TWO** or more criteria (see Recruitment Site MOP for specific values): • Positive kidney injury urine biomarker measured at the Recruitment Site • Urine microscopy suggestive of acute tubular necrosis. • Oliguria (less than 0.3mL/kg/hr) at least 1 hour after fluid resuscitation. • One or more exposure(s) known to cause acute kidney injury (major surgery not including index laparotomy, sepsis, nephrotoxic drugs, etc.).			

Screening Worksheet: Percutaneous AKI

Name:_____ MRN:_____

General Exclusion Criteria	Yes	No	Notes
Under 18 years of age			
Does not speak English or Spanish			
Severe allergy to iodinated contrast (any reaction)			
Pregnancy			
Transplant recipient (includes solid transplant and bone marrow)			
Additional vulnerable individuals (incarcerated, institutionalized, or otherwise unable to participate in the study)			
Inability to provide informed consent			
Clinical diagnosis of kidney disease from an autoimmune disease, dysproteinemia, viral disease or glomerular disease other than DKD or H-CKD			
Unwilling to receive blood transfusion (if needed)			
Any other imaging abnormality, which in the judgement of the operator, prevents biopsy being performed safely.			
Blood pressure above 160/100 mmHg			
Ventilator-dependent patient			
Hypotension or pressor support requirement			

Anatomical Imaging Exclusion Criteria	Yes	No	Notes
Kidney depth more than 13 cm (percutaneous biopsies only)			
Kidney size less than 8 cm (percutaneous biopsies only)			

Solitary or single functioning kidney			
Evidence of urinary tract obstruction or hydronephrosis			
Multiple bilateral kidney cysts			
Kidney infection, peri-renal infection, or cutaneous infection that overlies the kidney (percutaneous biopsies only)			

Bleeding Risk Exclusion Criteria	**Yes**	**No**	**Notes**
International Normalized Ratios (INR) greater than 1.4			
Platelet count less than 100,000/uL			
Hemoglobin less than 9 g/dL			
Chronic anticoagulation			
Inability to withdraw aspirin, clopidogrel, cilostazol, or similar anti-platelet agents for at least 7 days prior to biopsy (unless bleeding time is normal before open surgical biopsy); clinical judgement will be used in the case of nonsteroidal anti-inflammatory drugs (NSAID) exposure occurring less than 7 days before percutaneous biopsy.			

AKI Percutaneous Inclusion Criteria	**Yes**	**No**	**Notes**
Baseline estimated glomerular filtration rate greater than 45 mL/min/1.73m2. Baseline defined by the median of the last three outpatient serum creatinine measurements from day 7 to 365 prior to enrollment. OR If there are no sCr values available for 7 to 365 days prior to enrollment, the patient can be enrolled with an estimated baseline (as defined in the Recruitment Site MOP, but			

only if there is no past medical history of chronic kidney disease			
Elevated serum creatinine (greater than or equal to 1.5 times baseline as defined above).			
At least ONE of the following (see Recruitment Site MOP for specific values): • A repeat serum creatinine within 48 hours of initial serum creatinine, showing a further increase of 0.3 mg/dL • Positive kidney injury urine biomarker measured at the Recruitment Site • Urine microscopy suggestive of acute tubular necrosis.			

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4. Ali, H., et al., *Post renal biopsy complication rate and diagnostic yield comparing hands free (ultrasound-assisted) and ultrasound-guided biopsy techniques of renal allografts and native kidneys.* Springerplus, 2015. **4**: p. 491.
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